

**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 001-38210

**Krystal Biotech, Inc.**

(Exact name of Registrant as specified in its Charter)

**Delaware**

(State or other jurisdiction of  
incorporation or organization)

**2100 Wharton Street, Suite 701**

**Pittsburgh, Pennsylvania**

(Address of principal executive offices)

**81-0930882**

(I.R.S. Employer  
Identification No.)

**15203**

(Zip Code)

**Registrant's telephone number, including area code: (412) 586-5830**

Securities registered pursuant to Section 12(b) of the Act: Common Stock, Par Value \$0.00001 Per Share; Common stock traded on the NASDAQ stock 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, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	<input type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input type="checkbox"/> (Do not check if a smaller reporting company)	Smaller reporting company	<input checked="" type="checkbox"/>
Emerging growth company	<input checked="" type="checkbox"/>		

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 last business day of the Registrant's most recently completed second fiscal quarter, the Registrant's common equity was not listed on a domestic exchange or an over-the-counter market. The Registrant's common stock began trading on the NASDAQ Capital Market on September 20, 2017.

The number of shares of Registrant's Common Stock outstanding as of February 28, 2018 was 10,307,247.

Portions of the Registrant's Definitive Proxy Statement relating to the Annual Meeting of Shareholders, scheduled to be held on May 31, 2018, are incorporated by reference into Part III of this Report.

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## PART I

### Item 1. Business.

#### Overview

Krystal Biotech, Inc. (the “Company,” “we” or “us” or other similar pronouns) is a gene therapy company dedicated to developing and commercializing novel treatments for patients suffering from dermatological diseases. We have developed a proprietary gene therapy platform, which we refer to as the Skin TARgeted Delivery platform, or STAR-D platform, that consists of a patented engineered viral vector based on herpes simplex virus 1, or HSV-1, and skin-optimized gene transfer technology, to develop off-the-shelf treatments for dermatological diseases for which we believe there are no known effective treatments. We are initially using the STAR-D platform to develop treatments for rare or orphan dermatological indications caused by the absence of or a mutation in a single gene, and plan to leverage our platform to expand our pipeline to include other dermatological indications in the future.

Our lead candidate, KB103, a gene therapy product, is currently in preclinical development to treat dystrophic epidermolysis bullosa, or DEB, a rare and severe genetic disease, for which there is currently no approved treatment. Investigational New Drug (“IND”) enabling preclinical studies evaluating intradermal and topical delivery of KB103 have been completed, and we intend to file an IND application for KB103 with the U.S. Food and Drug Administration (“FDA”) in the first quarter of 2018.

DEB affects the skin and mucosal tissues, and is caused by one or more mutations in a gene called COL7A1, which is responsible for the production of protein type VII collagen, or COL7, that forms anchoring fibrils that bind the dermis, or inner layer of the skin, to the epidermis, or outer layer of the skin. In DEB patients, the genetic defect in COL7A1 results in loss or malfunctioning of these anchoring fibrils, leading to extremely fragile skin that blisters and tears from minor friction or trauma. Those born with DEB are sometimes called “butterfly children,” because their skin is likened to be as fragile as the wings of a butterfly. DEB patients may suffer from open wounds, skin infections, fusion of fingers and toes and gastrointestinal tract problems throughout their lifetime, and may eventually develop squamous cell carcinoma, a potentially fatal condition. Based on information from DEBRA International, a worldwide alliance of patient support groups for epidermolysis bullosa, or EB, of which DEB is a subset, we believe there may be as many as 125,000 patients worldwide who suffer from DEB. We estimate that there are presently 3,200 to 3,500 diagnosed DEB patients in the European Union, or EU, United States, Japan and Canada.

We believe our approach to treating DEB with KB103, which has not yet been approved by either the FDA, or the European Medicine Agency (“EMA”), is novel. The current standard of care for DEB patients is limited to palliative measures that seek to provide relief from some of the symptoms of DEB but do not meaningfully impact disease outcomes. Other known efforts to develop DEB treatments are employing autologous approaches to creating therapeutic products. Autologous treatments use a patient’s own tissues and cells to manufacture an individualized therapy. Such therapies are expensive, invasive and time consuming to use, and require highly sophisticated medical teams and procedures. In contrast, KB103 is designed to be an off-the-shelf treatment for DEB that can be applied as needed, either intra-dermally or topically to a patient’s skin. Unlike the current standard of care, KB103 seeks to treat DEB at the molecular level through gene therapy, and is intended to be a non-invasive treatment that can be used without requiring hospitalization or individually customized treatment.

KB103 is a replication-defective, non-integrating viral vector that has been engineered using our STAR-D platform to deliver functional human COL7A1 genes directly to patients’ dividing and non-dividing skin cells. Non-integrating vectors do not combine with the host cell’s DNA and express proteins separately from it. As a result, they do not disrupt the functioning of the host genes or present the cancer-causing risks associated with such disruption. We believe our STAR-D platform provides an optimal approach for treating dermatological conditions due to the nature of the HSV-1 viral vector we have created. Our viral vector has a natural tropism to the outermost layer of the epidermis, or skin epithelium, and we believe it can penetrate skin cells more efficiently than other viral vectors used in gene therapy. Our viral vector also has a high capacity or payload relative to most vectors, so it can accommodate multiple copies of large genes like COL7A1 and may allow us to insert multiple genes to develop combinatorial therapies for dermatological conditions like psoriasis and chronic wounds in the future.

#### Recent Developments

On November 2, 2017, the FDA granted Orphan Drug Designation to our lead product candidate, KB103, for the treatment of DEB. The FDA’s Office of Orphan Drug Products grants orphan drug designation to support the development of medicines for underserved patient populations, or rare disorders, that affect fewer than 200,000 people in the United States.

Orphan drug designation makes us eligible for a seven-year period of United States marketing exclusivity upon approval of KB103, tax credits for certain clinical research costs, and a waiver of the Prescription Drug User Fee Act (“PDUFA”) filing fees, subject to certain conditions.

On November 3, 2017, we announced receipt of an equity-based award totaling \$770,000 from the EB Research Partnership (“EBRP”) and the EB Medical Research Foundation (“EBMRF”). EBRP and EBMRF provided this funding following a highly competitive application and screening process overseen by EBRP’s Scientific Advisory Board (“SAB”), which is composed of leading scientists and physicians. The SAB recommends awards and grants to academic institutions and commercial parties based on its evaluation of the potential for development of commercially viable treatments and cures for EB.

Our success also depends in part on our ability to protect our intellectual property, including the STAR-D platform. We have adopted a strategy of seeking patent protection in the United States and abroad where appropriate with respect to certain of our technologies relating to our products and process. On January 16, 2018 we announced that the United States Patent Office (“USPTO”) has granted U.S. Patent No. 9,877,990 which covers compositions comprising herpes simplex viral (“HSV”) vectors and methods of using the same for providing prophylactic, palliative or therapeutic relief of a wound, disorder or disease of the skin in a subject. We believe that the granting of this patent, that is 100% owned by us, protects our core STAR-D viral platform and affords us freedom to use this platform for several skin diseases. We continue to actively develop our portfolio through the filing of new patent applications, divisionals and continuations relating to our technologies as we deem appropriate.

Our vision is to become a fully integrated biotechnology company. In pursuit of this goal, we are executing on our core strategic initiatives, which include the development of proprietary in-house manufacturing capabilities and the expansion of our pipeline. We maintain full global rights to all of our product candidates.

### **Our Strengths**

We believe we are the first biotechnology company to develop a gene therapy for dermatological indications that can be used without requiring individually customized treatment, which we refer to as an “off-the-shelf” treatment. We believe our organization and technology benefit from a singular set of strengths that will allow us to create and establish a leadership position in developing gene therapy treatments for dermatological indications. These strengths include:

- A first mover advantage in dermatological gene therapy with regards to:
  - An off-the-shelf gene therapy product candidate, and
  - Topical gene therapy application.
- Our STAR-D platform, a patented, proprietary, integrated gene therapy platform comprised of a library of optimized HSV-1 vectors and their complimentary cell lines with higher and more durable expression, lower immune response and improved manufacturability when compared with other viral vectors currently being used in dermatological gene therapy.
- The significant affinity to the skin and high payload capacity of our HSV-1 viral vector, which will allow us to efficiently deliver single and multiple genes to treat orphan and other dermatological indications.
- A proprietary process for both upstream (vector production) and downstream (purification) portions of the manufacturing process, which positions us to maximize scalability, quality and reliability.
- A scientific team with expertise in the HSV-1 viral vector.
- A strong patent estate that allows us the freedom to operate using modified HSV vectors for dermatological indications.
- A management team with a track record of developing drugs from research to approval.

## Our Strategy

Our objective is to develop and commercialize gene therapy treatments for dermatological indications. Our strategy to accomplish this objective is to initially focus on dermatological indications in the rare or orphan disease space, build out and leverage our in-house manufacturing capabilities, and then leverage our STAR-D platform to develop, manufacture and commercialize treatments for non-orphan indications within dermatology.

- **Why dermatology**—We believe the characteristics of our STAR-D platform are ideal for application in dermatology because of HSV-1’s high tropism, or natural affinity, for skin cells. This allows the viral vector to penetrate skin cells more efficiently than other gene therapy vectors which makes topical delivery of gene therapy possible. Dermatology is also attractive because treatments for diseases affecting the skin have clearly defined, objective clinical endpoints with validated measurement tools that are accepted by the FDA. We believe these clearly defined endpoints will help accelerate the process of clinical development and regulatory approval for our dermatological products.
- **Why rare or orphan diseases**—We believe there is significant unmet medical need for treatments for rare or orphan diseases, because the patient populations are not sizeable enough to attract the attention of large commercial entities. However, we believe there are advantages to developing in this space, including that these diseases are genetic and frequently affect children, and therefore have been studied extensively and have concentrated, supportive networks of key opinion leaders or KOLs, and patient advocacy groups. We have established strong relationships with such KOLs which we believe will aid us in obtaining data more rapidly and assist with the development and regulatory approval process. In addition, rare and orphan diseases, particularly monogenic ones like DEB, have defined clinical endpoints that have been validated by the FDA. There are also regulatory designations such as the FDA’s orphan drug designation, breakthrough drug designation, fast track drug designation and rare pediatric disease designation, one or more of which we believe, if successfully obtained, can provide certain regulatory and commercial advantages and incentives for developing treatments in this space. If we are able to successfully achieve one or more of these designations, we believe this will aid in the commercialization of our product candidates.
- **How we will manufacture**—While we currently outsource our manufacturing, we believe there is value in maintaining control of our entire manufacturing process. We intend to continue to devote substantial resources to developing the STAR-D platform and bringing our scalable manufacturing process in-house. Because of the high demand for contract manufacturing in gene therapy, we believe the focus on expanding the STAR-D platform and establishing current good manufacturing practices, or cGMP, manufacturing in-house will ultimately accelerate the process of regulatory approval for our products.
- **How we can expand**—We believe we can eventually expand beyond rare and orphan diseases by leveraging our STAR-D platform and expertise in viral vector selection and design, physical vector delivery and vector manufacturing to pivot into other gene therapy treatments for dermatological applications. For example, we believe that the large payload capacity of the viral “backbone” in the STAR-D platform will allow us to deliver multiple genes and other effectors using the platform and afford us an opportunity to treat non-monogenic diseases like psoriasis, as well as conditions which are not necessarily the result of an inherited genetic defect, such as chronic wounds. If we are able to successfully develop and commercialize products to treat non-orphan dermatological diseases, we intend to seek collaborative alliances towards commercializing these therapies among the broader population of patients in these indications.

## Background on Gene Therapy

Many diseases have a genetic aspect whereby a mutated gene linked to a disease is passed down from generation to generation. Genes produce proteins that perform a vast array of functions within all living organisms, through a process called gene expression. A mutation, or alteration, in the gene or in sequences that control the expression of that gene can cause aberrations in intracellular protein production, which can cause disease. Gene therapy seeks to introduce a functional copy of the defective gene into a patient’s own cells, a process called gene transfer. Gene therapy thereby has the potential to change the way patients are treated by correcting the underlying genetic defect that is the cause of their disease, rather than offering solutions that only address their symptoms.

In the gene transfer process, a functional gene is delivered and incorporated into a patient’s cells through a delivery system called a vector, which are most commonly based on naturally occurring viruses that have been modified to take advantage of the virus’ natural ability to introduce genes into cells. However, unlike naturally occurring viruses, which replicate following infection of a target cell and have the capacity to infect new cells, our viral vectors are modified to be

non-replicating by deleting that portion of the viral genome responsible for replication. Gene transfer using a viral vector is called transduction, and the resulting gene-modified cells are described as transduced cells.

A growing body of gene therapy-based clinical data, the establishment of regulatory guidelines to govern the development and approval of gene therapy products and increased investment from the biopharmaceutical industry suggest that gene therapy is being increasingly accepted as an important new therapeutic modality for patients with unmet medical need. We believe that if successful, our lead product candidate, KB103, together with the STAR-D platform, will help bring gene therapy to the treatment of dermatological indications. To date, only two gene therapy products have received marketing authorization from the FDA, and only two gene therapy products have received marketing authorization from the EMA.

### Our STAR-D Gene Therapy Platform

We believe that certain inherent features of the HSV-1 virus, combined with our ability to strategically modify the virus in the form we employ as our gene delivery backbone, provides our proprietary gene therapy platform, which we refer to as our STAR-D platform, with several advantages over other viral vector platforms for use in dermatological applications, including the following:

- **Non-Integrating Nature:** Conceptually, our STAR-D platform is similar in its simplicity, safety, and ease of use to other non-integrating gene therapy platforms like Adeno-Associated Virus, or AAV. Upon entry into cells, the HSV-1 vector persists as an episomal unit in the nucleus, meaning it remains physically separate from the host cell chromosome. Other vectors we are aware of currently being used in the development of gene therapy treatments for dermatological conditions, such as lentiviral and retroviral vectors, integrate into the host cell DNA in order to achieve gene expression. Integration into the host cell DNA carries the risk of disrupting host genes, and consequently can lead to a risk of causing cancer, or oncogenesis. In contrast, a non-integrating vector such as our HSV-1 vector does not carry the risk of disrupting the expression of host cell genes and the cancer-causing risks such disruptions could create.
- **Payload Capacity:** HSV-1 is a large virus, approximately 150 kilobase, or Kb, pairs of DNA in size. We have made strategic deletions within this genome to remove critical “immediate early”, or IE, genes. These IE genes are required for expression of most of the downstream genes that allow the HSV-1 virus to replicate and destroy host cells. Deletion of these IE genes inhibits expression of most of the viral proteins, making the resulting viral vector replication-deficient and non-toxic. These deletions also enable the vector to easily accommodate a payload of 30Kb or greater without any significant impact on yield or titer. In KB103, we have successfully inserted two functional copies of the complete ~9Kb human COL7A1 gene. In contrast, packaging capacity for most other viral vectors being used in dermatological indications is under 8Kb which limits their ability to package large genetic materials. In addition, we believe the high payload capacity of our viral vector will allow us to insert single and multiple genes, allowing for the potential treatment of non-monogenic dermatological conditions such as psoriasis, atopic eczema and chronic wounds.
- **Skin Tropism:** Poor infection of skin epithelia has remained a major hurdle for direct delivery of most viral vectors. HSV-1 has a natural affinity, or tropism, for the skin epithelium; therefore our viral vector penetrates skin cells much more efficiently than other viral vectors, resulting in transduction efficiencies or cell penetration as high as 95% in cell-based studies.

This efficient cell infection or penetration ability, along with the high payload capacity of our vector discussed above, are responsible for the high levels of transgene expression in animal models. In addition, these factors are critical contributors to our ability to create an off-the-shelf gene therapy treatment where others are taking autologous approaches. Because the genes that cause many dermatological diseases are quite large, many of our competitors can only fit a single gene, or in some cases may need to manipulate the genetic material in order to fit the limited payload capacity of their vectors. From our review of published research, we estimate that some of these autologous gene therapy approaches may have transduction efficiencies as low as 10% in skin. In order to develop an effective treatment in the face of payload capacity and transduction limitations, they may need to introduce the therapeutic gene into a patient’s tissues or cells *ex vivo* to create an individual treatment, which is re-administered back to the patient once the gene-modified tissues have achieved a sufficient level of gene expression. The greater payload capacity of our vector and the high transduction efficiencies achieved allow us to deliver a full gene directly to any patient’s tissues for *in vivo* gene expression without additional manipulation.

- **Immunogenicity:** One of the major challenges with other viral vector platforms is that the host immune system may recognize them as foreign bodies and launch a robust immune response, resulting in toxicity and rapid removal of the virus. Wild type HSV-1 is known to persist in the body by becoming latent and hiding from the immune system. We have harnessed the natural ability of HSV-1 to evade host-mediated immunogenicity, while

removing specific viral elements that exacerbate the host immunity, thus making the viral vector safer and allowing for repeat administration as needed to achieve durability of effect. Because the tendency of the viral vector to invoke an immune response is low, the ability of the HSV-1 vector to effectively deliver therapeutic genes is enhanced.

- **Stability:** HSV-1 is extremely stable and resistant to degradation by shear, solvents and enzymes, facilitating purification and final formulation of our product candidates. These characteristics of HSV-1 provide a stability advantage to our KB103 product candidate. Although frozen for long-term storage, it is also stable under refrigerated conditions for short-term storage and shipment, and stable over several freeze-thaw cycles.
- **Reproducible Manufacturing and Scalability:** Successful production of viral vectors involves two steps: (i) the 'upstream' process, which yields a bulk virus harvest; and (ii) the 'downstream' process, which involves purification and concentration of the clinical product. Successful and reproducible execution of both processes is critical for clinical manufacturing and scale-up. Our scientific team collectively has over 20 years of experience and expertise in HSV engineering and purification that has allowed us to successfully optimize our HSV-1 vector production process.
- **Existing Regulatory Precedent:** The first FDA- and EMA-approved oncolytic virus product, Imlygic® by Amgen, for treatment of melanoma, a skin cancer, is based on a genetically engineered HSV-1 virus. Because this product also employs an HSV-1 backbone, it has created a regulatory precedent for approval of an HSV-1-based therapy. In addition, Imlygic® is a chronic therapy, given bi-weekly, which provides support for the use of an HSV-1 backbone in chronic gene therapy of the type we are developing.

## **Our HSV-1 Product candidates**

### **KB103 for the treatment of Dystrophic Epidermolysis Bullosa**

#### *Background on Dystrophic Epidermolysis Bullosa*

DEB belongs to a group of genetic skin diseases known more broadly as epidermolysis bullosa, or EB, characterized by genetic defects of structural proteins of the skin, resulting in skin fragility and the formation of blisters. Blisters form as a result of rubbing, trauma or even in some cases from slight contact such as a simple hug. The subtypes of EB are distinguished by the location of the blister in the skin. DEB is associated with mutations in the gene coding for COL7, a major component of the anchoring fibrils which anchor the top layer of skin, called the epidermis, to an underlying layer, called the dermis, and provide structural adhesion in a normal individual. The lack of COL7 in DEB patients causes blisters to occur in the dermis as a result of separation from the epidermis. Genetic linkage studies have identified COL7A1 as the gene responsible for DEB. Over 200 distinct mutations in COL7A1 have been identified in DEB patients.

The most severe form of DEB is recessive DEB, or RDEB, in which both COL7 and anchoring fibrils are severely diminished in the patient's skin due to null mutations in the COL7A1 gene. As a result, RDEB is characterized by severe skin blistering, extremely fragile skin, mutilating scarring of the hands and feet, joint contractures, strictures of the esophagus, and often, eventually the development of aggressive squamous cell carcinomas which may shorten the patient's life. DEB also occurs in the form of dominant DEB, or DDEB, which is considered to be a more mild form of DEB. In DDEB blistering is often limited to the hands, feet, knees, and elbows, and often improves somewhat with age.

Currently, there is no effective therapy for any form of DEB, and RDEB patients have a low life expectancy. Nearly 10% of RDEB patients die before the age of 10, almost 40% die by the age of 20, and over 70% die before the age of 30. Persistent blistering begins at birth and contributes to the high mortality risk due to bacterial infection. In a study of 41 RDEB patients, the infectious causes of pneumonia and sepsis resulted in death in close to 15% and 10% of cases, respectively. Patients who survive bacterial sepsis during early infancy are at a high risk of later developing more severe complications such as growth retardation due to gastrointestinal involvement, multifactorial anemia, esophageal strictures, corneal scarring and/or progressive blindness, renal failure, progressive hand and foot deformities, muscle contractures that restrict movement, anemia, esophageal strictures, rapid tooth decay, nail deformities, and hair loss. The onset of aggressive squamous cell carcinoma, sepsis or malnutrition due to an inability or unwillingness to eat due to mouth or esophagus involvement, may also result in death among these patients.

#### *Existing Treatments for DEB*

At present, there are no FDA- or EMA-approved treatments for DEB. The management of DEB currently consists of palliative care, which generally consists of prevention of mechanical forces that produce new blisters, wound care, nutritional support, and infection control, all of which help treat the symptoms but not the causes of DEB. We estimate that the annual cost of palliative care for a DEB patient is in the range of approximately \$200,000 to \$400,000 per year. Wound care usually

includes treatment of new blisters by lancing and draining. Wounds are then dressed with a non-adherent material, covered with padding for stability and protection, and secured with an elastic wrap for integrity. Due to the increased risk of bacterial resistance, topical antibiotic ointments and antimicrobial dressings are typically reserved for those wounds that are colonized with bacteria and fail to heal, referred to as “critical colonization.”

Individuals with DEB have increased caloric and protein needs due to the increased energy utilized in wound healing. Involvement of the digestive system in RDEB may limit nutritional intake. Infants and children with RDEB may require nutritional support, including a gastrostomy feeding tube. Anemia is typically treated with iron supplements and transfusions as needed. Other nutritional supplements may include calcium, vitamin D, selenium, carnitine and zinc.

Surveillance is important for individuals with DEB. Biopsies of abnormal-appearing wounds that do not heal may be recommended in some types of DEB due to predisposition to squamous cell carcinoma, beginning in the second decade of life. Screening for deficiencies of iron, zinc, vitamin D, selenium, and carnitine is typically recommended after the first year of life. Routine echocardiograms are recommended to identify dilated cardiomyopathy, and bone mineral density studies are recommended to identify osteoporosis. It is also typically recommended to avoid activities and bandages (including all adhesives) that may traumatize the skin.

#### *Our approach to treating DEB*

Our gene therapy approach uses a modified HSV-1 vector designed to deliver fully functional COL7A1 gene into the patient’s skin cells. Upon direct delivery to the skin, KB103 can efficiently transduce both keratinocytes and fibroblasts. Following entry of KB103 into the cell, the drug is transported down microtubules to the nucleus, and the viral genome is deposited into the nucleus. Once in the nucleus, it recruits the host cellular machinery to initiate transcription of COL7A1. The COL7A1 transcripts allow for production of a precursor protein, Procollagen 7, that is secreted by the cell and processed by enzymes to remove extra protein segments from the ends. Once these molecules are processed, they arrange themselves into long, thin bundles of mature COL7 that form anchoring fibrils. The anchoring fibrils hold the epidermis and dermis together and are essential for maintaining the integrity of the skin.

The high payload capacity of the HSV-1 vector allows us to insert two copies of the COL7A1 gene into each viral vector backbone, facilitating high expression of Procollagen 7. Current autologous therapies in development for DEB use lentivirus or retrovirus which have limited payload capacity and low transduction efficiencies. In addition, those viral vectors can target either keratinocytes or fibroblasts for gene delivery, but not both. In order to develop an effective treatment in the face of these limitations, autologous approaches treat the patient’s tissues or cells *ex vivo* for re-administration once sufficient gene expression is achieved, which leads to an extremely expensive, invasive and time consuming treatment requiring highly sophisticated medical teams and procedures. We believe that the limited payload capacity of lentivirus and retrovirus along with low transduction efficiencies will make it very difficult, if not impossible, to develop off-the-shelf gene therapies for DEB with these viral vectors. In contrast, KB103 can transduce not only keratinocytes and fibroblasts but also all skin cells that it comes in contact with to produce optimum therapeutic levels of secreted COL7 protein. It has been shown in clinical and non-clinical studies that functional and durable replacement of COL7 protein is necessary and sufficient to correct the debilitating skin disease that inflicts these patients.

The persistence of KB103 in the skin depends on the rate of turnover of the cells where it resides. The vector has been engineered to be able to evade the host immune response and persist for the life of the cell. Additionally, we have also optimized its design to be safe and nontoxic to both dividing and non-dividing cells so that it can be reapplied as often as required.



Beyond the advantages surrounding the mechanism of action of KB103, it also has practical advantages as a therapy over autologous approaches. We believe that the major drawbacks of autologous therapies are subject discomfort during administration, a need for highly trained dermatologists, and a high cost of treatment including anesthesia, sophisticated equipment, and possible hospitalization. Additionally, because autologous treatments require time-consuming processing of a patient's own cells and tissues, there can be a significant lag of six months or more between diagnosis and commencement of treatment. As a result, we believe an off-the-shelf, non-invasive treatment such as KB103 will, if successful, be an effective alternative for treating DEB.

#### *Preclinical Proof of Concept for KB103*

The preclinical studies described below were conducted between September 2016 and December 2017. Detailed results from these studies can be found in the S-1 and suggest the following:

- **Robust levels of COL7 in KB103-administered RDEB patient-derived fibroblasts.** KB103 was evaluated for transduction efficiency, expression and functionality in 2-D and 3-D cell-based assays using normal and RDEB patient-derived fibroblasts, or HDFs. RDEB patient HDFs were infected with Multiplicity of Infection, or MOI, of 0.3, 1 or 3 viral particles per cell of KB103 to evaluate vector dose-dependent expression and toxicity. Transduction efficiency and COL7 expression were evaluated 48 hours post-infection using immunofluorescence, or IF, microscopy, a technique that uses fluorescent dye-conjugated antibodies that specifically bind to an antigen, to determine the localization and cellular expression of the antigens. After incubation with KB103, the HDFs were incubated with a fluorescent antibody that specifically recognizes and binds to human COL7 expressed by the cells, which is imaged by fluorescence microscopy. We detected high levels of COL7 expression at all three doses in fibroblasts administered with KB103.
- **Robust levels of COL7 in KB103 administered RDEB patient-derived keratinocytes.** KB103 was also evaluated for transduction efficiency, expression and functionality in 2-D and 3-D cell-based assays using normal and RDEB patient-derived keratinocytes, or HDKs. RDEB patient HDKs were infected with MOI of 0.3, 1, and 3 viral particles per cell of KB103 to evaluate vector dose-dependent expression and toxicity. Transduction efficiency and COL7 expression were evaluated 48 hours post-infection by IF microscopy, as described above. We detected high levels of COL7 expression at all three doses in keratinocytes administered with KB103 relative to endogenous COL7 expression in normal keratinocytes or N-HDK, or complete lack of COL7 expression in EB-HDKs that did not get transduced with KB103 (EB-HDK, Control).
- **Human COL7 expressed by KB103 in fibroblasts and keratinocytes is functionally active.** COL7 expressed by KB103 was confirmed to be functionally active as it increased the expression of a downstream target, Lysyl Hydroxylase 3, or LH3, in RDEB keratinocytes. Functional COL7 is also known to inhibit production of Thrombospondin-1, or TSP-1, an adhesive protein which is upregulated in the stroma of squamous cell carcinoma patients, and a marker for poor prognosis in RDEB patients who have developed squamous cell carcinoma. COL7 expressed by KB103 inhibited TSP-1 production in a dose-dependent manner, further confirming functional activity.
- **Confirmation of human COL7 in 3-D organotypic cultures.** Confirmation of expression and functionality in 2-D assays prompted assessment in 3-D organotypic cultures composed of RDEB fibroblasts and keratinocytes transduced with KB103. We believe that our 3-D organotypic culture study is the first study to show that KB103 infects both keratinocytes and fibroblasts and secretes COL7 from the dermis and the epidermis to optimize deposition of COL7 at the basement membrane zone, or BMZ. We believe that most ex-vivo viral approaches are only able to target either fibroblasts or keratinocytes due to limitations of their viral vector that result in inefficient transduction and/or difficulties in selection and expansion of either cell type. Our data suggests that KB103, due to its ability to transduce both cell types, has the potential to achieve therapeutic levels of COL7 following direct application to the skin.
- **Confirmation of COL7 expression in animal studies.** Immunocompetent mice were administered KB103 via intradermal injection to evaluate expression of COL7. Human COL7 was detected in the mouse skin and also in the BMZ.
- **Repeat administration of KB103 boosts COL7 levels.** KB103 was administered to mice on Day 1 and Day 5 and COL7 expression was assessed after one week. We observed that levels of COL7 expression were higher after one week following repeat administration.
- **Comparable expression levels of KB103 following intradermal and topical administration.** Efficacy of intradermal delivery vs. topical delivery to intact abraded skin was evaluated in immunocompetent mice one week

after administration. As shown in the figure below, both routes of administration yielded similar COL7A1 RNA and DNA levels in the skin.

- **Confirmation of COL7 expression in RDEB disease model.** KB103, administered by intradermal injection or topically, to COL7 deficient mice or mice grafted with RDEB patient-derived keratinocytes, showed robust COL7 expression and linear deposition at the BMZ

We believe that collectively these studies suggest robust expression of functional COL7 in in-vitro and in-vivo models. Previously, published studies showing robust deposition of COL7 in the BMZ in diseased animal models have shown strong clinical translation. In addition, recent publications from Stanford University using an autologous approach have shown strong correlation between COL7 expression in animal studies and efficacy in Phase 1 human trials. Consequently, we intend to complete the list of preclinical studies as requested by the FDA and file an IND application for KB103 with the FDA in the first quarter of 2018.

#### *Clinical Development Plan for KB103*

In October 2016, we had a pre-IND meeting with the FDA. Based on responses from the FDA, we plan to submit an IND to initiate a Phase 1/2 clinical trial of KB103 in the first quarter of 2018. Concurrent with our IND filing, we intend to apply for Fast Track designation. To date, we have reviewed preclinical results using an intradermal formulation of KB103 with FDA. Subsequent to our FDA meeting we completed preclinical studies that demonstrate equivalency in levels of COL7 expression between the intradermal KB103 formulation and a topical KB103 formulation. Therefore, we plan to use the topical formulation in our Phase 1/2 study. We plan to study three adult patients with RDEB in the initial stage of the Phase 1/2 trial and upon seeing a prospect of benefit will seek to enroll up to six RDEB patients who are five years and older. The Phase 1/2 trial will evaluate evidence of COL7 expression and the presence of mature anchoring fibrils as measured through skin biopsy. Based on our pre-IND discussions with the FDA to date, we believe that expression of COL7 resulting from the application of KB103 and the presence of anchoring fibrils will be sufficient to define clinical benefit. Results of this trial, which we expect to receive in second half of 2018, will guide us in finalizing the design of a pivotal Phase 3 clinical trial. In this planned pivotal Phase 3 trial, we anticipate enrolling both RDEB and DDEB patients. If successful, we believe the results of this Phase 3 trial could support submission of a Biologics License Application, or BLA, to the FDA in the United States and a Marketing Authorization Application, or MAA, to the EMA in Europe for our KB103 product candidate for the treatment of DEB. In December 2016, we received the designation of “rare pediatric disease” for KB103 and conditional designation of our marketing application as a “rare pediatric disease product application,” which, if granted, could qualify us to receive a Rare Pediatric Priority Review Voucher. A Rare Pediatric Priority Review Voucher can be redeemed to receive a priority review of a subsequent marketing application for a different product. In November 2017, we received notification from the NIH Recombinant DNA Advisory Committee (“RAC”) that the Phase 1/2 clinical protocol for KB103 completed the NIH protocol registration process and will not require additional review. In November 2017, we filed for orphan designation in the EU which will be reviewed by the Agency in the first quarter of 2018. In addition, we will pursue Regenerative Medicine Advanced Therapy (“RMAT”) designation and Breakthrough Therapy designation for KB103.

#### **Future Opportunities**

We believe our focus on the unique properties of dermatological diseases provides efficiencies as we select and pursue additional diseases associated with the skin. In addition, we will apply learnings from our near-term programs to future opportunities, which we believe will allow for rapid understanding and efficient drug development. We believe this will enable us to not only apply our gene therapy technology and specifically the STAR-D platform, across multiple severe, genetic diseases today, but across many broader indications associated with the skin, such as psoriasis, atopic dermatitis and chronic wound healing.

We are starting to conduct preclinical studies on our second pipeline compound, KB105, to treat Lamellar Ichthyosis (“LI”) an autosomal recessive disorder that is disfiguring and causes considerable psychological stress to affected patients. Patients with LI have accelerated epidermal turnover with proliferative hyperkeratosis and the majority of LI patients have a mutation in the transglutaminase 1 (“TGM1”) gene. We intend to file an IND on KB105 in the fourth quarter of 2018 and begin clinical studies in the first quarter of 2019.

Given the low prevalence of the rare or orphan diseases we are seeking to treat initially, we intend to internally establish a targeted commercial infrastructure that will be able to serve these patient population markets effectively. As we expand our portfolio to treat other non-orphan dermatological diseases, we intend to establish collaborative commercial alliances with other companies who are presently commercializing treatments for dermatological indications.

Following filing of an IND on KB103, we intend to design, build and validate a commercial-scale cGMP facility in Pittsburgh, Pennsylvania, for the upstream and downstream manufacturing processes of products based on our STAR-D platform.

## **Manufacturing**

Our proprietary manufacturing process for clinical grade KB103 was developed and optimized internally based on our STAR-D platform, and involves both an upstream production process and downstream purification step. Recombinant viral vectors are made safe by removal of most of the viral machinery, including packaging proteins, so that they are incapable of or attenuated for replicating in human cells. However, in order to produce the recombinant virus, these viral proteins have to be re-introduced to the process so that the viral vector can be packaged. In most other viral vector production systems, the missing viral proteins are supplied in one or more individual helper plasmids, along with the base viral vector plasmid. All the plasmids are then co-transfected into a production cell line in the presence of a transfection agent to facilitate viral vector production and packaging. The difficulty of this approach is that it requires cGMP-scale manufacturing and qualification of each of the packaging plasmids and optimization of the transfection method. Even with optimized reagents and methods, significant batch-to-batch variability is seen in viral vector yield and titer that, we believe, drives up the cost of viral vector manufacturing and scale-up, and increases the risk of failure during manufacturing.

Our proprietary upstream process for HSV-1 production avoids the aforementioned issues associated with AAV production systems. Our process requires three critical components:

- Production of a master virus seed stock, or MVSS;
- Production of complementing master cell bank, or MCB; and
- Optimized transduction parameters

The MVSS is scaled up from a single purified clone of the modified HSV-1 vector expressing the therapeutic COL7A1 gene. The MCB is a complementing cell line that stably expresses the HSV-1 viral proteins that are required for HSV-1 growth but have been deleted from the recombinant HSV-1 backbone. By introducing the deleted proteins into the MCB, as opposed to including them in the viral replication process via co-transfection of individual plasmids, we eliminate the need for multiple cGMP qualifications of the plasmids or variability in transfection efficiency from batch to batch, that other production processes face. Infection of the MCB with the MVSS at the optimal concentration results in production of the viral particle. Once the MCB and MVSS and the conditions of infection are established, virus production and resultant yield and titer are highly reproducible and scalable over multiple runs and the risk of failure is minimal.

Optimization of MCB, MVSS and production methods requires extensive knowledge and technical experience with the HSV-1 genome and significant upfront effort to design and select the best virus seed stock and complementing cell line. To date we have screened through hundreds of cell line clones to find the best complementing cell lines, and similarly designed and generated the optimal virus seed stocks for our portfolio candidates. The viral seed stock expresses the therapeutic proteins under the control of strong constitutive or tissue-specific promoters, and additional non-coding regulatory sequences have been included to optimize gene expression. We have also optimized the transduction conditions to reproducibly obtain high yields of the virus.

Unlike the upstream process, steps used to purify and concentrate the viral vector product are often common across different viral vector platforms, and usually involve multiple stages of clarification, concentration, and diafiltration with the ultimate goal to remove contaminants and concentrate the product. We believe that we have successfully developed a robust and reproducible process for purifying our viral vector to required concentrations for clinical use, while successfully removing contaminants to meet FDA guidelines.

We believe that the MVSS and MCB are a vital part of the production of KB103, as they will ensure the reproducible production of multiple clinical batches in a short six week cycle time frame and in a cost-effective manner.

We have made significant investments in developing the most comprehensive and optimized manufacturing process for our vector product candidate including:

- sufficient scale to support stability of KB103 with sufficient longevity that a small number of initial batches will likely provide adequate clinical supply up to pivotal Phase 3 trials;
- a proprietary vector manufacturing technique that produces a highly purified KB103;
- approximately 10 assays to accurately characterize our process and the HSV-1 vectors we produce; and

- a series of high-efficiency purification processes, which can be adapted and customized for our HSV-1 platform products.

We believe these improvements and our continued investment in our STAR-D platform will enable us to develop best in class, next generation gene therapy products for dermatological indications.

Our entire manufacturing process has been successfully transferred to a contract manufacturing organization, and cGMP manufacturing for our lead candidate, KB103, is scheduled for later this year. However, our long-term strategy is to bring our cGMP manufacturing in-house in order to maximally control our intellectual property.

### Competition

The biotechnology and pharmaceutical industries are highly competitive. In particular, the field of gene therapy is characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. Some of our competitors have substantially greater financial resources and larger research and development organizations. In addition, our experience in clinical trials, obtaining FDA and other regulatory approvals, manufacturing and commercialization of products may be more limited. At this time, there is no FDA- or EMA-approved treatment for EB. However, a number of companies are developing drug candidates for EB. At this time, there is no FDA- or EMA-approved treatment for DEB. However, with respect to companies and institutions developing a treatment for DEB we do not believe that we have any direct competitors who provide an allogeneic approach to treating this disease in the way we seek. As a result, we believe our competitors are more indirect and general in nature and fall into three broad categories:

- **Autologous Approaches:** We are aware of less than five companies and research institutions including Abeona, Fibrocell and Kings College who are developing autologous or grafting gene therapy approaches to treating DEB.
- **Palliative Treatments:** We are aware of companies such as Castle Creek Pharma who are developing product candidates taking a palliative approach to treating the disease.
- **Non-Gene Therapy:** We are aware that ProQR Therapeutics has a product candidate in preclinical development that intends to treat some forms of RDEB with a topical RNA-based treatment.

We believe that the major drawbacks of autologous therapies are patient discomfort, the need for highly trained dermatologists, and high cost of treatment including sophisticated equipment, and possible hospitalization. Additionally, because autologous treatments require processing patient's own cells and tissues that takes time, there is a significant delay of six months or more between diagnosis and commencement of patient's treatment. Potential palliative approaches may help mitigate some of the symptoms of the disease but do not treat the underlying disease at a molecular level. We expect that ProQR's preclinical candidate will be able to treat only a subset of the many genetic defects that cause RDEB. Even if our competitors are able to successfully develop approved products for DEB, we believe there will remain a need for an off-the-shelf treatment such as KB103.

### Intellectual Property

Protection of our intellectual property is an important part of our business. We seek patent protection in the United States and in other countries for our inventions and discoveries, and we develop and protect our key know-how and trade secrets relating to our platform technology and the products we are developing using our platform.

We have adopted a strategy of seeking patent protection in the United States and in other jurisdictions globally that we deem appropriate with respect to certain of our technologies relating to our products and process. On January 16, 2018 we announced that the USPTO has granted U.S. Patent No. 9,877,990 which covers compositions comprising HSV vectors and methods of using the same for providing prophylactic, palliative or therapeutic relief of a wound, disorder or disease of the skin in a subject. We believe that the granting of this patent, that is 100% owned by the Company, protects our core STAR-D viral platform and affords us freedom to use this platform for several skin diseases. A corresponding international patent application has been filed in accordance with the Paris Cooperation Treaty. We continue to actively develop our portfolio through the filing of new patent applications, divisionals and continuations relating to our technologies as we deem appropriate.

In addition to patents and licenses, we rely on trade secrets and know-how to develop and maintain our competitive position. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, and obtain and maintain ownership of certain technologies, in part, through confidentiality agreements and invention assignment agreements with our employees, consultants and commercial partners. We also seek to preserve the integrity and confidentiality of our data, trade secrets and know-how, as well as that of our licensees, including by implementing measures

intended to maintain the physical security of research facilities and the physical and electronic security of our information technology systems.

### **Government Regulation and Product Approval**

In the United States, the FDA regulates biologic products including gene therapy products under the Federal Food, Drug, and Cosmetic Act, or the FDCA, the Public Health Service Act, or the PHS Act, and regulations and guidance implementing these laws. The FDCA, PHS Act and their corresponding regulations govern, among other things, the testing, manufacturing, safety, efficacy, labeling, packaging, storage, record keeping, distribution, reporting, advertising and other promotional practices involving biologic products. Applications to the FDA are required before conducting human clinical testing of biologic products. Additionally, each clinical trial protocol for a gene therapy product candidate is reviewed by the FDA, and in limited instances the National Institutes of Health, or the NIH, through its RAC. FDA approval also must be obtained before marketing of biologic products. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources and we may not be able to obtain the required regulatory approvals to successfully develop and commercialize our product candidates.

Within the FDA, the Center for Biologics Evaluation and Research, or CBER, regulates gene therapy products. Within CBER, the review of gene therapy and related products is in the Office of Cellular, Tissue and Gene Therapies, or the OCTGT, and the FDA has established the Cellular, Tissue and Gene Therapies Advisory Committee, or the CTGTAC, to advise CBER on its reviews. 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. To date, the FDA has only approved one human gene therapy product for sale. The FDA has provided guidance for the development of gene therapy products generally, including a growing body of guidance documents on chemistry, manufacturing and control, or CMC, clinical investigations and other areas of gene therapy development, all of which are intended to facilitate the industry's development of gene therapy products.

Ethical, social and legal concerns about gene therapy, genetic testing and genetic research could result in additional regulations restricting or prohibiting the processes we may use. Federal and state agencies, congressional committees and foreign governments have expressed interest in further regulating biotechnology. More restrictive regulations or claims that our products are unsafe or pose a hazard could prevent us from commercializing any products. New government requirements may be established that could delay or prevent regulatory approval of our product candidates under development. It is impossible to predict whether legislative changes will be enacted, regulations, policies or guidance changed, or interpretations by agencies or courts changed, or what the impact of such changes, if any, may be.

#### *U.S. Biologic Products Development Process*

The FDA must approve a product candidate before it may be legally marketed in the United States. The process required by the FDA before a biologic product candidate may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests and in vivo studies in accordance with the FDA's current Good Laboratory Practice, or GLP, regulations and applicable requirements for the humane use of laboratory animals or other applicable regulations;
- submission to the FDA of an IND application, which allows human clinical trials to begin unless FDA objects within 30 days;
- approval by each clinical trial site's institutional review board ("IRB") and institutional biosafety committee ("IBC") before the clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials according to the FDA's GCP regulations, and any additional requirements for the protection of human research subjects and their health information, to establish the safety and efficacy of the proposed biologic product candidate for its intended use;
- preparation and submission to the FDA of a biologics license application, or BLA, for marketing approval that includes substantial evidence of safety, purity and potency from results of nonclinical testing and clinical trials;
- review of the product by an FDA advisory committee, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the biologic product candidate is produced to assess compliance with cGMP requirements and to assure that the facilities, methods and

controls are adequate to preserve the biologic product candidate's identity, safety, strength, quality, potency and purity;

- potential FDA audit of the nonclinical and clinical trial sites that generated the data in support of the BLA; and
- payment of user fees and FDA review and approval, or licensure, of the BLA.

Before testing any biologic product candidate in humans, including a gene therapy product candidate, the product candidate must undergo preclinical testing. Preclinical tests, also referred to as nonclinical studies, include laboratory evaluations of product chemistry, toxicity and formulation, as well as in vivo studies to assess the potential safety and activity of the product candidate and to establish a rationale for therapeutic use. The conduct of the preclinical tests must comply with federal regulations and requirements including GLPs.

Concurrent with clinical trials, companies usually must complete some long-term preclinical testing, such as animal studies of reproductive adverse events and carcinogenicity, and must also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the drug in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final drug product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

The clinical trial sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of an IND. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. With gene therapy protocols, if the FDA allows the IND to proceed, but the RAC decides that full public review of the protocol is warranted, the FDA will request at the completion of its IND review that sponsors delay initiation of the protocol until after completion of the RAC review process. The FDA also may impose clinical holds on a biologic product candidate at any time before or during clinical trials due to safety concerns or non-compliance. If the FDA imposes a clinical hold, trials may not recommence without FDA authorization and then only under terms authorized by the FDA. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical studies to begin, or that, once begun, issues will not arise that suspend or terminate such studies.

#### *Human Clinical Trials Under an IND*

Clinical trials involve the administration of the biologic product candidate to healthy volunteers or patients under the supervision of qualified investigators which generally are physicians not employed by, or under, the control of the trial sponsor. Clinical trials are conducted under written study protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters to be used to monitor subject safety, including stopping rules that assure a clinical trial will be stopped if certain adverse events should occur. Each protocol and any amendments to the protocol must be submitted to the FDA as part of the IND. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to a proposed clinical trial and places the trial on clinical hold, including concerns that human research subjects will be exposed to unreasonable health risks. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Accordingly, submission of an IND may or may not result in the FDA allowing clinical trials to commence. Clinical trials must be conducted and monitored in accordance with the FDA's regulations comprising the GCP requirements, including the requirement that all research subjects provide informed consent. Further, each clinical trial must be reviewed and approved by an IRB and IBC at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers items such as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the form and content of the informed consent that must be signed by each clinical trial subject, or their legal representative, reviews and approves the study protocol, and must monitor the clinical trial until completed. Clinical trials involving recombinant DNA also must be reviewed by an IBC, a local institutional committee that reviews and oversees basic and clinical research that utilizes recombinant DNA at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment.

Human clinical trials typically are conducted in three sequential phases that may overlap or be combined:

- Phase 1. The biologic product candidate initially is introduced into a small number of healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion and, if possible, to gain an early understanding of its effectiveness. In the case of some product candidates for severe or life-threatening diseases, especially when the product candidate may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients. Phase 1 clinical trials of gene therapies are typically conducted in patients rather than healthy volunteers.
- Phase 2. The biologic product candidate is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product candidate for specific targeted diseases and to determine dosage tolerance, optimal dosage and dosing schedule.
- Phase 3. Phase 3 clinical trials are commonly referred to as “pivotal” studies, which typically denotes studies that present the data the FDA or other relevant regulatory agencies will use to determine whether or not to approve a biologic product. In Phase 3 studies, the biologic product candidate is administered to an expanded patient population, generally at multiple geographically dispersed clinical trial sites in adequate and well-controlled clinical trials to generate sufficient data to statistically confirm the potency and safety of the product for approval. These clinical trials are intended to establish the overall risk/benefit ratio of the product candidate and provide an adequate basis for product labeling.
- Post-approval clinical trials, sometimes referred to as Phase 4 clinical trials, may be conducted after marketing approval. These clinical trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication, particularly for long-term safety follow-up.

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data and clinical trial investigators. Annual progress reports detailing the results of the clinical trials must be submitted to the FDA.

#### *Additional Regulation for Gene Therapy Clinical Trials*

In addition to the regulations discussed above, there are a number of additional standards that apply to clinical trials involving the use of gene therapy. The FDA has issued various guidance documents regarding gene therapies, which outline 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 CMC 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. The NIH and the FDA have a publicly accessible database, the Genetic Modification Clinical Research Information System, which includes information on gene therapy trials and serves as an electronic tool to facilitate the reporting and analysis of adverse events on these trials.

#### *U.S. Review and Approval Processes*

The results of the preclinical tests and clinical trials, together with detailed information relating to the product’s CMC and proposed labeling, among other things, are submitted to the FDA as part of a BLA requesting approval to market the product for one or more indications. For gene therapies, selecting patients with applicable genetic defects is a necessary condition to effective treatment. For the therapy we are currently developing, we believe that diagnoses based on existing genetic tests developed and administered by laboratories certified under the Clinical Laboratory Improvement Amendments, or CLIA, are sufficient to select appropriate patients and will be permitted by the FDA. Under the PDUFA, each BLA must be accompanied by a significant user fee. The FDA adjusts the PDUFA user fees on an annual basis. The PDUFA also imposes an annual product fee for biologics and an annual establishment license fee on facilities used to manufacture prescription biologics. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on BLAs for product candidates designated as orphan drugs, unless the product candidate also includes a non-orphan indication.

The FDA reviews a BLA within 60 days of submission to determine if it is substantially complete before it accepts it for filing. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In that event, the BLA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for

filing, the FDA begins an in-depth, substantive review of the BLA. The FDA reviews the BLA to determine, among other things, whether the proposed product candidate is safe and potent, or effective, for its intended use, has an acceptable purity profile and whether the product candidate is being manufactured in accordance with cGMP to assure and preserve the product candidate's identity, safety, strength, quality, potency and purity. 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 a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. During the product approval process, the FDA also will determine whether a REMS is necessary to assure the safe use of the product candidate.

REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events, and whether the product is a new molecular entity. A REMS could include medication guides, physician communication plans and elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. If the FDA concludes a REMS is needed, the sponsor of the BLA must submit a proposed REMS; the FDA will not approve the BLA without a REMS, if required.

Before approving a BLA, the FDA will inspect the facilities at which the product candidate is manufactured. The FDA will not approve the product candidate unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product candidate within required specifications. Additionally, before approving a BLA, the FDA typically will inspect one or more clinical sites to assure that the clinical trials were conducted in compliance with IND trial requirements and GCP requirements.

On the basis of the BLA and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the biologic product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the BLA, the FDA will issue an approval letter.

If a product candidate receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. The FDA may impose restrictions and conditions on product distribution, prescribing or dispensing in the form of a REMS, or otherwise limit the scope of any approval. In addition, the FDA may require post-marketing clinical trials, sometimes referred to as Phase 4 clinical trials, designed to further assess a biologic product's safety and effectiveness, and testing and surveillance programs to monitor the safety of approved products that have been commercialized.

The FDA has agreed to specified performance goals in the review of BLAs under the PDUFA. One such goal is to review standard BLAs in 10 months after the FDA accepts the BLA for filing, and priority BLAs in six months, whereupon a review decision is to be made. The FDA does not always meet its PDUFA goal dates for standard and priority BLAs and its review goals are subject to change from time to time. The review process and the PDUFA goal date may be extended by three months if the FDA requests or the BLA sponsor otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

#### *Orphan Drug Designation*

On November 2, 2017, the FDA granted Orphan Drug Designation to the Company's lead product candidate, KB103, for the treatment of DEB. The FDA's Office of Orphan Drug Products grants orphan drug designation to support the development of medicines for underserved patient populations, or rare disorders, that affect fewer than 200,000 people in the United States. Orphan drug designation may allow Krystal Biotech to be eligible for a seven-year period of U.S. marketing exclusivity upon approval of KB103, tax credits for certain clinical research costs, and a waiver of the PDUFA filing fees, subject to certain conditions.

Under the Orphan Drug Act, the FDA may designate a biologic product as an "orphan drug" if it is intended to treat a rare disease or condition (generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a biologic product available in the United States for treatment of the disease or condition will be recovered from sales of the product). Orphan product



designation must be requested before submitting a BLA. After the FDA grants orphan product designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan product designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

If a product with orphan status receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, meaning that the FDA may not approve any other applications to market the same drug or biologic product for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity or if the party holding the exclusivity fails to assure the availability of sufficient quantities of the drug to meet the needs of patients with the disease or condition for which the drug was designated. Competitors, however, may receive approval of different products for the same indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity.

Orphan medicinal product status in the EU has similar, but not identical, benefits. In November 2017, we filed for Orphan Drug Designation for KB103 with the EMA. The application is scheduled for review by the EMA in the first quarter of 2018.

#### *Expedited Development and Review Programs*

In addition, the FDA is authorized to expedite the review of BLAs in several ways.

##### *Fast Track Program*

Under the Fast Track program, the sponsor of a biologic product candidate may request the FDA to designate the product for a specific indication as a Fast Track product concurrent with or after the filing of the IND. Biologic products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to the combination of the product candidate and the specific indication for which it is being studied. In addition to other benefits, such as the ability to have greater interactions with the FDA, the FDA may initiate review of sections of a Fast Track BLA before the application is complete, a process known as rolling review. Any product submitted to FDA for marketing, including under a Fast Track program, may be eligible for other types of FDA programs intended to expedite development and review, such as breakthrough therapy designation, Regenerative Medicine Advanced Therapy designation, priority review and accelerated approval.

##### *Breakthrough Therapy Designation*

To qualify for the breakthrough therapy program, product candidates must be intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence must indicate that such product candidates may demonstrate substantial improvement on one or more clinically significant endpoints over existing therapies. The FDA will seek to ensure the sponsor of a breakthrough therapy product candidate receives intensive guidance on an efficient drug development program; intensive involvement of senior managers and experienced staff on a proactive, collaborative and cross-disciplinary review; and rolling review.

##### *Regenerative Medicine Advanced Therapy ("RMAT") Designation*

To qualify for the RMAT program, product candidates must be intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence must indicate that such product candidates have the potential to address unmet medical needs for such disease or condition. The designation gives the sponsor access to increased meeting opportunities with FDA, in a manner comparable to those offered to sponsors of breakthrough-designated therapies. Because the designated products meet the criteria for unmet medical need in the treatment of a serious condition, they may be eligible for priority review, in which the initial assessment of the BLA is reduced from ten months to six months, and accelerated approval, which bases approval on an effect on a predictive surrogate endpoint or an intermediate clinical endpoint. RMATs qualifying for accelerated approval may be able to satisfy licensing requirements through commitment to post-approval clinical studies as well as real-world data such as patient registries and health record analysis.

##### *Accelerated Approval*

Drug or biologic products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval. Accelerated approval means that a product candidate may be approved on the basis of adequate and well-controlled clinical trials establishing that the product candidate has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the

basis of an effect on a clinical endpoint other than survival or irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity and prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, FDA may require that a sponsor of a drug or biologic product candidate receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. In addition, FDA currently requires as a condition for accelerated approval pre-approval of promotional materials.

Fast Track designation, breakthrough therapy designation and accelerated approval do not change the standards for approval but may expedite the development or approval process.

#### *Rare Pediatric Disease Priority Review Voucher*

The FDA also offers a rare pediatric disease drug designation. If a drug receives the designation of a “rare pediatric disease” drug, it is eligible during the FDA marketing process to apply for a Rare Pediatric Disease Priority Review Voucher. According to the FDA website, under the Rare Pediatric Priority Review Voucher Program, a sponsor who receives an approval for a drug or biologic for a “rare pediatric disease” may qualify for a voucher that can be redeemed to receive a priority review of a subsequent marketing application for a different product. In December 2016, we received the designation of “rare pediatric disease” for KB103 and conditional designation of our marketing application as a “rare pediatric disease product application,” which, if granted, could qualify us to receive a Rare Pediatric Priority Review Voucher. According to the FDA website, a Rare Pediatric Priority Review Voucher can be redeemed to receive a priority review of a subsequent marketing application for a different product.

#### *Post-Approval Requirements*

Rigorous and extensive FDA regulation of biologic products continues after approval, particularly with respect to cGMP requirements. Manufacturers are required to comply with applicable requirements in the cGMP regulations, including quality control and quality assurance and maintenance of records and documentation. Other post-approval requirements applicable to biologic products include reporting of cGMP deviations that may affect the identity, potency, purity and overall safety of a distributed product; recordkeeping requirements; reporting of adverse effects; reporting updated safety and efficacy information; and complying with electronic record and signature requirements. After a BLA is approved, the product also may be subject to official lot release. If the product is subject to official release by the FDA, the manufacturer submits samples of each lot of product to the FDA, together with a release protocol, showing a summary of the history of manufacture of the lot and the results of all tests performed on the lot. The FDA also may perform certain confirmatory tests on lots of some products before releasing the lots for distribution. In addition, the FDA conducts laboratory research related to the regulatory standards on the safety, purity, potency and effectiveness of biologic products. A sponsor also must comply with the FDA’s advertising and promotion requirements, such as the prohibition on promoting products for uses or in patient populations that are not described in the product’s approved labeling (known as “off-label use”).

Discovery of previously unknown problems or the failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a product or withdrawal of the product from the market as well as possible civil or criminal sanctions. In addition, changes to the manufacturing process or facility generally require prior FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

#### *U.S. Patent Term Restoration and Marketing Exclusivity*

Depending upon the timing, duration and specifics of FDA approval of product candidates, some of a sponsor’s U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product’s approval date. The patent term restoration period generally is one-half the time between the effective date of an IND and the submission date of a BLA plus the time between the submission date of a BLA and the approval of that application. Only one patent applicable to an approved biologic product is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. Moreover, a given patent may only be extended once based on a single product. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration.

### *Government Regulation Outside of the United States*

In addition to regulations in the United States, sponsors are subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of biologic products. Because biologically sourced raw materials are subject to unique contamination risks, their use may be restricted in some countries.

Whether or not a sponsor obtains FDA approval for a product, a sponsor must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application, much like the IND, prior to the commencement of human clinical trials. In the EU, for example, a request for a Clinical Trial Authorization, or CTA, must be submitted to the competent regulatory authorities and the competent Ethics Committees in the EU Member States in which the clinical trial takes place, much like FDA and the IRB, respectively. Once the CTA request is approved in accordance with the EU and the EU Member State's requirements, clinical trial development may proceed. The requirements and processes governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials are conducted in accordance with GCPs and the applicable regulatory requirements of the country or countries in which the clinical trial is performed, as well as the ethical principles that have their origin in the Declaration of Helsinki (whichever provides the greater protection to the clinical trial participants).

Failure to comply with applicable foreign regulatory requirements may result in, among other things, fines; suspension, variation or withdrawal of regulatory approvals; product recalls; seizure of products; operating restrictions; and criminal prosecution.

### *Other Healthcare Laws and Regulations*

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and use of pharmaceutical products that are granted marketing approval. Arrangements with third-party payors, existing or potential customers and referral sources are subject to broadly applicable fraud and abuse and other healthcare laws and regulations, and these laws and regulations may constrain the business or financial arrangements and relationships through which manufacturers market, sell and distribute the products for which they obtain marketing approval. Such restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in cash or kind, in exchange for, or to induce, either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers, on the one hand, and prescribers, purchasers and formulary managers on the other. The Patient Protection and Affordable Care Act, or PPACA, amended the intent requirement of the federal Anti-Kickback Statute. A person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to commit a violation;
- the federal false claims and civil monetary penalties laws, including the civil False Claims Act, or the FCA, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid or other third-party payors that are false or fraudulent, or making a false statement to avoid, decrease, or conceal an obligation to pay money to the federal government. Certain marketing practices, including off-label promotion, also may implicate the FCA. In addition, the PPACA codified case law that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the FCA;
- the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services, or the CMS, information related to payments and other transfers of value to physicians, certain other healthcare providers and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and its implementing regulations, which imposes obligations, including mandatory contractual terms, with respect to safeguarding the transmission, security and privacy of protected health information;
- 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; and
- state and foreign law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Violation of the laws described above or any other governmental laws and regulations may result in penalties, including civil and criminal penalties, damages, fines, the curtailment or restructuring of operations, the exclusion from participation in federal and state healthcare programs, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, and imprisonment. Furthermore, efforts to ensure that business activities and business arrangements comply with applicable healthcare laws and regulations can be costly.

#### *Coverage and Reimbursement*

Significant uncertainty exists as to the coverage and reimbursement status of any products for which we may obtain regulatory approval. In the United States, sales of any product candidates for which regulatory approval for commercial sale is obtained will depend in part on the availability of coverage and adequate reimbursement from third-party payors. Third-party payors include government authorities and health programs in the United States such as Medicare and Medicaid, managed care providers, private health insurers and other organizations. These third-party payors are increasingly reducing reimbursements for medical products and services. The process for determining whether a payor will provide coverage for a drug product may be separate from the process for setting the reimbursement rate that the payor will pay for the drug product. Third-party payors may limit coverage to specific drug products on an approved list, or formulary, which might not include all of FDA-approved drugs for a particular indication. Additionally, the containment of healthcare costs has become a priority of federal and state governments, and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic 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 we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

In the EU, 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. EU 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 company profits. The downward pressure on health care costs has become intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert competitive pressure that may reduce pricing within a country. Any country that has price controls or reimbursement limitations may not allow favorable reimbursement and pricing arrangements.

#### *Health Reform*

The United States and some foreign jurisdictions are considering or have enacted a number of reform proposals to change the healthcare system. There is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality or expanding access. In the United States, for example, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected and continues to face major uncertainty due to the status of major legislative initiatives surrounding healthcare reform.

### *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 other countries that impose similar obligations.

### *U.S. Foreign Corrupt Practices Act*

The U.S. Foreign Corrupt Practices Act, or FCPA, prohibits U.S. corporations and individuals from engaging in certain activities to obtain or retain business abroad or to influence a person working in an official capacity. It is illegal to pay, offer to pay or authorize the payment of anything of value to any foreign government official, government staff member, political party or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity. The scope of the FCPA includes interactions with certain healthcare professionals in many countries. Equivalent laws have been adopted in other foreign countries that impose similar obligations.

### **Employees**

As of January 31, 2018, we had twelve employees, eight of whom were primarily engaged in research and development activities. None of our employees are represented by a labor union and we consider our employee relations to be good.

### **Corporate Information**

We were organized in December 2015 in the State of California and commenced operations on April 15, 2016. On March 31, 2017, we converted from a California limited liability company to a Delaware C-corporation, and changed our name from Krystal Biotech, LLC to Krystal Biotech, Inc. Our principal offices are located at 2100 Wharton Street, Suite 701, Pittsburgh, PA 15203, and our telephone number is 412-586-5830. Our website address is [www.krystalbio.com](http://www.krystalbio.com). Our website and the information contained on, or that can be accessed through, the website will not be deemed to be incorporated by reference in, and are not considered part of, this Annual Report on Form 10-K. You should not rely on any such information in making your decision whether to purchase our common stock. Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, are available free of charge on our investor relations website as soon as reasonably practicable after we electronically file such material with, or furnish it to the Securities and Exchange Commission, or SEC. The SEC also maintains a website that contains our SEC filings. The address of the website is [www.sec.gov](http://www.sec.gov). Further, a copy of this Annual Report on Form 10-K is located at the SEC's Public Reference Room at 100 F Street, NE, Washington, DC 20549. Information on the operation of the Public Reference Room can be obtained by calling the SEC at 1-800-SEC-0300.

### **Implications of Being an Emerging Growth Company**

We qualify as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. An emerging growth company may take advantage of relief from certain reporting requirements and other burdens that are otherwise applicable generally to public companies. These provisions include:

- Reduced obligations with respect to financial data, including presenting only two years of audited financial statements and only two years of selected financial data in this Form 10-K;
- An exception from compliance with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act;
- Reduced disclosure about our executive compensation arrangements in our periodic reports, proxy statements and registration statements; and
- Exemptions from the requirements of holding non-binding advisory votes on executive compensation or golden parachute arrangements.

We may take advantage of these provisions for up to five years or such earlier time that we no longer qualify as an emerging growth company. We would cease to be an emerging growth company if we have more than \$1.07 billion in annual revenue, have more than \$700 million in market value of our capital stock held by non-affiliates or issue more than \$1.0 billion of non-convertible debt over a three-year period. We may choose to take advantage of some but not all of these reduced reporting burdens. For example, we intend to take advantage of the reduced reporting requirements with respect to

disclosure regarding our executive compensation arrangements, have presented only two years of audited financial statements and only two years of related “Management’s Discussion and Analysis of Financial Condition and Results of Operations” elsewhere in this Annual Report on Form 10-K, and have taken advantage of the exemption from auditor attestation on the effectiveness of our internal control over financial reporting. To the extent that we take advantage of these reduced reporting burdens, the information that we provide stockholders may be different than you might obtain from other public companies in which you hold equity interests.

In addition, under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards until such time as those standards 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.

#### **Item 1A. Risk Factors.**

##### **RISKS RELATED TO OUR FINANCIAL POSITION AND NEED FOR ADDITIONAL CAPITAL**

###### ***We have never generated revenue and may never be profitable.***

Since inception, we have incurred recurring losses and negative cash flows from operations and, at December 31, 2017, we have an accumulated deficit of \$9.1 million. Our ability to achieve profitability depends on our ability to successfully complete the development of, and obtain the regulatory approvals necessary to commercialize, KB103 and any additional product candidates that we may pursue in the future. We do not anticipate generating revenues from product sales for the next several years, if ever. We have devoted substantially all of our efforts to research and development of our gene therapy product candidate, KB103, as well as to building out our infrastructure. We expect that it could be several years, if ever, before we have a commercialized product candidate. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially if, and as, we:

- continue our research and the preclinical and clinical development of KB103, including our planned clinical trials;
- initiate additional clinical trials and preclinical studies for any additional product candidates that we may pursue in the future;
- prepare our BLA, and marketing authorization application for KB103;
- manufacture current good manufacturing practices, or cGMP, material for clinical trials or potential commercial sales;
- establish and validate a commercial-scale cGMP manufacturing facility;
- further develop our gene therapy product candidate portfolio;
- establish a sales, marketing and distribution infrastructure to commercialize any product candidate for which we may obtain marketing approval;
- develop, maintain, expand and protect our intellectual property portfolio;
- acquire or in-license other product candidates and technologies; and
- seek marketing approval for KB103 in the EU and in other key geographies.

To become and remain profitable, we must develop and eventually commercialize one or more product candidates with significant market potential. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials of KB103, developing and validating commercial scale manufacturing processes, obtaining marketing approval for this product candidate, manufacturing, marketing and selling any future product candidates for which we may obtain marketing approval and satisfying any post-marketing requirements. In addition, if we were required to discontinue development of KB103, if KB103 does not receive regulatory approval, if we do not obtain our targeted indications for KB103 or if KB103 fails to achieve sufficient market acceptance for any indication, we could be delayed by many years in our ability to achieve profitability, if ever, and would materially adversely affect our business prospects and financial condition. Moreover, if we decide to leverage any success with our KB103 product candidate to develop other product opportunities, we may not be successful in such efforts. In any such event, our business will be materially adversely affected.

We currently only have two product candidates, KB103 and KB105, and we may never develop, acquire or in-license additional product candidates. We may never succeed in any or all of these activities and, even if we do, we may never generate revenues that are significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company also could cause you to lose all or part of your investment.

Because of the numerous risks and uncertainties associated with pharmaceutical product and biological development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. If we are required by the FDA, or EMA, or other regulatory authorities to perform studies in addition to those currently expected, or if there are any delays in completing our clinical trials or the development of KB103, our expenses could increase and revenue could be further delayed.

***We will need to raise additional funding in order to receive approval for KB103 or any other product candidate. Such funding may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate certain of our product development efforts or other operations.***

In order to complete the process of obtaining regulatory approval for KB103 and to build the sales, marketing and distribution infrastructure that we believe will be necessary to commercialize KB103, if approved, we will require substantial additional funding. In addition, if we obtain marketing approval for KB103, we expect to incur significant expenses related to product sales, medical affairs, marketing, manufacturing and distribution. Furthermore, we expect to incur additional costs associated with operating as a public company. We anticipate that we will need additional funding to complete the development of KB103 and any future product candidates and to commercialize any such approved products.

Our future capital requirements will depend on many factors, including:

- the progress and results of our planned clinical trials of KB103;
- the scope, progress, results and costs of drug discovery, laboratory testing, manufacturing, preclinical development and clinical trials for any other product candidates that we may pursue in the future, if any;
- the costs, timing and outcome of regulatory review of KB103 and any other product candidates we may develop;
- the costs of establishing and maintaining our own commercial-scale cGMP manufacturing facility;
- the costs associated with the manufacturing process development and evaluation of third-party manufacturers;
- the costs of future activities, including product sales, medical affairs, marketing, manufacturing and distribution, in the event we receive marketing approval for KB103 or any other product candidates we may develop;
- the extent to which the costs of our product candidates, if approved, will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or will be reimbursed by government authorities, private health coverage insurers and other third-party payors;
- revenue, if any, received from commercial sale of KB103 or other product candidates, should any of our product candidates receive marketing approval;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- our current license agreements remaining in effect and our achievement of milestones under those agreements;
- our ability to establish and maintain collaborations and licenses on favorable terms, if at all; and
- the extent to which we acquire or in-license other product candidates and technologies.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our product revenues, if any, will be derived from or based on sales of product candidates that may not be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. 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. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders 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 stockholders. The incurrence of indebtedness would result in increased fixed payment obligations and a portion of our operating cash flows, if any, being dedicated to the payment of principal and interest on such indebtedness, 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. Furthermore, existing stockholders may not agree with our financing plans or the terms of such financings. Adequate additional financing may not be available to us on acceptable terms, or at all.

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

We are a development-stage company that commenced operations in 2016. Our efforts to date, with respect to the development of KB103, have been limited to organizing and staffing our company, business planning, raising capital, developing our STAR-D platform and related technologies, identifying KB103 as a potential gene therapy product candidate and undertaking preclinical trials of KB103. We have not yet demonstrated the ability to complete clinical trials of KB103 or any other product candidate, obtain marketing approvals, manufacture a commercial-scale product or conduct sales and marketing activities necessary for successful commercialization. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had more experience developing gene therapy products.

We do not currently have the ability to perform the sales, marketing and manufacturing functions necessary for the production and sale of KB103 on a commercial scale. Our lead product candidate, KB103, will be required to undergo significant clinical trials before it can be commercialized, if at all. The successful commercialization of KB103 will require us to perform a variety of functions, including:

- clinical development of KB103;
- obtaining required regulatory approvals;
- formulating and manufacturing product candidates; and
- conducting sales and marketing activities.

We expect our financial condition and operating results to continue to fluctuate from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. We will need to transition at some point from a company with a research and development focus to a company capable of undertaking commercial activities. We may encounter unforeseen expenses, difficulties, complications and delays and may not be successful in such a transition.

#### **RISKS RELATED TO OUR BUSINESS**

***We are early in our development efforts and our lead product candidate, KB103, is still in preclinical development. If we are unable to advance KB103 to clinical trials, obtain regulatory approval and ultimately commercialize KB103, or if we experience significant delays in doing so, our business will be materially harmed.***

We are early in our development efforts and KB103 is still in preclinical development. Pending additional regulatory approvals, we plan to initiate a Phase 1/2 clinical trial in the first quarter of 2018. The development and commercialization of KB103 or any other product candidate we may develop is subject to many uncertainties, including the following:

- successful completion of additional preclinical studies and successful enrollment and completion of clinical trials;
- an effective IND and CTA, that allow us to commence our planned clinical trials for KB103;
- positive results from our planned clinical trials;
- receipt of regulatory approvals from applicable regulatory authorities;
- maintenance of our existing arrangements with third-party manufacturers for clinical supply and successful development of our internal manufacturing processes on an ongoing basis;
- commercial launch of KB103, if and when approved, whether alone or in collaboration with others;
- acceptance of KB103, if and when approved, by patients, the medical community and third-party payors;
- enforcement and defense of intellectual property rights and claims; and
- maintenance of a continued acceptable safety profile of our product candidates following approval.



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 KB103, which would materially harm our business. If we do not receive regulatory approvals for KB103, our business, financial condition, results of operations and prospects could be materially and adversely affected.

***We have not tested KB103 in clinical trials. Success in early preclinical studies may not be indicative of results obtained in later preclinical studies and clinical trials.***

KB103 has never been evaluated in human clinical trials, and we may experience unexpected or adverse results in the future. We will be required to demonstrate through adequate and well-controlled clinical trials that KB103 is safe for humans and effective for indicated uses before we can seek regulatory approvals for commercial sale.

The positive results we have observed for KB103 in preclinical trials may not be predictive of outcomes in our future clinical trials. KB103, or other product candidates, may also fail to show the desired safety and efficacy in later stages of clinical development even if they successfully advance through initial clinical trials. The clinical trial process may fail to demonstrate that KB103 is safe for humans and effective for indicated uses, which may cause us to abandon KB103, which is currently our lead product candidate.

Many companies in the biotechnology industry have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development and there is a high failure rate for product candidates proceeding through clinical trials. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. Regulatory delays or rejections may be encountered as a result of many factors, including changes in regulatory policy during the period of product development, failure to perform in accordance with FDA good clinical practices or applicable regulatory guidelines in the EU and other countries, selection of clinical endpoints that require prolonged periods of clinical observation or analysis of the resulting data, or changes in regulatory requirements and guidance that require amending or submitting new clinical protocols. In addition, the design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We cannot be certain that we will not face these or similar setbacks.

***We may find it difficult to enroll an adequate number of patients in our clinical trials, which could delay or prevent us from proceeding with clinical trials of KB103.***

Identifying and qualifying patients to participate in clinical trials of KB103 is critical to our success. The timing of our clinical trials depends on our ability to recruit an adequate number of patients to participate as well as completion of required follow-up periods. If patients are unwilling to participate in our gene therapy studies because of competitive clinical trials for similar patient populations, negative publicity from adverse events related to the biotechnology or gene therapy fields or for other reasons, the timeline for recruiting patients, conducting studies and obtaining regulatory approval of KB103 may be delayed. These delays could result in increased costs, delays in advancing KB103, delays in testing the effectiveness of KB103 or termination of clinical trials altogether.

***Even if we complete the necessary clinical trials, we cannot predict when, or if, we will obtain regulatory approval to commercialize KB103 and the approval may be for a more narrow indication than we seek.***

We cannot commercialize a product candidate until the appropriate regulatory authorities have reviewed and approved the product candidate. Even if KB103 meets its safety and efficacy endpoints in clinical trials, the regulatory authorities may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Additional delays may result if an FDA Advisory Committee or other regulatory authority recommends non-approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory authority policy during the period of product development, clinical trials and the review process.

Regulatory authorities also may approve a product candidate for more limited indications than requested or they may impose significant limitations in the form of narrow indications, warnings or a Risk Evaluation and Mitigation Strategy, or REMS. These regulatory authorities may require precautions or contra-indications with respect to conditions of use or they may grant approval subject to the performance of costly post-marketing clinical trials. In addition, regulatory authorities may not approve the labeling claims that are necessary or desirable for the successful commercialization of KB103. Any of the foregoing scenarios could materially harm the commercial prospects for KB103 and materially and adversely affect our business, financial condition, results of operations and prospects.

***KB103 is based on a novel technology, which makes it difficult to predict the time and cost of development and of subsequently obtaining regulatory approval.***

The clinical trial requirements of the FDA, 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 such product candidates. The regulatory approval process for novel product candidates such as ours can be more expensive and take longer than for other, better known or more extensively studied product candidates. To date, only two gene therapy products, Novartis' Kymriah and Spark Therapeutics's Luxurna, have received marketing approval by the FDA, and only two gene therapy products, uniQure N.V.'s Glybera® and GlaxoSmithKline's Strimvelis™, have received marketing authorization from the European Commission. 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 EU or how long it will take to commercialize our product candidates. Approvals by the European Commission may not be indicative of what FDA may require for approval.

Regulatory requirements governing gene and cell therapy products have changed frequently and may continue to change in the future. The FDA has established the Office of Cellular, Tissue and Gene Therapies within its Center for Biologics Evaluation and Research, or CBER, to consolidate the review of gene therapy and related products, and has established the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER in its review. Gene therapy clinical trials conducted at institutions that receive funding for recombinant DNA research from the NIH, also are potentially subject to review by the NIH Office of Biotechnology Activities' RAC; however, the NIH recently announced that the RAC will only publicly review clinical trials if the trials cannot be evaluated by standard oversight bodies and pose unusual risks. Although the FDA decides whether individual gene therapy protocols may proceed, 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 approved its initiation. Conversely, the FDA can put an IND on a clinical hold even if the RAC has provided a favorable review or an exemption from in-depth, public review. If we were to engage an NIH-funded institution to conduct a clinical trial, that institution's IBC as well as its IRB, 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 our product candidates. Similarly, the EMA may issue new guidelines concerning the development and marketing authorization for gene therapy medicinal products and require that we comply with these new guidelines.

These regulatory review committees and advisory groups and the new guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of KB103 or future product candidates or lead to significant post-approval limitations or restrictions. As we advance KB103, we will be required to consult with these regulatory and advisory groups, and comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of KB103. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product revenue, and our business, financial condition, results of operations and prospects would be materially and adversely affected.

***KB103 may cause undesirable side effects or have other properties that could delay or prevent its regulatory approval, limit the commercial potential or result in significant negative consequences following any potential marketing approval.***

There have been several significant adverse side effects in gene therapy trials using other vectors in the past. Gene therapy is still a relatively new approach to disease treatment and additional adverse side effects could develop. There also is the potential risk of delayed adverse events following exposure to gene therapy products 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 therapy products include an immunologic reaction early after administration which, while not necessarily adverse to the patient's health, could substantially limit the effectiveness of the treatment. In previous clinical trials involving vectors derived from adeno-associated virus for gene therapy, some subjects experienced the development of a T-cell response, whereby after the vector is within the target cell, the cellular immune response system triggers the removal of transduced cells by activated T-cells. If our vectors demonstrate a similar effect we may decide or be required to halt or delay further clinical development of KB103.

In addition to side effects caused by the product candidate, the administration process or related procedures also can cause adverse side effects. If any such adverse 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 the administration process or related procedures,

the FDA, the European Commission, the EMA or other regulatory authorities could order us to cease further development of, or deny approval of, KB103 for any or all targeted indications. Even if we are able to demonstrate that any 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 KB103, the commercial prospects of such product candidate may be harmed and our ability to generate product revenues from this product candidate may be delayed or eliminated. Any of these occurrences may harm our ability to develop other product candidates, and may harm our business, financial condition and prospects significantly.

Additionally, if KB103 receives marketing approval, the FDA could require us to adopt a REMS to ensure that the benefits outweigh its risks, which may include, among other things, a medication guide outlining the risks of the product for distribution to patients and a communication plan to health care practitioners. Furthermore, if we or others later identify undesirable side effects caused by KB103, several potentially significant negative consequences could result, including:

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

Any of these events could prevent us from achieving or maintaining market acceptance of KB103 and could significantly harm our business, financial condition, results of operations and prospects.

***We may encounter substantial delays in our clinical trials or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities.***

Before obtaining marketing approval from regulatory authorities for the sale of our drug candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the drug candidate for its intended indications. Clinical trials are expensive, time consuming and uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. A failure of one or more clinical trials can occur at any stage of testing. Events that may prevent successful or timely completion of clinical development include:

- delays in reaching a consensus with regulatory authorities on trial design;
- delays in opening sites and recruiting suitable patients to participate in our clinical trials;
- imposition of a clinical hold by regulatory authorities as a result of a serious adverse event or concerns with a class of drug candidates, or after an inspection of our clinical trial operations or trial sites;
- delays in having patients complete participation in a trial or return for post-treatment follow-up;
- occurrence of serious adverse events associated with the drug candidate that are viewed to outweigh its potential benefits; or
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols.

In addition, if we make manufacturing or formulation changes to KB103, we may need to conduct additional studies to bridge our modified product candidate to earlier versions. Clinical trial delays could also shorten any periods during which we may have the exclusive right to commercialize KB103 or allow our competitors to bring products to market before we do, which could limit our potential revenue or impair our ability to successfully commercialize KB103 and may harm our business, financial condition, results of operations and prospects. Any delays, setbacks or failures in our clinical trials could materially and adversely affect our business, financial condition, results of operations and prospects.

Additionally, if the results of our clinical trials are inconclusive or if there are safety concerns or serious adverse events associated with our drug candidates, we may:

- be delayed in obtaining marketing approval, if at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing requirements;

- be required to perform additional clinical trials to support approval or be subject to additional post-marketing testing requirements;
- have regulatory authorities withdraw, or suspend, their approval of the drug or impose restrictions on its distribution;
- be subject to the addition of labeling statements, such as warnings or contraindications;
- be sued; or
- experience damage to our reputation

Our drug development costs will also increase if we experience delays in testing or obtaining marketing approvals. We do not know whether any of our preclinical studies or clinical trials will begin as planned, need to be restructured or be completed on schedule, if at all.

Further, we, the FDA or an IRB, may suspend our clinical trials at any time if it appears that we or our collaborators are failing to conduct a trial in accordance with regulatory requirements, including the FDA's current Good Clinical Practice, or GCP, regulations, that we are exposing participants to unacceptable health risks, or if the FDA finds deficiencies in our IND applications or the conduct of these trials. Therefore, we cannot predict with any certainty the schedule for commencement and completion of future clinical trials. If we experience delays in the commencement or completion of our clinical trials, or if we terminate a clinical trial prior to completion, the commercial prospects of our drug candidates could be negatively impacted, and our ability to generate revenues from our drug candidates may be delayed.

***Negative public opinion and increased regulatory scrutiny of gene therapy may damage public perception of the safety of our gene therapy product candidates and adversely affect our ability to conduct our business or obtain regulatory approvals for our product candidates.***

Gene therapy remains a novel technology, with only two gene therapy products approved to date in the United States and only two gene therapy products approved to date in the EU. Public perception may be influenced by claims that gene therapy is unsafe, and gene therapy may not gain the acceptance of the public or the medical community. In particular, our success will depend upon physicians who specialize in the treatment of genetic diseases targeted by our product candidates prescribing treatments that involve the use of our product candidates in lieu of, or in addition to, existing treatments with which they are familiar and for which greater clinical data may be available. More restrictive government regulations or negative public opinion would have an adverse effect on our business, financial condition, results of operations and prospects and may delay or impair the development and commercialization of our product candidates or demand for any products we may develop. For example, earlier gene therapy trials led to several well-publicized adverse events, including cases of leukemia and death seen in trials using other vectors. Serious adverse events in our clinical trials, or other clinical trials involving gene therapy products or our competitors' products, even if not ultimately attributable to the relevant product candidates, and the resulting publicity, could result in increased government regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates.

In addition, our success will depend upon physicians who specialize in the treatment of DEB prescribing treatments that involve the use of KB103 in lieu of, or in addition to, other treatments with which they are more familiar and for which greater clinical data may be available. More restrictive government regulations or negative public opinion would have an adverse effect on our business, financial condition, results of operations and prospects and may delay or impair the development and commercialization of KB103 or demand for any product candidate we may develop. Serious adverse events in our clinical trials, or other clinical trials involving gene therapy products or our competitors' products, even if not ultimately attributable to the relevant product candidates, and the resulting publicity, could result in increased government regulation, unfavorable public perception, potential regulatory delays in the testing or approval of KB103, stricter labeling requirements for KB103 if approved and a decrease in demand for KB103.

***If the market opportunities for KB103 or our future product candidates are smaller than we believe they are, our product revenues may be adversely affected and our business may suffer.***

We are currently focusing our research and product development efforts on our KB103 treatment for DEB. Our understanding of both the number of people who have this disease, as well as the subset of people with this disease who have the potential to benefit from treatment with KB103, are based on estimates in published literature. These estimates may prove to be incorrect and new studies may reduce the estimated incidence or prevalence of this disease. The number of patients in the United States, the EU and elsewhere may turn out to be lower than expected or these patients may not be otherwise

amenable to treatment with KB103 or may become increasingly difficult to identify and access, all of which would adversely affect our business, financial condition, results of operations and prospects.

Further, there are several factors that could contribute to making the actual number of patients who receive KB103 less than the potentially addressable market. These include the lack of widespread availability of, and limited reimbursement for, new therapies in many underdeveloped markets. Further, the severity of the progression of a disease up to the time of treatment will likely diminish the therapeutic benefit conferred by a gene therapy due to irreversible cell damage. Lastly, certain patients' immune systems might prohibit the successful delivery of certain gene therapy products to the target tissue, thereby limiting the treatment outcomes.

***The commercial success of KB103 and any future 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 KB103. Even with the requisite approvals from the FDA in the United States, the EMA in the EU and other regulatory authorities internationally, the commercial success of KB103 will depend, in part, on the acceptance of physicians, patients and health care payors of gene therapy products in general, and KB103 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. If these products do not achieve an adequate level of acceptance, we may not generate significant product revenue and may not become profitable. The degree of market acceptance of gene therapy products and, in particular, KB103, if approved for commercial sale, will depend on several factors, including:

- the efficacy and safety of KB103 as demonstrated in clinical trials;
- the efficacy, potential and perceived advantages of KB103 over alternative treatments;
- the cost of KB103 relative to alternative treatments;
- the clinical indications for which KB103 is approved by the FDA or the European Commission;
- 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 the FDA, the EMA or other regulatory authorities, including any limitations or warnings contained in a product's approved labeling;
- relative convenience and ease of administration;
- the strength of marketing and distribution support;
- the timing of market introduction of competitive products;
- the availability of products and their ability to meet market demand;
- publicity concerning our product candidates or competing products and treatments;
- any restrictions on the use of our products together with other medications; and
- favorable third-party payor coverage and adequate reimbursement.

Even if a potential product displays a favorable efficacy and safety profile in preclinical studies and clinical trials, market acceptance of the product will not be fully known until after it is launched.

***Even if we obtain and maintain approval for our product candidates from the FDA, we may never obtain approval for them outside of the United States, which would limit our market opportunities and adversely affect our business.***

Approval of a product candidate in the United States by the FDA does not ensure approval of such product candidate by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA. Sales of KB103 or other future product candidates outside of the United States will be subject to foreign regulatory requirements governing clinical trials and marketing approval. Even if the FDA grants marketing approval for a product candidate, comparable regulatory authorities of foreign countries also must approve the manufacturing and marketing of the product candidate in those countries. Approval

procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and more onerous than, those in the United States, including additional preclinical studies or clinical trials. In many countries outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that country. In some cases, the price that we intend to charge for our product candidates, if approved, is also subject to approval. We intend to submit a marketing authorization application to the EMA for approval of KB103 in the EU, but obtaining such approval from the European Commission following the opinion of the EMA is a lengthy and expensive process. Even if a product candidate is approved, the FDA or the European Commission, as the case may be, may limit the indications for which the product may be marketed, require extensive warnings on the product labeling or require expensive and time-consuming additional clinical trials or reporting as conditions of approval. Regulatory authorities in countries outside of the United States and the EU also have requirements for approval of product candidates with which we must comply prior to marketing in those countries. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our product candidates in certain countries.

Further, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. Also, regulatory approval for any of our product candidates may be withdrawn. If we fail to comply with the regulatory requirements, our target market will be reduced and our ability to realize the full market potential of KB103 or our future product candidates will be harmed and our business, financial condition, results of operations and prospects will be adversely affected.

***We have a limited number of employees and limited corporate infrastructure, and may experience difficulties in managing growth.***

We are a small company with a limited number of employees and corporate infrastructure. For example, we currently do not have a full-time chief financial officer or principal accounting officer in-house, and rely on professional service providers for these functions. We expect to experience a period of significant expansion in headcount, facilities, infrastructure and overhead as we mature and to meet our new reporting requirements under the Exchange Act. Future growth will impose significant added capital requirements, as well as added responsibilities on members of management, including the need to identify, recruit, maintain and integrate new personnel. Our future financial performance and our ability to compete effectively will depend, in part, on our ability to manage any future growth effectively.

***Even if we obtain regulatory approval for a product candidate, our product candidates will remain subject to regulatory oversight.***

Even if we obtain any regulatory approval for KB103, our lead product candidate, it will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping and submission of safety and other post-market information. Any regulatory approvals that we receive for KB103 may also be subject to a REMS, limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the quality, safety and efficacy of the product. For example, the holder of an approved BLA is obligated to monitor and report adverse events and any failure of a product to meet the specifications in the BLA. FDA guidance advises that patients treated with some types of gene therapy undergo follow-up observations for potential adverse events for as long as 15 years, and our current and each of our proposed clinical trials for KB103 includes a 15 year long-term follow-up phase, limited to confirmed data collection from annual visits with standard care physicians. The holder of an approved BLA also must submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. Advertising and promotional materials must comply with FDA rules and are subject to FDA review, in addition to other potentially applicable federal and state laws.

In addition, product manufacturers and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP requirements and adherence to commitments made in the BLA or foreign marketing application. If we, or a regulatory authority, discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured or disagrees with the promotion, marketing or labeling of that product, a regulatory authority may impose restrictions relative to that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.

If we fail to comply with applicable regulatory requirements following approval of KB103 or any future product candidate, a regulatory authority may:

- issue a warning letter asserting that we are in violation of the law;
- seek an injunction or impose administrative, civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve a pending BLA or comparable foreign marketing application (or any supplements thereto) submitted by us or our strategic partners;
- restrict the marketing or manufacturing of the product;
- seize or detain the product or otherwise require the withdrawal of the product from the market;
- refuse to permit the import or export of product candidates; or
- refuse to allow us to enter into supply contracts, including government contracts.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize KB103 and adversely affect our business, financial condition, results of operations and prospects.

In addition, the FDA's policies, and those of equivalent foreign regulatory agencies, may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of KB103. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would materially and adversely affect our business, financial condition, results of operations and prospects.

***While we have obtained orphan drug designation for KB103, it may not effectively protect us from competition and we may be unable to obtain orphan drug exclusivity for our future product candidates. If our competitors are able to obtain orphan drug exclusivity for products that constitute the same drug and treat the same indications as our product candidates before us, we may not be able to have competing products approved by the applicable regulatory authority for a significant period of time.***

On November 2, 2017, the FDA granted orphan drug designation to our lead product candidate, KB103, for the treatment of DEB and we may seek orphan drug designation from the FDA for our future product candidates. Regulatory authorities in some jurisdictions, including the United States and the EU, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act of 1983, the FDA may designate a product candidate as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as having a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the EU, the EMA's Committee for Orphan Medicinal Products grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than 5 in 10,000 persons in the EU. Additionally, orphan designation is granted for products intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the EU would be sufficient to justify the necessary investment in developing the drug or biologic product.

Generally, if a product candidate with an orphan drug designation receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the European Commission from approving another marketing application for a product that constitutes the same drug treating the same indication for that marketing exclusivity period, except in limited circumstances. If another sponsor receives such approval before we do (regardless of our orphan drug designation), we will be precluded from receiving marketing approval for our product for the applicable exclusivity period. The applicable period is seven years in the United States and 10 years in the EU. The exclusivity period in the EU can be reduced to nine years if a product no longer meets the criteria for orphan drug designation or if the product is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be revoked if any regulatory agency determines that the request for designation was materially

defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition.

Even though we have obtained orphan drug exclusivity for KB103, that exclusivity may not effectively protect the product candidate from competition because different drugs can be approved for the same condition. In the United States, even after an orphan drug is approved, the FDA may subsequently approve another drug for the same condition if the FDA concludes that the latter drug is not the same drug or is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. In the EU, marketing authorization may be granted to a similar medicinal product for the same orphan indication if:

- the second applicant can establish in its application that its medicinal product, although similar to the orphan medicinal product already authorized, is safer, more effective or otherwise clinically superior;
- the holder of the marketing authorization for the original orphan medicinal product consents to a second orphan medicinal product application; or
- the holder of the marketing authorization for the original orphan medicinal product cannot supply sufficient quantities of orphan medicinal product.

***Breakthrough therapy designation, RMAT designation, Fast Track designation or Rare Pediatric Disease designation by the FDA, even if granted for any of our product candidates, may not lead to a faster development, regulatory review or approval process, and it does not increase the likelihood that any of our product candidates will receive marketing approval in the United States.***

We may, in the future, apply for breakthrough therapy designation or Fast Track designation in the United States for our product candidates. We plan to apply for Fast Track designation and RMAT designation in the first quarter of 2018 and breakthrough therapy designation in the second quarter of 2018 for KB103. We have been granted rare pediatric disease designation for KB103. Each of these designations is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for breakthrough therapy designation, Fast Track designation or rare pediatric disease designation, the FDA may disagree. In any event, the receipt of any of these designations for a product candidate may not result in a faster development process, review or approval compared to products considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA.

A breakthrough therapy product candidate is defined as a product candidate that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that such product candidate may demonstrate substantial improvement on one or more clinically significant endpoints over existing therapies. Drugs designated as breakthrough therapies by the FDA are eligible for accelerated approval and increased interaction and communication with the FDA designed to expedite the development and review process. If a drug, or biologic in our case, is intended for the treatment of a serious or life-threatening condition and the biologic demonstrates the potential to address unmet medical needs for this condition, the biologic sponsor may apply for FDA Fast Track designation. Even if we do receive Fast Track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. In addition, the FDA may withdraw Fast Track designation if it believes that the designation is no longer supported by data from our clinical development program. Many biologics that have received Fast Track designation have failed to obtain approval. A sponsor who receives an approval for a drug or biologic for a “rare pediatric disease” may qualify for a voucher that can be redeemed to receive a priority review of a subsequent marketing application for a different product. In December 2016, we received the designation of “rare pediatric disease” for KB103 and conditional designation of our marketing application as a “rare pediatric disease product application,” which, if granted, could qualify us to receive a Rare Pediatric Priority Review Voucher. According to the FDA website, a Rare Pediatric Priority Review Voucher can be redeemed to receive a priority review of a subsequent marketing application for a different product.

There is no assurance we will receive breakthrough therapy or Fast Track designations for any of our product candidates and the receipt of any of these designations for a product candidate may not result in a faster development process, review or approval and does not assure ultimate approval by the FDA. Further, even though we have received rare pediatric disease designation for KB103, we may not experience a faster development process, review or approval for a subsequent marketing application.



***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.

***If we are not successful in discovering, developing and commercializing additional product candidates, our ability to expand our business and achieve our strategic objectives would be impaired.***

Although a substantial amount of our efforts focuses on the potential approval of KB103, a key component our strategy is to discover, develop and potentially commercialize a portfolio of product candidates to treat orphan diseases and ultimately, non-orphan diseases. Identifying new product candidates requires substantial technical, financial and human resources, whether or not any product candidates are ultimately identified. Even if we identify product candidates that initially show promise, we may fail to successfully develop and commercialize such product candidates for many reasons, including the following:

- the research methodology used may not be successful in identifying potential product candidates;
- competitors may develop alternatives that render our product candidates obsolete;
- product candidates we develop may nevertheless be covered by third parties' patents or other exclusive rights;
- a product candidate may, on further study, be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; and
- a product candidate may not be accepted as safe and effective by patients, the medical community or third-party payors.

If we are unsuccessful in identifying and developing additional product candidates, our potential for growth may be impaired.

***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 adversely affect our financial condition and our ability to successfully market or commercialize KB103.***

At this time, there are no known FDA or EMA approved treatments for DEB, or any approved gene therapy treatment for dermatological indications, generally. However, we are aware of several companies and institutions that are currently developing alternative autologous or palliative gene therapy approaches for DEB. Many of our potential competitors, alone or with their strategic partners, have substantially greater financial, technical and other resources, such as larger research and development, clinical, marketing and manufacturing organizations. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of competitors. Our commercial opportunity could be reduced or eliminated if 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 product candidate that we may develop. Competitors also may obtain FDA or other regulatory approval for their products more rapidly or earlier 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 KB103 uneconomical or obsolete, and we may not be successful in marketing KB103 against competitors.

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

***Delays in obtaining regulatory approvals of the process and facilities needed to manufacture KB103 or disruptions in our manufacturing process may delay or disrupt our product development and commercialization efforts.***

Before we can begin to commercially manufacture KB103, whether in a third-party facility or in our own facility, once established, we must obtain regulatory approval from FDA for our manufacturing process and facility. A manufacturing authorization must also be obtained from the appropriate EU regulatory authorities. The timeframe required for us to obtain such approvals is uncertain. In addition, we must pass a pre-approval inspection of our manufacturing facility by the FDA before KB103 can obtain marketing approval. In order to obtain approval, we will need to ensure that all of our processes, methods and equipment are compliant with cGMP, and perform extensive audits of vendors, contract laboratories and suppliers. If any of our vendors, contract laboratories or suppliers is found to be out of compliance with cGMP, we may experience delays or disruptions in manufacturing while we work with these third parties to remedy the violation or while we work to identify suitable replacement vendors. The cGMP requirements govern quality control of the manufacturing process and documentation policies and procedures. In complying with cGMP, we will be obligated to expend time, money and effort in production, record keeping and quality control to assure that the product meets applicable specifications and other requirements. If we fail to comply with these requirements, we would be subject to possible regulatory action and may not be permitted to sell any product candidate that we may develop.

In addition, the manufacturing process used to produce KB103 is complex, novel and has not been validated for commercial use. In order to produce sufficient quantities of KB103 for future clinical trials and initial U.S. commercial demand, we will need to increase the scale of our manufacturing process. The production of KB103 requires processing steps that are more complex than those required for most chemical pharmaceuticals. Moreover, unlike chemical pharmaceuticals, the physical and chemical properties of a biologic such as ours generally cannot be fully characterized. As a result, assays of the finished product may not be sufficient to ensure that the product will perform in the intended manner. Accordingly, we employ multiple steps to control our manufacturing process to assure that the process works and that KB103 is made strictly and consistently in compliance with the process. Problems with the manufacturing process, even minor deviations from the normal process, could result in product defects or manufacturing failures that result in lot failures, product recalls, product liability claims or insufficient inventory. We may encounter problems achieving adequate quantities and quality of clinical-grade materials that meet FDA, EMA or other applicable standards or specifications with consistent and acceptable production yields and costs.

***Although we intend to establish our own KB103 manufacturing facility, we expect to utilize third parties to conduct our product manufacturing for the near future. Therefore, we are subject to the risk that these third parties may not perform satisfactorily.***

Until such time as we establish our manufacturing facility that has been properly validated to comply with FDA cGMP requirements, we will not be able to independently manufacture material for our planned preclinical and clinical programs. Even following our establishment of a validated cGMP manufacturing facility, we intend to maintain third-party manufacturing capabilities in order to provide multiple sources of supply. In the event that the establishment of our own manufacturing facility is delayed and if these third-party manufacturers do not successfully carry out their contractual duties, meet expected deadlines or manufacture KB103 in accordance with regulatory requirements or if there are disagreements between us and these third-party manufacturers, we will not be able to complete, or may be delayed in completing, the preclinical studies required to support future IND submissions and the clinical trials required for approval of KB103. In such instances, we may need to locate an appropriate replacement third-party relationship, which may not be readily available or on acceptable terms, which would cause additional delay or increased expense prior to the approval of KB103 and would thereby have a material adverse effect on our business, financial condition, results of operations and prospects.

Building our own manufacturing facility will require additional investment, will be time consuming and may be subject to delays, including because of shortage of labor or compliance with regulatory requirements. In addition, building a manufacturing facility may cost more than we currently anticipate. Delays or problems in the build out of our manufacturing facility may adversely impact our ability to obtain regulatory approval and provide supply for the development and commercialization of KB103 as well as our financial condition.

If we or our third-party manufacturer fails to comply with applicable cGMP regulations, the FDA and foreign regulatory authorities can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new product candidate or suspension or revocation of a pre-existing approval. Such an occurrence may cause our business, financial condition, results of operations and prospects to be materially harmed.

***Any contamination in our manufacturing process, shortages of raw materials or failure of any of our key suppliers to deliver necessary components could result in delays in our clinical development or marketing schedules.***

Given the nature of biologics manufacturing, there is a risk of contamination. Any contamination could materially adversely affect our ability to produce KB103 on schedule and could, therefore, harm our results of operations and cause reputational damage.

Some of the raw materials required in our manufacturing process are derived from biologic sources. Such raw materials are difficult to procure and may be subject to contamination or recall. A material shortage, contamination, recall or restriction on the use of biologically derived substances in the manufacture of KB103 could adversely impact or disrupt the commercial manufacturing or the production of clinical material, which could materially and adversely affect our development timelines and our business, financial condition, results of operations and prospects.

***Our future success depends on our ability to retain key employees and scientific advisors and to attract, retain and motivate qualified personnel.***

We are highly dependent on members of our executive team, the loss of whose services may adversely impact the achievement of our objectives. Our employees and scientific advisors are at-will employees and consultants, and the loss of one or more of them might impede the achievement of our research, development and commercialization objectives.

Recruiting and retaining other qualified employees and scientific advisors for our business, including scientific and technical personnel, also will be critical to our success. There currently is a shortage of skilled individuals with substantial gene therapy experience, which is likely to continue. As a result, competition for skilled personnel, including in gene therapy research and vector manufacturing, is intense and the turnover rate can be high. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies and academic institutions for individuals with similar skill sets. In addition, failure to succeed in preclinical or clinical trials or applications for marketing approval may make it more challenging to recruit and retain qualified personnel. The inability to recruit, or loss of services of certain executives, key employees or advisors, may impede the progress of our research, development and commercialization objectives and have a material adverse effect on our business, financial condition, results of operations and prospects.

***Our employees, principal investigators and advisors 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, principal investigators and advisors. Misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in the EU and other jurisdictions, provide accurate information to the FDA, the European Commission and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Such misconduct also could involve the improper use of information obtained in the course of clinical trials or interactions with the FDA or other regulatory authorities, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from government investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, financial condition, results of operations and prospects, including the imposition of significant fines or other sanctions.

In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA. The FDA may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the trial. The FDA may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA and may ultimately lead to the denial of marketing approval of our current and future drug candidates.

***Healthcare legislative reform measures may have a material adverse effect on our business and results of operations.***

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities, and affect our ability to profitably sell any product candidates for which we obtain marketing approval.

For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or the PPACA, was passed, which substantially changes the way healthcare is financed by both the government and private insurers, and significantly impacts the U.S. pharmaceutical industry. The PPACA, among other things: (i) addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; (ii) increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations; (iii) establishes annual fees and taxes on manufacturers of certain branded prescription drugs; (iv) expands the availability of lower pricing under the 340B drug pricing program by adding new entities to the program; and (v) establishes a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the PPACA. As a result, there have been delays in the implementation of, and action taken to repeal or replace, certain aspects of the PPACA. In January 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the PPACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. Further, in January 2017, Congress adopted a budget resolution for fiscal year 2017, or the Budget Resolution, that authorizes the implementation of legislation that would repeal portions of the PPACA. Following the passage of the Budget Resolution, in March 2017, the U.S. House of Representatives introduced legislation known as the American Health Care Act, which, if enacted, would amend or repeal significant portions of the PPACA. Among other changes, the American Health Care Act would repeal the annual fee on certain brand prescription drugs and biologics imposed on manufacturers and importers, eliminate penalties on individuals and employers that fail to maintain or provide minimum essential coverage, and create refundable tax credits to assist individuals in buying health insurance. The American Health Care Act would also make significant changes to Medicaid by, among other things, making Medicaid expansion optional for states, repealing the requirement that state Medicaid plans provide the same essential health benefits that are required by plans available on the exchanges, modifying federal funding, including implementing a per capita cap on federal payments to states, and changing certain eligibility requirements. While it is uncertain when or if the provisions in the American Health Care Act will become law, or the extent to which any changes may impact our business, it is clear that concrete steps are being taken to repeal and replace certain aspects of the PPACA.

Additionally, in the United States, the Biologics Price Competition and Innovation Act of 2009 created an abbreviated approval pathway for biologic products that are demonstrated to be "highly similar" or "biosimilar or interchangeable" with an FDA-approved biologic product. This new pathway could allow competitors to reference data from biologic products already approved after 12 years from the time of approval. This could expose us to potential competition by lower-cost biosimilars even if we commercialize a product candidate faster than our competitors. Moreover, the creation of this abbreviated approval pathway does not preclude or delay a third party from pursuing approval of a competitive product candidate via the traditional approval pathway based on their own clinical trial data. Other legislative changes have been proposed and adopted in the United States since the PPACA was enacted. For example, in August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least \$1.2 trillion for the years 2012 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2025 unless additional Congressional action is taken. In January 2013, the American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to certain providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Additionally, there have been several recent U.S. Congressional inquiries and proposed bills designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs.

Additional changes that may affect our business include those governing enrollment in federal healthcare programs, reimbursement changes, fraud and abuse enforcement, and expansion of new programs, such as Medicare payment for performance initiatives.

We expect that these initiatives, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms could result in reduced demand for KB103 or additional pricing pressures, and may prevent us from being able to generate revenue, attain profitability, or commercialize our products.

***We may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws and health information privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.***

If we obtain FDA approval for KB103 and begin commercializing it in the United States, our operations will be directly, or indirectly through our prescribers, customers and purchasers, subject to various federal and state fraud and abuse laws and regulations, including, without limitation, the federal Health Care Program Anti-Kickback Statute, the federal civil and criminal laws and Physician Payments Sunshine Act and regulations. These laws will impact, among other things, our proposed sales, marketing and educational programs. In addition, we may be subject to patient privacy laws by both the federal government and the states in which we conduct our business. The laws that will affect our operations include, but are not limited to:

- the federal Health Care Program Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, in return for the purchase, recommendation, leasing or furnishing of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand, and prescribers, purchasers and formulary managers on the other. The PPACA amended the intent requirement of the federal Anti-Kickback Statute. A person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it;
- federal civil and criminal false claims laws and civil monetary penalty laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid or other government payors that are false or fraudulent. The PPACA provides and recent government cases against pharmaceutical and medical device manufacturers support the view that Federal Anti-Kickback Statute violations and certain marketing practices, including off-label promotion, may implicate the False Claims Act;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit a person from knowingly and willfully executing a scheme or from making false or fraudulent statements to defraud any healthcare benefit program, regardless of the payor (e.g., public or private);
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, and as amended again by the final HIPAA omnibus rule, Modifications to the HIPAA Privacy, Security, Enforcement, and Breach
- Notification Rules Under HITECH and the Genetic Information Nondiscrimination Act; Other Modifications to HIPAA, published in January 2013, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization by entities subject to the rule, such as health plans, health care clearinghouses and health care providers;
- federal transparency laws, including the federal Physician Payment Sunshine Act, that require certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services, or CMS, information related to: (i) payments or other "transfers of value" made to physicians and teaching hospitals and (ii) ownership and investment interests held by physicians and their immediate family members;
- state and foreign law equivalents of each of the above federal laws, state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures and state laws governing the privacy and security of health information in certain

circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts in certain circumstances, such as specific disease states; and

- state and foreign laws that 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.

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 ability to operate our business and our results of operations.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations.

The risk of our being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. The shifting compliance environment and the need to build and maintain a robust and expandable systems to comply with multiple jurisdictions with different compliance and/or reporting requirements increases the possibility that a healthcare company may run afoul of one or more of the requirements.

***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 have a material adverse effect on the success of our business.***

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the generation, handling, use, storage, treatment, manufacture, transportation and disposal of, and exposure to, hazardous materials and wastes, as well as laws and regulations relating to occupational health and safety. Our operations involve the use of hazardous and flammable materials, including chemicals and biologic materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended.

Although we maintain workers' compensation insurance for certain costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for toxic tort claims that may be asserted against us in connection with our storage or disposal of biologic, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations, which have tended to become more stringent over time. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions or liabilities, which could materially adversely affect our business, financial condition, results of operations and prospects.

***Our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.***

Natural disasters could severely disrupt our operations or the operations of manufacturing facilities and have a material adverse effect on our business, financial condition, results of operations and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as manufacturing facilities, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and may not prove adequate in the event of a serious disaster or similar event. Our third-party manufacturing facility, as well as substantially all of our current supply of KB103 is located in Pittsburgh, Pennsylvania, and we do not have any existing back-up facilities in place or plans for such back-up facilities. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

**RISKS RELATED TO OUR INTELLECTUAL PROPERTY**

***If we are unable to obtain and maintain patent protection for our lead product candidate, KB103, any future product candidates we may develop and our STAR-D platform, 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 our current product candidate, any future product candidates we may develop and our technology may be adversely affected.***

We currently have one issued patent in the United States. Our success depends, in large part, on our ability to obtain and maintain patent protection in the United States and other countries with respect to both KB103 and future innovations related to our STAR-D platform. 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 and issued patents at a reasonable cost or in a timely manner. We are actively prosecuting a patent application in front of the U.S. Patent and Trademark Office, or USPTO, directed, in part, to pharmaceutical formulations and methods of treating dystrophic epidermolysis bullosa using our KB103 product. A corresponding international application has also been filed in accordance with the Paris Cooperation treaty. In addition, we are seeking patent protection for key aspects of our viral platform technologies through a second patent application on file at the USPTO. We do not, however, yet know the outcome of these patent applications.

Even if we are granted the patents we are currently pursuing, they may not issue in a form that will provide us with the full scope of protection we desire, they may not prevent competitors or other third parties from competing with us, and/or they may not otherwise provide us with a competitive advantage. 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. Even assuming patents issue from our pending and future patent applications, changes in either the patent laws or interpretation of the patent laws in the United States and foreign jurisdictions may diminish the value of our patents, or narrow their scope of protection.

In addition, we may not be aware of all third-party intellectual property rights potentially relating to technologies similar to KB103. Publications of discoveries in the scientific literature often lag behind their 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, it is impossible to be certain that we were the first to develop the specific technologies as claimed in any owned patents or pending patent applications, or that we were the first to file for patent protection of such inventions.

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

Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and intellectual property rights in some countries outside the United States may differ in scope from those eventually granted in the United States. Thus, in some cases, we will not have the opportunity to obtain patent protection for certain technologies in some jurisdictions outside the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, even in jurisdictions where we do pursue patent protection. 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.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biotechnology products. Such challenges in enforcing rights in these countries could make it difficult for us to stop the infringement of our patents, if pursued and obtained, or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our future patent rights in foreign jurisdictions could result in substantial costs and may 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 any future patent applications, including continuation and divisional 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 any intellectual property rights around the world stemming from intellectual property that we develop or license may be inadequate to obtain a significant commercial advantage in these foreign jurisdictions.

***Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.***

Our commercial success depends upon our ability (and the ability of any potential future collaborators) to develop, manufacture, market and sell our product candidates, and to use our proprietary technologies without infringing the rights and intellectual property of others. Many companies and institutions have filed, and continue to file, patent applications related to various aspects of gene therapy. Some of these patent applications have already been allowed or issued, while others may issue in the future. Since the areas of gene delivery and gene therapeutics are competitive and of strong interest to pharmaceutical and biotechnology companies, there will likely be additional patent applications filed, and additional patents granted, in the future, as well as additional gene therapy research and development programs. Furthermore, because patent applications can take many years to issue, may be confidential for 18 months or more after filing, and can be revised before issuance, there may be applications now pending which may later result in issued patents that a third party asserts are infringed by the manufacture, use, sale, or importation of our products. The biotechnology and pharmaceutical industries are characterized by extensive and complex litigation regarding patents and other intellectual property rights. We may in the future become party to, or be threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to KB103 or related technologies, including, for example, interference proceedings, post grant review challenges, and inter partes review before the USPTO. Our competitors or other third parties may assert infringement claims against us, alleging that our therapeutics, manufacturing methods, formulations or administration methods are covered by their patents. Moreover, we may face patent infringement claims from non-practicing entities that have no relevant product revenue, and against whom our licensed patent portfolio may therefore have no deterrent effect.

Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit. There is a risk that third parties may choose to engage in litigation with us to enforce or to otherwise assert their patents or other intellectual property rights against us. Even if we believe such claims are without merit, 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 KB103. 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. In such a hypothetical situation, there is no assurance that a court of competent jurisdiction would find that KB103 or our other product candidates or technologies do not infringe a third-party patent.

Patent and other types of intellectual property litigation can involve complex factual and legal questions, and their outcomes are uncertain. If we are found, or believe there is a risk that we may be found, to infringe a third party's valid and enforceable intellectual property rights, we could be required (or may choose) to obtain a license from such a third party to continue developing, manufacturing and marketing our technologies. However, we may not be able to obtain any required license on commercially reasonable terms, if 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 further, it could require us to make substantial licensing and royalty payments. We could be forced, including by court order, to cease developing, manufacturing and commercializing the infringing technologies, including KB103. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right. A finding of infringement could prevent us from manufacturing and commercializing KB103, or force us to cease some or all of our business operations. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact 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. Competitors may infringe our patents, should such patents issue, or we may be required to defend against claims of infringement. Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our scientific and management personnel from their normal responsibilities. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions, or other proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, or distribution activities.

We may not have sufficient financial or other resources to 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, 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.

***We may be subject to claims asserting that our employees 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.***

Certain of our employees or advisors are currently, or were previously, employed at universities or other biotechnology or pharmaceutical companies, including potential competitors. Although we try to ensure that our employees 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 these individuals, or we, 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. Moreover, any such litigation, or the threat thereof, may adversely affect our ability to hire new employees or contract with independent contractors. A loss of key personnel or their work product could hamper or prevent our ability to commercialize our technologies, which would have an adverse effect on our business, results of operations, and financial condition. 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 of intellectual property to execute agreements assigning such intellectual property rights to us, unforeseen complications may arise when fully and adequately executing such an agreement with each party who, in fact, conceives of intellectual property that we regard as our own. Examples of such complications may include, for example, when we obtain agreements assigning intellectual property to us, the assignment of intellectual property rights may not be self-executing or the assignment agreements may be breached. Such complications may lead to us being 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. Moreover, individuals executing agreements with us may have preexisting or competing obligations to a third party, such as an academic institution, and thus an agreement with us may be insufficient in fully perfecting ownership of inventions developed by that individual. Disputes about the ownership of intellectual property that we may own may have a material adverse effect on our business.

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

Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. For example, on September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act included several significant changes to U.S. patent law, including provisions that affected the way patent applications are prosecuted, and altered strategies regarding patent litigation. These provisions also switched the United States from a "first-to-invent" system to a "first-to-file" system, allowed third-party submission of prior art to the USPTO during patent prosecution, and set forth additional procedures to attack the validity of a patent through various post grant proceedings administered by the USPTO. As patent reform legislation can

inject serious uncertainty into the patent prosecution and litigation processes, it is not clear what impact future patent reform legislation will have on the operation of our business. However, such future legislation, and its implementation, could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of any issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

Moreover, the patent positions of companies engaged in the development and commercialization of biologics and pharmaceuticals are particularly uncertain given the ever evolving and constantly shifting nature of precedential patent cases decided by both the U.S. Court of Appeals for the Federal Circuit and the U.S. Supreme Court. For instance, two cases involving diagnostic method claims and “gene patents” have recently been decided by the Supreme Court. On March 20, 2012, the Supreme Court issued a decision in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, or *Prometheus*, a case involving patent claims directed to a process of measuring a metabolic product in a patient to optimize a drug dosage for the patient. According to the Supreme Court, the addition of well-understood, routine or conventional activity such as “administering” or “determining” steps was not enough to transform an otherwise patent-ineligible natural phenomenon into patent-eligible subject matter. On July 3, 2012, the USPTO issued a guidance memo to patent examiners indicating that process claims directed to a law of nature, a natural phenomenon or a naturally occurring relation or correlation that do not include additional elements or steps that integrate the natural principle into the claimed invention such that the natural principle is practically applied (and thus, the claim amounts to significantly more than the natural principle itself) should be rejected as directed to patent-ineligible subject matter. On June 13, 2013, the Supreme Court issued its decision in *Association for Molecular Pathology v. Myriad Genetics, Inc.*, or *Myriad*, a case involving patent claims held by Myriad Genetics, Inc. relating to the breast cancer susceptibility genes BRCA1 and BRCA2. In its decision, the US Supreme Court held that an isolated segment of naturally occurring DNA, such as the DNA constituting the BRCA1 or BRCA2 genes, is not patent eligible subject matter; however, complementary DNA may be patent eligible.

Although the Supreme Court held in *Myriad* that isolated segments of naturally occurring DNA are not patent-eligible subject matter, certain third parties could allege that potential activities that we undertake in the future may infringe other gene-related patent claims, and we may deem it necessary to defend ourselves against these claims by asserting non-infringement and/or invalidity positions, or paying to obtain a license to these claims. In any situation involving third-party intellectual property rights, such as those directed to gene-related patent claims, if we are unsuccessful in defending against claims of patent infringement (e.g., by asserting invalidity of the infringed patent in view of the Supreme Court’s *Myriad* decision), we could be forced to pay damages or be subjected to an injunction that would prevent us from utilizing the patented subject matter. Such outcomes could harm our business, financial condition, results of operations or prospects.

Moreover, we cannot assure you that our efforts to seek patent protection for our technology and product candidates will not be negatively impacted by the decisions described above, rulings in other cases, or changes in guidance or procedures issued by the USPTO. These decisions, the guidance issued by the USPTO (or changes thereto), and rulings in other cases could have a material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property rights in the future.

***If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.***

We are currently in the process of registering our trademarks and trade names. Once registered, our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely impact our financial condition or results of operations.

***Intellectual property rights and regulatory exclusivity 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 our product candidates but that are not covered by the claims of the patents that we may own or license in the future;
- we, or any future license partners or collaborators, might not have been the first to develop the specific technologies covered by the issued patents or pending patent applications that we may own or license in the future;
- we, or any future license partners or collaborators, might not have been the first to file patent applications covering certain aspects of the concerned technologies;
- others may independently develop similar or alternative technologies, or duplicate any of our technologies, potentially without falling within the scope of our future issued claims, thus not infringing our intellectual property rights;
- others may circumvent our regulatory exclusivities, such as by pursuing approval of a competitive product candidate via the traditional approval pathway based on their own clinical data, rather than relying on the abbreviated pathway provided for biosimilar applicants;
- it is possible that our filed or future patent applications will not lead to issued patents;
- issued patents to which we hold rights in the future may be held invalid or unenforceable, including as a result of legal challenges by our competitors;
- others may have access to any future intellectual property rights licensed to us on a non-exclusive basis;
- our competitors might conduct research and development activities in countries where we do not have or pursue 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 or other intellectual property rights of others may have an adverse effect on our business; and
- we may choose not to file a patent for 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 significantly harm our business, financial condition, results of operations and prospects.

**RISKS RELATED TO OWNERSHIP OF OUR COMMON STOCK**

***Our Chief Executive Officer and Chairman of the Board of Directors and our founder, Chief Operating Officer and director will maintain the ability to substantially influence all matters submitted to stockholders for approval.***

As of December 31, 2017, Krish S. Krishnan and Suma M. Krishnan, our Chief Executive Officer and Chairman of the Board and our founder, Chief Operating Officer and director, respectively, in the aggregate, beneficially owned shares representing approximately 38.6% of our capital stock. As a result, they will be able to substantially influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons would substantially influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of voting power could delay or prevent an acquisition of our company on terms that other stockholders may desire or result in management of our company that our public stockholders disagree with.

***A significant portion of our total outstanding shares are restricted from immediate resale following our initial public offering or IPO but may be sold into the market in the near future, which could cause the market price of our common stock to drop significantly, even if our business is performing well.***

Sales of a substantial number of shares of our common stock in the public market could occur at any time, subject to certain restrictions described below. These sales, or the perception in the market that holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. As of December 31, 2017, we had outstanding 10,307,247 shares of common stock. However, the resale of an aggregate of 5,883,247 shares will be restricted as a result of lock-up agreements executed in connection with our IPO. We have registered all shares of common stock that we may

issue under our equity compensation plans on a Registration Statement on Form S-8. These shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates and the lock-up agreements.

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

The trading market for our common stock will rely, in part, on the research and reports that industry or financial analysts publish about us or our business. If securities analysts do not commence coverage of us, the trading price of our stock could decrease. Additionally, if one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

***The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for holders of our common stock.***

Our stock price is likely to be volatile. The stock market in general and the market for biopharmaceutical or pharmaceutical companies in particular, has experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your common stock at or above the price that you paid for it. The market price of our common stock may be influenced by many factors, including:

- our ability to successfully proceed to and conduct clinical trials;
- results of clinical trials of our product candidates or those of our competitors;
- the success of competitive products or technologies;
- commencement or termination of collaborations;
- 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 product candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- our inability to obtain or delays in obtaining adequate product supply for any approved product or inability to do so at acceptable prices;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- significant lawsuits, including patent or stockholder litigation;
- variations in our financial results or those of companies that are perceived to be similar to us;
- 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.

***We have broad discretion in the use of our cash, including the net proceeds from our IPO, and may not use them effectively.***

Our management will have broad discretion in the application of our cash, including the net proceeds from our IPO, and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of KB103, KB105 and any other product candidates we may develop. Pending their use, we may invest our cash, including the net proceeds from our IPO, in a manner that does not produce income or that loses value.

***Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our technologies or KB103.***

We may seek additional capital through a combination of public and private equity offerings, debt financings, collaborations and licensing arrangements. To the extent that we raise additional capital through the sale of equity or debt securities, your ownership interest will be diluted and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. The incurrence of indebtedness would result in increased fixed payment obligations and could involve restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. If we raise additional funds through strategic partnerships and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or KB103, or grant licenses on terms unfavorable to us.

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

We are an “emerging growth company,” as defined in the JOBS Act, and we may take advantage of certain exemptions and relief from various reporting requirements that are applicable to other public companies that are not “emerging growth companies.” In particular, while we are an “emerging growth company: (i) we will not be required to comply with the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act; (ii) we will be exempt from any rules that may be adopted by the Public Company Accounting Oversight Board requiring mandatory audit firm rotations or a supplement to the auditor’s report on financial statements; (iii) we will be subject to reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements; and (iv) we will not be required to hold nonbinding advisory votes on executive compensation or stockholder approval of any golden parachute payments not previously approved. Investors may find our common stock less attractive if we rely on the exemptions and relief granted by the JOBS Act. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may decline or become more volatile.

In addition, the JOBS Act provides that an emerging growth company may 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 will incur increased costs as a result of operating as a smaller reporting public company, and our management will be required to devote substantial time to new compliance initiatives.***

As a smaller reporting 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. In addition, the Sarbanes-Oxley Act and rules subsequently implemented by the SEC and NASDAQ have imposed 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 to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance.

Pursuant to Section 404, we will be 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 Section 404 within the prescribed period, we will be 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 and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

***Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.***

Provisions in our corporate charter and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions also could limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that not all members of the board are elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from the board;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a stockholder rights plan, or so-called “poison pill,” that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 80% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

***Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain.***

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

We currently are not a party to any material litigation or other material legal proceedings. We may, from time to time, be subject to legal proceedings and claims arising from the normal course of business activities.

***Cyber-security incidents, including data security breaches or computer viruses, could harm our business by disrupting our delivery of services, damaging our reputation or exposing us to liability.***

We receive, process, store, and transmit, often electronically, confidential data of others. Unauthorized access to our computer systems or stored data could result in the theft or improper disclosure of confidential information, the deletion or modification of records, or could cause interruptions in our operations. These cyber-security risks increase when we transmit information from one location to another, including transmissions over the Internet or other electronic networks. Despite implemented security measures, our facilities, systems, and procedures, and those of our third-party service providers, may be vulnerable to security breaches, acts of vandalism, software viruses, misplaced or lost data, programming and/or human errors, or other similar events which may disrupt our delivery of services or expose the confidential information of our customers and others. Any security breach involving the misappropriation, loss or other unauthorized disclosure or use of confidential information of others, whether by us or a third party, could: (i) subject us to civil and criminal penalties; (ii) have a negative impact on our reputation; or (iii) expose us to liability to our customers, third parties or government authorities.

Any of these developments could have a material adverse effect on our business, financial condition, and results of operations.

***The Tax Cuts and Jobs Act could have material effects on the Company.***

The Tax Cuts and Jobs Act of 2017, or the Tax Act, which was signed into law on December 22, 2017, makes significant changes to the taxation of U.S. business entities. These changes include a permanent reduction to the federal corporate income tax rate and changes in the deductibility of interest on corporate debt obligations, among others. The Company is currently evaluating the Tax Act with its professional advisers; the full impact of the Tax Act on the Company in future periods cannot be predicted at this time and no assurances in that regard are made by the Company.

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

None.

**Item 2. Properties.**

We lease approximately 5,000 square feet of combined laboratory and office space in Pittsburgh, Pennsylvania that we use in our research and development efforts. We established the geographic locations of our research and development operations based on proximity to the relevant market expertise and access to available talent pools. We presently plan on extending our current lease, which ends in October 2018.

**Item 3. Legal Proceedings.**

We currently are not a party to any material litigation or other material legal proceedings. We may, from time to time, be subject to legal proceedings and claims arising in the normal course of business.

**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 has been listed on the Nasdaq Capital Market under the symbol "KRY5" since September 20, 2017. Prior to that time, there was no public market for our common stock. The following table sets forth for the indicated periods the high and low intra-day sales prices per share for our common stock on the Nasdaq Capital Market.

<u>Fiscal Quarter 2017</u>	<u>High</u>	<u>Low</u>
Third Quarter (from September 20, 2017)	\$ 11.31	\$ 9.42
Fourth Quarter	\$ 11.98	\$ 8.03

On February 28, 2018, there were 20 stockholders of record of our common stock. We are unable to estimate the total number of stockholders represented by these record holders, as many of our shares are held by brokers and other institutions on behalf of our stockholders. The closing price of our common stock was \$10.08 per share as reported on the Nasdaq Capital Market.

#### Dividend Policy

We have never declared or paid cash dividends on our capital stock. We currently intend to retain any future earnings for use in the operation of our business and do not intend to declare or pay any cash dividends in the foreseeable future. Any further determination to pay dividends on our capital stock will be at the discretion of our board of directors, subject to applicable laws, and will depend on our financial condition, results of operations, capital requirements, general business conditions and other factors that our board of directors considers relevant.

#### Purchases of Equity Securities by the Issuer or Affiliated Purchasers

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

#### 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.

#### Sales of Unregistered Securities

From April 15, 2016, the date we began operations, through December 31, 2017, we granted to employees, consultants and directors options to purchase an aggregate of 213,754 shares of common stock pursuant to our equity incentive plans, having exercise prices ranging from \$2.46 to \$10.00 per share.

On November 1, 2017, the Company entered into a stock purchase agreement (the "Agreement") with the Epidermolysis Bullosa Medical Research Foundation, a California not-for-profit corporation ("EBMRF"), and EB Research Partnership, Inc., a New York not-for-profit corporation ("EBRP" and together with EBMRF, the "Purchasers"), pursuant to which the Company has agreed to issue and sell, and the Purchasers have agreed to purchase, an aggregate of 70,000 shares of the Company's common stock, par value \$0.00001 per share, for a purchase price of \$11.00 per share, resulting in aggregate gross proceeds to the Company of \$770,000 (the "Transaction"). The Company intends to commence work on or before September 1, 2018 and to use the proceeds exclusively to complete the research plan pursuant to the Agreement. There is a redemption feature whereby the Company shall repurchase all or a portion of the shares at a purchase price of \$11.00 per share or the closing trading price of the common stock on the redemption request date, whichever is higher, should the Company not commence work on or before September 1, 2018 or cease commercially reasonable efforts. The offer, sale and issuance of the shares of the Company are exempt from registration pursuant to Rule 506 of Regulation D and Section 4(a)(2) of the Securities Act of 1933, as amended. Pursuant to the Agreement, the Purchasers have agreed they are acquiring the securities for investment only and not with a view to or for sale in connection with any distribution thereof and appropriate legends are to be affixed to the securities to be issued in conjunction with the Agreement. The Purchasers are subject to a six month lock-up, and the shares purchased under the terms of the Agreement will be subject to restrictions on selling, transferring or otherwise disposing of such shares. The Transaction closed on November 2, 2017.



Except as previously reported above and in our quarterly reports on Form 10-Q and current reports on Form 8-K filed with the SEC, during the year ended December 31, 2017, there were no unregistered sales of equity securities by us during the year ended December 31, 2017.

The offers, sales and issuances of the securities described above were deemed to be exempt from registration under the Securities Act of 1933, as amended, or the Securities Act, under either (a) Rule 701 promulgated under the Securities Act as offers and sale of securities pursuant to certain compensatory benefit plans and contracts relating to compensation in compliance with Rule 701 or (b) Section 4(2) of the Securities Act as transactions by an issuer not involving any public offering. The recipients of securities in each of these transactions represented their intention to acquire the securities for investment only and not with view to or for sale in connection with any distribution thereof and appropriate legends were affixed to the stock certificates and instruments issued in such transactions. All recipients had adequate access, through their relationships with us, to information about us.

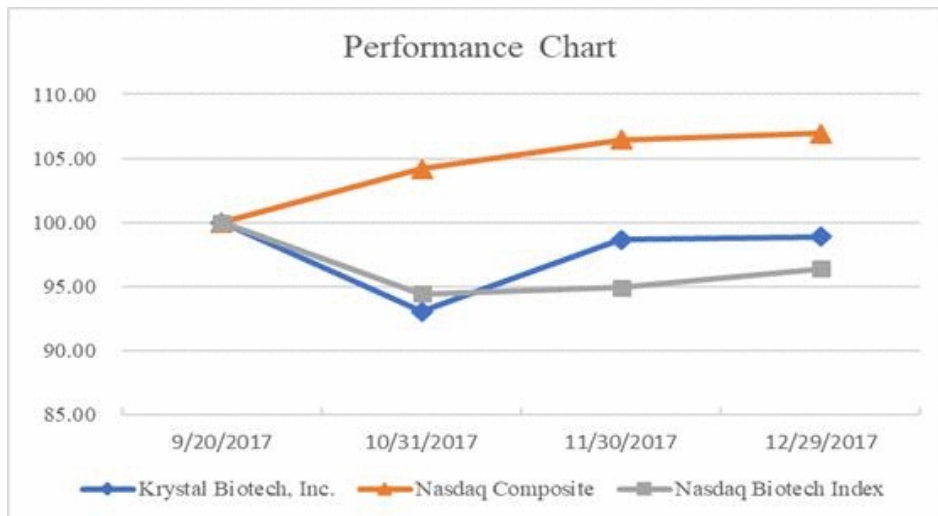
#### **Use of Proceeds from Initial Public Offering of Common Stock**

On September 22, 2017, the Company completed its IPO of 4,554,000 shares of its common stock at a price to the public of \$10.00 per share, which includes the sale of 594,000 shares of the Company's common stock pursuant to the underwriters' full exercise of their option to purchase additional shares. The total proceeds from the offering to the Company, net of underwriting discounts and commissions of approximately \$3.2 million, were approximately \$42.3 million. After deducting offering expenses payable by the Company of approximately \$1.6 million, net proceeds to the Company were approximately \$40.7 million. There has been no material change in the planned use of proceeds from our IPO as described in our final prospectus filed with the SEC on September 20, 2017 pursuant to Rule 424(b) under the Securities Act. Pending the uses described, we have invested the net proceeds in short-term, investment-grade interest-bearing securities such as money market funds.

#### **Stock Performance Graph**

Set forth below is a graph comparing the cumulative total return on an indexed basis of a \$100 investment in the Company's common stock, the Nasdaq Composite Index and the Nasdaq Biotechnology Index commencing on September 20, 2017 (the date our common stock began trading on The Nasdaq Stock Market) and continuing through December 31, 2017. The graph assumes our closing sale price on September 20, 2017 of \$10.64 per share as the initial value of our common stock for indexing purposes. Points on the graph represent the performance as of the last business day of each of the fiscal quarters indicated.

This performance graph shall not be deemed “soliciting material” or to be “filed” with the SEC for purposes of Section 18 of the Exchange Act or incorporated by reference into any filing of Krystal Biotech, Inc. under the Securities Act or the Exchange Act, except to the extent we specifically incorporate it by reference into such filing. The past performance of our common stock is no indication of future performance.



Trade Date	Krystal Biotech, Inc.	Nasdaq Composite	Nasdaq Biotech Index
9/20/2017	100.00	100.00	100.00
10/31/2017	93.05	104.21	94.45
11/30/2017	98.68	106.47	94.93
12/29/2017	98.87	106.93	96.41

**Item 6. Selected Financial Data.**

The following selected financial data of the Company for each of the periods indicated are derived from the Company's audited financial statements. The financial statements of the Company as of December 31, 2017 and 2016 and for the years ended December 31, 2017 and 2016, and the related reports of the independent registered public accounting firm are included elsewhere in this Annual Report on Form 10-K. The data presented below should be read in conjunction with the Company's financial statements, the notes thereto, and "Management's Discussion and Analysis of Financial Condition and Results of Operations" included elsewhere in this report.

(In thousands, except shares, units, per share and per unit data)	Year Ended December 31,	
	2017	2016
<b>Expenses</b>		
Research and development	\$ 3,208	\$ 741
General and administrative	1,564	402
Total operating expenses	4,772	1,143
Loss from operations	(4,772)	(1,143)
<b>Other Expense</b>		
Interest and other expense, net	(3,148)	(7)
Total other expense	(3,148)	(7)
Net loss	(7,920)	(1,150)
Net loss applicable to stockholders and members	\$ (7,920)	\$ (1,150)
Net loss attributable to common stockholders and members per share:		
Basic and diluted	\$ (1.48)	\$ (1.31)
Weighted-average common shares and common units outstanding: Basic and diluted	5,360,536	877,490
(In thousands)	December 31, 2017	December 31, 2016
<b>Balance sheet data:</b>		
Cash	\$ 49,591	\$ 1,923
Working capital	49,274	2,126
Total assets	50,114	2,182
Accrued expenses and other current liabilities	447	1
Related party promissory notes	—	698
Total liabilities	640	1,893
Total stockholders' and members' equity	49,474	289

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

*The following discussion and analysis of financial condition and results of operations should be read together with the financial statements and the related notes included in Item 8 of Part II of this Annual Report on Form 10-K. This discussion and analysis contains certain forward-looking statements that involve risks and uncertainties. Our actual results may differ materially from those discussed below. Factors that could cause or contribute to such differences include, but are not limited to, those identified below and those set forth under the section entitled "Risk Factors" in Item 1A, and other documents we file with the SEC. Historical results are not necessarily indicative of future results.*

### Overview

We are a gene therapy company dedicated to developing and commercializing novel treatments for patients suffering from dermatological diseases. We have developed a proprietary gene therapy platform, our STAR-D platform, that consists of an engineered patent pending viral vector based on herpes simplex virus 1, or HSV-1, and skin-optimized gene transfer technology, to develop off-the-shelf treatments for dermatological diseases for which we believe there are no known effective treatments. We are initially using our STAR-D platform to develop treatments for rare or orphan dermatological indications caused by the absence of or a mutation in a single gene, and plan to leverage our platform in the future to expand our pipeline to include other dermatological indications.

Our lead product candidate, KB103, is currently in preclinical development and seeks to use gene therapy to treat DEB, a rare and severe genetic disease, for which there is currently no approved treatment. DEB affects the skin and mucosal tissues, and is caused by one or more mutations in a gene called COL7A1, which is responsible for the formation of protein type VII collagen, or COL7, that forms anchoring fibrils that bind the dermis to the epidermis. In DEB patients, the genetic defect in COL7A1 results in loss or malfunctioning of these anchoring fibrils, leading to extremely fragile skin that blisters and tears from minor friction or trauma. Those who are born with DEB are sometimes called "butterfly children", because their skin is likened to be as fragile as the wings of a butterfly. DEB patients may suffer from open wounds, skin infections, fusion of fingers and toes, and gastrointestinal tract problems throughout their lifetime, and may eventually develop squamous cell carcinoma, a potentially fatal condition. Based on information from DEBRA International, a worldwide alliance of patient support groups for EB, of which DEB is a subset, we believe there may be as many as 125,000 patients worldwide who suffer from DEB. We estimate that there are 3,200 to 3,500 diagnosed DEB patients in the EU, United States, Japan and Canada.

Our company was organized in December 2015 in the State of California and commenced operations on April 15, 2016. On March 31, 2017, we converted from a California limited liability company to a Delaware C-corporation, and changed our name from Krystal Biotech, LLC to Krystal Biotech, Inc. To date, our operations have been limited to organizing and staffing our company, developing our proprietary STAR-D platform, identifying potential product candidates and undertaking preclinical studies and preparing for clinical trials of our product candidates.

On September 19, 2017, the Company's registration statement on Form S-1 (File No. 333-220085) relating to the IPO was declared effective by the SEC. On September 22, 2017, the Company completed its IPO of 4,554,000 shares of its common stock at a price to the public of \$10.00 per share, which includes the sale of 594,000 shares of the Company's common stock pursuant to the underwriters' full exercise of their option to purchase additional shares. Total proceeds from the offering to the Company, net of underwriting discounts and commissions of \$3.2 million, were \$42.3 million. After deducting offering expenses payable by the Company of \$1.6 million, net proceeds to the Company were \$40.7 million. At December 31, 2017, our cash balance was approximately \$49.6 million.

On November 1, 2017, the Company entered into a stock purchase agreement with EBMRP and EBRP pursuant to which the Company agreed to issue and sell, and the Purchasers agreed to purchase, an aggregate of 70,000 shares of the Company's common stock, par value \$0.00001 per share, for a purchase price of \$11.00 per share, resulting in aggregate gross proceeds to the Company of \$770,000.

On November 2, 2017, the FDA granted Orphan Drug Designation to the Company's lead product candidate, KB103, for the treatment of DEB. The FDA's Office of Orphan Drug Products grants orphan drug designation to support the development of medicines for underserved patient populations, or rare disorders, that affect fewer than 200,000 people in the United States. Orphan drug designation may allow Krystal Biotech to be eligible for a seven-year period of U.S. Marketing exclusivity upon approval of KB103, tax credits for certain clinical research costs, and a waiver of the Prescription Drug User Fee Act ("PDUFA") filing fees, subject to certain conditions.

On November 3, 2017, the Office of Science Policy or OSP at the NIH indicated that the Company's Phase 1/2 protocol for KB103 has completed the RAC protocol registration process.

Since operations began, we have incurred operating losses. Our net losses were \$7.9 million and \$1.2 million for the years ended December 31, 2017 and 2016, respectively. At December 31, 2017, we had accumulated a deficit of \$9.1 million. We expect to incur significant expenses and increasing operating losses for the foreseeable future. Our net losses may fluctuate significantly from quarter to quarter and year to year. We will need to generate significant revenue to achieve profitability, and we may never generate revenue or enough revenue to achieve profitability.

Costs related to clinical trials can be unpredictable and therefore there can be no guarantee that we will have sufficient proceeds from our IPO and from other sources to fund our planned preclinical and clinical studies or our operations. Our funds may not be sufficient to enable us to conduct pivotal clinical trials for, seek marketing approval for or commercially launch KB103 or any other product candidate. Accordingly, to obtain marketing approval for and to commercialize this or any other product candidates, we may be required to obtain further funding through public or private equity offerings, debt financings, collaboration and licensing arrangements or other sources. Adequate additional financing may not be available to us on acceptable terms, if at all. Our failure to raise capital when needed would have a negative effect on our financial condition and our ability to pursue our business strategy.

#### ***Revenue***

We currently have no approved products for commercial marketing or sale and have not generated any revenue from the sale of products or other sources to date. In the future, we may generate revenue from product sales, royalties on product sales, or license fees, milestones, or other upfront payments if we enter into any collaborations or license agreements. We expect that our future revenue will fluctuate from quarter to quarter for many reasons, including the uncertain timing and amount of any such payments and sales.

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

Research and development expenses consist primarily of costs incurred to advance our preclinical candidates, which include:

- expenses incurred under agreements with contract manufacturing organizations, consultants and other vendors that conduct our preclinical activities;
- costs of acquiring, developing and manufacturing clinical trial materials and lab supplies; and
- facility costs, depreciation and other expenses, which include direct expenses for rent and maintenance of facilities and other supplies.

We expense internal research and development costs to operations as incurred. We expense third party costs for research and development activities, such as the manufacturing of preclinical and clinical materials, based on an evaluation of the progress to completion of specific tasks such as manufacturing of drug substance, fill/finish and stability testing, which is provided to us by our vendors.

We expect our research and development expenses will increase as we continue the manufacture of preclinical and clinical materials and manage the clinical trials of, and seek regulatory approval for, our product candidates and expand our product portfolio. In the near term, we expect that our research and development expenses will increase as we conduct our ongoing preclinical trials and our planned Phase 1/2 clinical trial for KB103. Due to the numerous risks and uncertainties associated with product development, we cannot determine with certainty the duration, costs and timing of this clinical trial, and, as a result, the actual costs to complete this planned clinical trial may exceed the expected costs.

#### ***General and Administrative Expenses***

General and administrative expenses consist principally of professional fees associated with corporate and intellectual property legal expenses, consulting and accounting services and facility-related costs. Other general and administrative costs include stock-based compensation and travel expenses.

We anticipate that our general and administrative expenses will increase in the future to support the continued research and development of our product candidates and to operate as a public company. These increases will likely include increased costs for insurance, costs related to the hiring of additional personnel and payments to outside consultants, lawyers and accountants, among other expenses. Additionally, if and when we believe a regulatory approval of our first product candidate

appears likely, we anticipate that we will increase our salary and personnel costs and other expenses as a result of our preparation for commercial operations.

### ***Interest Expense, Net***

Interest expense, net consists primarily of interest expense on our convertible promissory notes, which is partially offset by interest earned on our cash. Interest expense includes a beneficial conversion feature as a result of our convertible promissory notes having a conversion price into preferred stock that was lower than the market price of each share of preferred stock on the date of conversion.

### **Critical Accounting Policies and Significant Judgments and Estimates**

Our management's discussion and analysis of our financial position and results of operations is based on our financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles, or GAAP. The preparation of financial statements in conformity with GAAP requires us to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. On an ongoing basis, we evaluate estimates which include, but are not limited to, estimates related to contract manufacturing prepayments and accruals, stock-based compensation expense, and reported amounts of expenses during the reported period. We base our estimates on historical experience and other market-specific or other relevant assumptions that we believe to be reasonable under the circumstances. Actual results may differ materially from those estimates or assumptions.

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

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

As part of the process of preparing our financial statements, we are required to estimate our accrued research and development expenses, current assets and other current liabilities. This process involves reviewing open contracts and commitments, communicating with our personnel to identify services that have been performed for us and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued research and development expenses, current assets and other current liabilities as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. Examples of estimated accrued research and development expenses, prepaid assets and other current liabilities include fees paid to contract manufacturers made in connection with the manufacturing of clinical trials materials.

We base our expenses related to clinical manufacturing on our estimates of the services performed pursuant to contracts with the entities producing clinical materials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. Payments under these types of contracts depend heavily upon the successful completion of many separate tasks involved in the manufacturing of drug product. In accruing service fees, we estimate the time period over which services will be performed, and the actual services performed in each period. If our estimates of the status and timing of services performed differs from the actual status and timing of services performed we may report amounts that are too high or too low in any particular period. To date, there have been no material differences from our estimates to the amount actually incurred.

### ***Stock-Based Compensation***

We have applied the fair value recognition provisions of Financial Accounting Standards Board Accounting Standards Codification, or ASC, Topic 718, *Compensation—Stock Compensation*, or ASC 718, to account for stock-based compensation for employees and ASC 718 and ASC 505, *Equity*, or ASC 505, for non-employees. We recognize compensation costs related to stock options granted to employees based on the estimated fair value of the awards on the date of grant. Stock compensation related to non-employee awards is re-measured at each reporting period until the awards are vested. Described below is the methodology we have utilized in measuring stock-based compensation expense.

Determining the amount of stock-based compensation to be recorded requires us to develop estimates of the fair value of stock-based awards as of their measurement date. We recognize stock-based compensation expense over the requisite service period, which is the vesting period of the award. Calculating the fair value of stock-based awards requires that we make highly subjective assumptions. We use the Black-Scholes option pricing model to value our stock option awards. Use of this valuation methodology requires that we make assumptions as to the volatility of our common stock, the fair value of

our common stock on the measurement date, the expected term of our stock options, the risk-free interest rate for a period that approximates the expected term of our stock options and our expected dividend yield. Because we are a privately held company with a limited operating history, we utilize data from a representative group of publicly traded companies to estimate expected stock price volatility. We selected representative companies from the biopharmaceutical industry with characteristics similar to us. We use the simplified method as prescribed by the SEC Staff Accounting Bulletin No. 107, *Share-Based Payment* as we do not have sufficient historical stock option activity data to provide a reasonable basis upon which to estimate the expected term of stock options granted to employees. For non-employee grants, we use an expected term equal to the remaining contractual term of the award. We utilize a dividend yield of zero based on the fact that we have never paid cash dividends and have no current intention of paying cash dividends. The risk-free interest rate used for each grant is based on the U.S. Treasury yield curve in effect at the time of grant for instruments with a similar expected life.

Under ASC 718, we are required to estimate the level of forfeitures expected to occur and record stock-based compensation expense only for those awards that we ultimately expect will vest. For all periods presented, our estimated annual forfeiture rate was 0%.

#### *Determination of the Fair Value of Common Stock on Grant Dates*

As there has been no public market for our equity instruments prior to the completion of our IPO on September 22, 2017, the estimated fair value of our pre-IPO common shares prior had been determined by our board of directors as of the grant date, with input from management, considering our most recently available third-party valuations of common shares and our board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent valuation through the date of the grant. Following the completion of our IPO, the fair value of our common stock will be determined based on the quoted market price of our common stock. We engaged an independent third-party valuation specialist to perform contemporaneous valuations as of September 30, 2016 and May 31, 2017. The third-party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*, or AICPA's Practice Aid. In conducting the valuations, the independent third-party valuation specialist considered all objective and subjective factors that it believed to be relevant for each valuation conducted in accordance with AICPA's Practice Aid, including our best estimate of our business condition, prospects and operating performance at each valuation date. Other significant factors included:

- the rights, preferences and privileges of our preferred stock as compared to those of our common stock, including the liquidation preferences of our preferred stock;
- our results of operations, financial position and the status of research and development efforts;
- the composition of, and changes to, our management team and board of directors;
- the lack of liquidity of our common stock;
- our stage of development and business strategy and the material risks related to our business and industry;
- the valuation of publicly traded companies in the life sciences and biotechnology sectors, as well as recently completed mergers and acquisitions of guideline companies;
- any external market conditions affecting the life sciences and biotechnology industry sectors;
- the likelihood of achieving a liquidity event for the holders of our common stock and stock options, such as an IPO, or a sale of our company, given prevailing market conditions; and
- the state of the IPO market for similarly situated privately held biotechnology companies.

The dates of our contemporaneous valuations have not always coincided with the dates of our stock option grants. In determining the exercise prices of the stock options, our board of directors considered, among other things, the most recent contemporaneous valuation of our common stock and their assessment of additional objective and subjective factors that were relevant as of the grant dates. The additional factors considered when determining whether any changes in the fair value of our common stock had occurred between the most recent contemporaneous valuation and the grant dates included our stage of research and preclinical development, our operating and financial performance and current business conditions.

There are significant judgments and estimates inherent in the determination of the fair value of our common stock. These judgments and estimates include assumptions regarding our future operating performance, the time to completing an IPO or other liquidity event, the related valuations associated with such events, and the determinations of the appropriate

valuation methods at each valuation date. If we had made different assumptions, our stock-based compensation expense, net loss and net loss per share applicable to common stockholders could have been materially different.

### JOBS Act Accounting Election

We are an emerging growth company, as defined in the JOBS Act. Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

### Results of Operations

#### Years Ended December 31, 2017 and 2016

(in thousands)	Year Ended December 31,		Change
	2017	2016	\$
<b>Expenses</b>			
Research and development	\$ 3,208	\$ 741	\$ 2,467
General and administrative	1,564	402	1,162
Total operating expenses	4,772	1,143	3,629
Loss from operations	(4,772)	(1,143)	(3,629)
<b>Other Expense</b>			
Interest and other expense, net	(3,148)	(7)	(3,141)
Total other expense	(3,148)	(7)	(3,141)
Net loss	<u>\$ (7,920)</u>	<u>\$ (1,150)</u>	<u>\$ (6,770)</u>

#### Research and Development Expenses

Research and development expenses increased \$2.5 million for the year ended December 31, 2017 as compared to the year ended December 31, 2016. Higher research and development spending was due largely to increases in professional services related to outsourced manufacturing and in-vivo studies of \$1.4 million, lab supplies and expensed lab equipment of \$411 thousand, payroll and employee benefits of \$454 thousand, stock-based compensation of \$126 thousand, and other research and development expenses of \$89 thousand. We expect research and development expenses to continue to increase.

#### General and Administrative Expenses

General and administrative expenses increased \$1.2 million for the year ended December 31, 2017 as compared to the year ended December 31, 2016. Higher general and administrative spending was due largely to increases in legal and professional services of \$614 thousand, payroll and employee benefits of \$221 thousand, insurance expenses of \$104 thousand, stock-based compensation of \$87 thousand, travel and related costs of \$40 thousand and other administrative costs of \$95 thousand.

#### Interest Expense, Net

Interest expense, net was \$3.1 million for the year ended December 31, 2017 which consists of \$3.2 million in interest expense incurred in connection with the conversion of promissory notes to shares of preferred stock, partially offset by \$115 thousand in interest income earned from our cash. Interest expense, net was approximately \$7 thousand for the year ended December 31, 2016.

### Liquidity and Capital Resources

#### Overview

As of December 31, 2017 and 2016, we had accumulated deficits of \$9.1 million and \$1.2 million, respectively. On September 22, 2017, we received net proceeds of approximately \$40.7 million from our IPO. We believe that our cash of approximately \$49.6 million as of December 31, 2017 will be sufficient to allow us to fund our operations for at least 12 months from the filing date of this Annual Report on Form 10-K. As we continue to incur losses, a transition to profitability is dependent upon the successful development, approval and commercialization of our product candidates and the achievement of a level of revenues adequate to support our cost structure. We may never achieve profitability, and unless and



until it does, we will continue to need to raise additional capital or obtain financing from other sources, such as partnerships. Management intends to fund future operations through equity and debt financings and may also seek additional capital through arrangements with strategic partners or other sources. There can be no assurances, however, that additional funding will be available on terms acceptable to us, if at all.

In November 2017, we closed the sale of common stock to EBMRF, a California not-for-profit corporation and EB Research Partnership, Inc., a New York not-for-profit corporation for aggregate proceeds of \$770,000.

In August 2017, we closed the sale of preferred stock to a single investor for aggregate proceeds of \$7.0 million, and the sale of 130,590 shares of our common stock with a party related to a member of our board of directors for aggregate proceeds of \$1.0 million.

Prior to August 2017, we had received \$1.4 million in gross proceeds from the issuance of equity securities and \$4.1 million in gross proceeds from debt financings.

### ***Debt Financings***

On November 16, 2016, we executed a note purchase agreement pursuant to which convertible promissory notes were issued. Each note bore interest at a rate of 6% per annum, which accrued based on a 365 day year and matured on May 14, 2018, unless sooner paid or converted. As of December 31, 2016, the outstanding principal balance of the notes was \$1.8 million.

In connection with the sale and issuance of the preferred stock on August 8, 2017, the convertible promissory notes were converted into 968,053 shares of preferred stock (inclusive of accrued interest thereon), in accordance with the conversion features of the notes. Upon the closing of the IPO, all shares of preferred stock, including previously converted promissory notes, converted into 2,061,773 shares of common stock on a 1-to-1 basis.

### ***Operating Capital Requirements***

Our primary uses of capital are, and we expect will continue to be for the near future, compensation and related expenses, manufacturing costs for preclinical and clinical materials, third party clinical trial research and development services, laboratory and related supplies, clinical costs, legal and other regulatory expenses and general overhead costs.

We believe that our available funds will be sufficient to enable us to obtain clinical data from our planned Phase 1/2 clinical trial for KB103. We expect that these funds will not be sufficient to enable us to seek marketing approval for or commercialize any of our product candidates.

We have based our projections of operating capital requirements on assumptions that may prove to be incorrect and we may use all of our available capital resources sooner than we expect. Because of the numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical products, we are unable to estimate the exact amount of our operating capital requirements. Our future funding requirements will depend on many factors, including, but not limited to:

- the timing and costs of our ongoing planned Phase 1/2 clinical trial for KB103;
- the progress, timing and costs of manufacturing of KB103 for planned clinical trials;
- the initiation, progress, timing, costs and results of preclinical studies and clinical trials for our other product candidates and potential product candidates;
- the outcome, timing and costs of seeking regulatory approvals;
- the costs of commercialization activities for KB103 and other product candidates if we receive marketing approval, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- subject to receipt of marketing approval, revenue received from commercial sales of our product candidates;
- the terms and timing of any future collaborations, licensing, consulting or other arrangements that we may establish;

- the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights, including milestone and royalty payments and patent prosecution fees that we are obligated to pay pursuant to our license agreements;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against intellectual property related claims; and
- the extent to which we in-license or acquire other products and technologies.

We expect that we will need to obtain substantial additional funding in order to receive regulatory approval and to commercialize KB103 or any other product candidates. To the extent that we raise additional capital through the sale of common stock, convertible securities or other equity securities, the ownership interests of our existing stockholders may be materially diluted and the terms of these securities could include liquidation or other preferences that could adversely affect the rights of our existing stockholders. In addition, debt financing, if available, would result in increased fixed payment obligations and may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, that could adversely affect our ability to conduct our business. If we are unable to raise capital when needed or on attractive terms, we could be forced to significantly delay, scale back or discontinue the development or commercialization of KB103 or our other product candidates, seek collaborators at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available, and relinquish or license, potentially on unfavorable terms, our rights to KB103 or our other product candidates that we otherwise would seek to develop or commercialize ourselves.

## Cash Flows

The following table summarizes our sources and uses of cash (in thousands):

	<b>Year Ended December 31,</b>	
	<b>2017</b>	<b>2016</b>
Net cash used in operating activities	\$ (3,890)	\$ (1,311)
Net cash used in investing activities	(210)	(15)
Net cash provided by financing activities	51,768	3,249
Net increase in cash	<u>\$ 47,668</u>	<u>\$ 1,923</u>

### *Operating Activities*

Net cash used in operating activities was \$3.9 million for the year ended December 31, 2017 and consisted primarily of a net loss of \$7.9 million adjusted for non-cash items including interest expense incurred of \$3.3 million primarily due to the beneficial conversion feature upon conversion of promissory notes to shares of preferred stock, depreciation and stock-based compensation expense of \$269 thousand and a net decrease in operating assets and liabilities of approximately \$0.5 million.

Net cash used in operating activities was \$1.3 million for the year ended December 31, 2016 and consisted primarily of a net loss of \$1.2 million adjusted for non-cash items including nominal depreciation expenses, stock-based compensation expense of \$33 thousand, non-cash interest expense of \$7 thousand and a net increase in operating assets and liabilities of approximately \$203 thousand.

### *Investing Activities*

During the year ended December 31, 2017 and 2016, our investing activities used net cash of approximately \$210 thousand and \$15 thousand, respectively, primarily from the purchase of computer and laboratory equipment.

### *Financing Activities*

Net cash provided by financing activities was \$51.8 million for the year ended December 31, 2017, which consisted of total proceeds of approximately \$42.3 million from the sale of common stock in our IPO on September 22, 2017 net of underwriting discounts and commissions of approximately \$3.2 million, less offering expenses paid by the Company of \$1.6 million, \$7.0 million in proceeds from the sale of Series A Preferred Stock to a single investor, \$2.3 million in proceeds from the issuance of convertible promissory notes, \$1.0 million in proceeds from the sale of shares of common stock to an affiliate of a member of the Board and \$0.7 million in proceeds from a stock purchase agreement with the EBMRP and EB Research Partnership, Inc.

Net cash provided by financing activities was \$3.2 million for the year ended December 31, 2016, which consisted of \$1.4 million from the issuance of preferred and common stock and \$1.8 million from the issuance of convertible promissory notes.

#### Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements as defined in Item 303(a)(4)(ii) of Regulation S-K promulgated by the SEC.

#### Contractual Obligations

The following table summarizes our outstanding contractual obligations as of payment due date by period at December 31, 2016 (in thousands):

	Total	Less than 1 year	Years 1-3	Years 4-5	More Than 5 Years
Future minimum operating lease payments (1)	\$ 102	\$ 102	\$ —	\$ —	\$ —
Less: minimum payments to be received from non-cancelable subleases	(18)	(18)	—	—	—
Total minimum lease payment, net	\$ 84	\$ 84	\$ —	\$ —	\$ —
Obligation to contract manufacturing organization	\$ 289	\$ 289	\$ —	\$ —	\$ —

(1) In May 2016, we leased office and laboratory space at 2100 Wharton St., Suite 701, Pittsburgh, PA that expires in October 2018.

#### Recent Accounting Pronouncements

In February 2016, the FASB issued *ASU 2016-02 Leases (Topic 842)* (“ASU 2016-02”), which replaces the existing lease accounting standards. The new standard requires a dual approach for lessee accounting under which a lessee would account for leases as finance (also referred to as capital) leases or operating leases. Both finance leases and operating leases will result in the lessee recognizing a right-of-use asset and corresponding lease liability. For finance leases the lessee would recognize interest expense and amortization of the right-of-use asset and for operating leases the lessee would recognize straight-line total lease expense. ASU 2016-02 is effective for fiscal years, and periods within those years, beginning after December 15, 2018. The Company generally does not finance purchases of equipment but it does lease office and lab facilities. The Company is in the process of evaluating the effect that this ASU will have on its financial statements and related disclosures.

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

Our cash is held in an operating account as of December 31, 2017. The investments in these financial instruments are made in accordance with an investment policy which specifies the categories, allocations and ratings of securities we may consider for investment. The primary objective of our investment activities is to preserve principal while at the same time maximizing the income we receive without significantly increasing risk. Some of the financial instruments in which we invest could be subject to market risk. This means that a change in prevailing interest rates may cause the value of the instruments to fluctuate. For example, if we purchase a security that was issued with a fixed interest rate and the prevailing interest rate later rises, the value of that security will probably decline. To minimize this risk, we intend to maintain a portfolio which may include cash, cash equivalents and investment securities available-for-sale in a variety of securities which may include money market funds, government and non-government debt securities and commercial paper, all with various maturity dates. Based on our current investment portfolio, we do not believe that our results of operations or our financial position would be materially affected by an immediate change of 10% in interest rates.

We do not hold or issue derivatives, derivative commodity instruments or other financial instruments for speculative trading purposes. Further, we do not believe our cash has significant risk of default or illiquidity. While we believe our cash account does not contain excessive risk, we cannot provide absolute assurance that any investments we make in the future will not be subject to adverse changes in market value. Our cash is recorded at fair value.

**Item 8. Financial Statements and Supplementary Data.**

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## REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and  
Stockholders of Krystal Biotech, Inc.:

### Opinion on the Financial Statements

We have audited the accompanying balance sheets of Krystal Biotech, Inc. ("Company") as of December 31, 2017 and 2016, and the related statements of operations, convertible preferred stock and stockholders' and members' equity and cash flows for each of the two 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 financial position of the Company as of December 31, 2017 and 2016, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2017, in conformity with accounting principles generally accepted in the United States of America.

### 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/ Mayer Hoffman McCann P.C.

We have served as the Company's auditor since 2017.  
San Diego, California  
March 12, 2018

**Krystal Biotech, Inc. (formerly Krystal Biotech, LLC)**

**Balance Sheets**

(In thousands, except shares, units, per share and per unit data)	December 31, 2017	December 31, 2016
<b>Assets</b>		
Current assets		
Cash	\$ 49,591	\$ 1,923
Prepaid assets	304	246
Other current assets	19	—
Total current assets	49,914	2,169
Property and equipment, net	200	13
Total assets	\$ 50,114	\$ 2,182
<b>Liabilities, Convertible Preferred Stock and Stockholders' and Members' Equity</b>		
Current liabilities		
Accounts payable	\$ 193	\$ 42
Accrued expenses and other current liabilities	447	1
Total current liabilities	640	43
Accrued interest	—	7
Related party convertible promissory notes	—	698
Convertible promissory notes	—	1,145
Total liabilities	640	1,893
Commitments and contingencies (Note 7)		
Preferred stock		
Preferred stock; \$0.00001 par value; 20,000,000 shares authorized, 2,061,773 shares issued, and no shares outstanding at December 31, 2017; no shares authorized, issued, or outstanding at December 31, 2016	—	—
Total preferred stock	—	—
Stockholders' and members' equity		
Common stock; \$0.00001 par value; 80,000,000 shares authorized, 10,307,247 shares issued and outstanding at December 31, 2017; no shares authorized, issued, or outstanding at December 31, 2016	—	—
Common units; no par value; no common units authorized, issued, or outstanding at December 31, 2017; 3,490,884 units authorized, issued, and outstanding at December 31, 2016	—	—
Preferred units; no par value; no preferred units authorized, issued, or outstanding at December 31, 2017; 179,613 units authorized, issued, and outstanding at December 31, 2016 (aggregate liquidation preference of \$1,406)	—	1,406
Additional paid-in capital	58,544	33
Accumulated deficit	(9,070)	(1,150)
Total stockholders' and members' equity	49,474	289
Total liabilities, convertible preferred stock and stockholders' and members' equity	\$ 50,114	\$ 2,182

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

**Krystal Biotech, Inc. (formerly Krystal Biotech, LLC)**

**Statements of Operations**

(In thousands, except shares, units, per share and per unit data)	Year Ended December 31,	
	2017	2016
<b>Expenses</b>		
Research and development	\$ 3,208	\$ 741
General and administrative	1,564	402
Total operating expenses	4,772	1,143
Loss from operations	(4,772)	(1,143)
<b>Other Expense</b>		
Interest and other expense, net	(3,148)	(7)
Total other expense	(3,148)	(7)
Net loss	(7,920)	(1,150)
Net loss applicable to stockholders and members	\$ (7,920)	\$ (1,150)
Net loss attributable to common stockholders per share:		
Basic and diluted	\$ (1.48)	\$ (1.31)
Weighted-average common shares and common units outstanding:		
Basic and diluted	5,360,536	877,490

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

Krystal Biotech, Inc. (formerly Krystal Biotech, LLC)

Statements of Convertible Preferred Stock, Stockholders' and Members' Equity

(In thousands, except shares and units)	Statements of Convertible Preferred Stock, Stockholders' and Members' Equity										Total Stockholders' and Members' Equity (Deficit)	
	Convertible Preferred Stock		Common Stock		Common Units		Preferred Units		Additional			
	Shares	Amount	Shares	Amount	Units	Amount	Units	Amount	Paid-in Capital	Accumulated Deficit		
<b>Balances at January 1, 2016</b>	—	\$ —	—	\$ —	—	\$ —	—	\$ —	—	\$ —	—	\$ —
Issuance of common units	—	—	—	—	450	100	—	—	—	—	—	—
Conversion from common units to preferred units	—	—	—	—	(450)	(100)	12,771	100	—	—	—	—
Issuance of preferred and common units	—	—	—	—	3,490,884	—	166,842	1,306	—	—	—	1,306
Stock-based compensation expense	—	—	—	—	—	—	—	—	33	—	—	33
Net loss	—	—	—	—	—	—	—	—	—	(1,150)	—	(1,150)
<b>Balances at December 31, 2016</b>	—	\$ —	—	\$ —	3,490,884	\$ —	179,613	\$ 1,406	\$ 33	\$ (1,150)	\$ —	\$ 289
Conversion of preferred units to preferred stock	179,613	1,406	—	—	—	—	(179,613)	(1,406)	—	—	—	(1,406)
Conversion of common units to common stock	—	—	3,490,884	—	(3,490,884)	—	—	—	—	—	—	—
Conversion of convertible promissory notes to preferred stock	968,053	4,255	—	—	—	—	—	—	3,158	—	—	3,158
Issuance of preferred stock	914,107	7,000	—	—	—	—	—	—	—	—	—	—
Issuance of common stock	—	—	4,754,590	—	—	—	—	—	42,446	—	—	42,446
Conversion of preferred stock to common stock	(2,061,773)	(12,661)	2,061,773	—	—	—	—	—	12,661	—	—	12,661
Stock-based compensation expense	—	—	—	—	—	—	—	—	246	—	—	246
Net loss	—	—	—	—	—	—	—	—	—	(7,920)	—	(7,920)
<b>Balances at December 31, 2017</b>	—	\$ —	10,307,247	\$ —	—	\$ —	—	\$ —	\$ 58,544	\$ (9,070)	\$ —	\$ 49,474

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



**Krystal Biotech, Inc. (formerly Krystal Biotech, LLC)**

**Statements of Cash Flows**

(In thousands)	Year Ended December 31,	
	2017	2016
<b>Operating Activities</b>		
Net loss	\$ (7,920)	\$ (1,150)
Adjustments to reconcile net loss to net cash used in operating activities		
Depreciation	23	2
Stock-based compensation expense	246	33
Non-cash interest expense	3,263	7
(Increase) decrease in		
Prepaid and other assets	(77)	(246)
Accounts payable	133	42
Accrued expenses and other current liabilities	442	1
Net cash used in operating activities	(3,890)	(1,311)
<b>Investing Activities</b>		
Purchases of property and equipment	(210)	(15)
Net cash used in investing activities	(210)	(15)
<b>Financing Activities</b>		
Proceeds from the issuance of convertible promissory notes	1,299	1,145
Proceeds from the issuance of related party convertible promissory notes	1,000	698
Issuance of common stock and common units, net	42,469	100
Issuance of preferred stock and preferred units	7,000	1,306
Net cash provided by financing activities	51,768	3,249
Net increase in cash	47,668	1,923
Cash at beginning of period	1,923	—
Cash at end of period	\$ 49,591	\$ 1,923
<b>Supplemental Disclosures of Non-Cash Investing and Financing Activities</b>		
Conversion of common units to preferred units	\$ —	\$ 100
Conversion of convertible promissory notes to preferred stock	\$ 4,142	\$ —
Conversion of preferred stock to common stock	\$ 12,661	\$ —
Unpaid deferred offering costs	\$ 23	\$ —

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

**Krystal Biotech, Inc. (formerly Krystal Biotech, LLC)**  
**Notes to Financial Statements**

**1. Organization**

Krystal Biotech, Inc. (the “Company,” or “we” or other similar pronouns) was formed on December 20, 2015 in the State of California as Krystal Biotech, LLC and began operations on April 15, 2016. On March 31, 2017, the Company converted from a limited liability company (“LLC”) to a C-corporation in the state of Delaware, and changed its name to Krystal Biotech, Inc. The Company seeks to use gene therapy to develop novel treatments for patients suffering from dermatological diseases. The Company is currently conducting preclinical studies evaluating its lead product candidate, KB103, which is intended to treat dystrophic epidermolysis bullosa, or DEB, a rare and severe genetic disease for which there is currently no approved treatment.

***Stock Split and Increase in Authorized Shares***

On September 5, 2017, in connection with our initial public offering (the “IPO”), the Company’s board of directors (the “Board”) approved a 1-to-4.5 forward stock split, in the form of a dividend, of all outstanding shares of common stock and preferred stock. Except as otherwise noted, all references to share and per share amounts related to common stock, common units, preferred stock, preferred units and stock options in these financial statements reflect the stock split. The par value per share of our capital stock was not adjusted as a result of the stock split. Additionally, the Board approved an increase in authorized shares of common stock and preferred stock to 80,000,000 shares and 20,000,000 shares, respectively. The stock split and the increase in the number of authorized common and preferred shares occurred immediately prior to the effectiveness of our registration statement on Form S-1 (File No. 333-220085) relating to the IPO on September 19, 2017.

***Initial Public Offering***

On September 22, 2017, the Company completed its IPO of 4,554,000 shares of its common stock at a price to the public of \$10.00 per share, which includes the sale of 594,000 shares of the Company’s common stock pursuant to the underwriters’ full exercise of their option to purchase additional shares. The total proceeds from the offering to the Company, net of underwriting discounts and commissions of approximately \$3.2 million, were approximately \$42.3 million. After deducting offering expenses paid by the Company of approximately \$1.6 million, net proceeds to the Company were approximately \$40.7 million. Immediately prior to the closing of the IPO, all outstanding shares of the Company’s preferred stock converted into 2,061,773 shares of common stock on a 1-to-1 basis.

***Liquidity and Risks***

As of December 31, 2017, the Company had an accumulated deficit since inception of \$9.1 million. With the net proceeds raised upon the close of IPO, the Company believes that its cash of approximately \$49.6 million as of December 31, 2017 will be sufficient to allow the Company to fund its operations for at least 12 months from the filing date of this Annual Report on Form 10-K. As the Company continues to incur losses, a transition to profitability is dependent upon the successful development, approval and commercialization of its product candidates and the achievement of a level of revenues adequate to support the Company’s cost structure. The Company may never achieve profitability, and unless and until it does, the Company will continue to need to raise additional capital or obtain financing from other sources, such as partnerships. Management intends to fund future operations through the sale of equity and debt financings and may also seek additional capital through arrangements with strategic partners or other sources. There can be no assurances that additional funding will be available on terms acceptable to the Company, if at all.

The Company is subject to risks common to companies in the biotechnology industry, including, but not limited to, development of technological innovations by its competitors, risks of failure of clinical studies, dependence on key personnel, protection of proprietary technology, compliance with government regulations, and ability to transition from preclinical manufacturing to commercial production of products.

**2. Summary of Significant Accounting Policies**

***Basis of Presentation***

The accompanying financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America (“GAAP”) as found in the Accounting Standards Codification (“ASC”) and Accounting Standards Update (“ASU”) of the Financial Accounting Standards Board (“FASB”).

**Krystal Biotech, Inc. (formerly Krystal Biotech, LLC)**  
**Notes to Financial Statements — Continued**

***Use of Estimates***

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts in the financial statements and accompanying notes. Actual results could materially differ from those estimates. Management considers many factors in selecting appropriate financial accounting policies and controls, and in developing the estimates and assumptions that are used in the preparation of these financial statements. Management must apply significant judgment in this process. In addition, other factors may affect estimates, including: expected business and operational changes, sensitivity and volatility associated with the assumptions used in developing estimates, and whether historical trends are expected to be representative of future trends. The estimation process often may yield a range of potentially reasonable estimates of the ultimate future outcomes and management must select an amount that falls within that range of reasonable estimates. This process may result in actual results differing materially from those estimated amounts used in the preparation of the financial statements. Estimates are used in the following areas, among others: stock-based compensation expense, accrued research and development expenses, the fair value of financial instruments, and the valuation allowance included in the deferred income taxes calculations.

***Segment and Geographical 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 view the Company's operations and manage its business in one operating segment, which is the business of developing and commercializing pharmaceuticals. The Company operates in only one geographic segment.

***Concentrations of Credit Risk and Off-Balance Sheet Risk***

Financial instruments that potentially subject the Company to credit risk consist of cash. The Company's policy is to invest its cash in money market funds and various bank deposit accounts. These financial instruments were held in Company accounts at two financial institutions. The counterparties to the agreements relating to the Company's investments consist of financial institutions of high credit standing. The Company is exposed to credit risk in the event of default by the financial institutions to the extent of amounts recorded on the balance sheets which may be in excess of insured limits. The Company has not experienced any credit losses in such accounts and does not believe it is exposed to any significant credit risk on these funds. The Company has no financial instruments with off-balance sheet risk of loss.

***Cash***

Cash consists of money market funds and bank deposits.

***Deferred Issuance Costs***

Deferred public offering costs, which consist primarily of direct, incremental legal and accounting fees relating to the IPO, are offset against IPO proceeds at December 31, 2017.

***Fair Value of Financial Instruments***

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*, 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 fair value hierarchy applies only to the valuation inputs used in determining the reported or disclosed fair value of the financial instruments and is not a measure of the investment credit quality. Fair value measurements are classified and disclosed in one of the following three categories:

- *Level 1*—Valuations based on unadjusted quoted prices in active markets for identical assets or liabilities that the Company has the ability to access at the measurement date.
- *Level 2*—Valuations based on quoted prices for similar assets or liabilities in markets that are not active or for which all significant inputs are observable, either directly or indirectly.

**Krystal Biotech, Inc. (formerly Krystal Biotech, LLC)**  
**Notes to Financial Statements — Continued**

- *Level 3*—Valuations that require inputs that reflect the Company’s own assumptions that are both significant to the fair value measurement and are unobservable.

To the extent that a 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 within 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.

There have been no changes to the valuation methods utilized by the Company during the years ended December 31, 2017 and 2016. The Company evaluates transfers between levels at the end of each reporting period. There were no transfers of financial instruments between levels during the years ended December 31, 2017 and 2016.

The carrying amounts of financial instruments consisting of cash, prepaid expenses, accounts payable and accrued expenses, related party convertible promissory notes and convertible promissory notes included in the Company’s financial statements, are reasonable estimates of fair value due to their short maturities.

***Property and Equipment, net***

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, while costs of major additions and betterments are capitalized. 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:

Computer equipment and software	3 years
Lab equipment	3 years

***Impairment of Long-Lived Assets***

The Company evaluates long-lived assets for potential impairment when events or changes in circumstances indicate the carrying value of the assets may not be recoverable. Recoverability is measured by comparing the book values of the assets to the expected future net undiscounted cash flows that the assets are expected to generate. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the book value of the assets exceed their fair value. The Company has not recognized any impairment losses for the years ended December 31, 2017 and 2016.

***Convertible Preferred Stock***

In accordance with the guidance in FASB ASC Topic 480, *Distinguishing Liabilities from Equity*, shares of preferred stock (Note 8), were classified outside of permanent equity and within temporary equity, as of December 30, 2016 due to their associated redemption features and liquidation preferences. There were no shares of preferred stock outstanding as of December 31, 2017 and 2016.

The Company evaluated its preferred stock and determined that it is considered an equity host under ASC 815. In making this determination, the Company’s analysis followed the whole instrument approach which compares an individual feature against the entire preferred stock instrument which includes that feature. The Company’s analysis was based on a consideration of the economic characteristics and risks of the preferred stock. More specifically, the Company evaluated all of the stated and implied substantive terms and features, including: (i) whether the preferred stock included redemption features; (ii) how and when any redemption features could be exercised; (iii) whether the holders of the preferred stock were entitled to dividends and how those dividends were calculated; (iv) the voting rights of the Preferred stock; and (v) the existence and nature of any conversion rights. As a result of the Company’s conclusion that the preferred stock both represent an equity host, the redemption features of the preferred stock are considered to be clearly and closely related to the associated equity host instruments. Accordingly, the redemption features of the preferred stock are not considered embedded derivatives that require bifurcation. The Company also concluded that the conversion rights under the preferred stock are clearly and closely related to the equity host instruments and are not considered embedded derivatives that require bifurcation.

**Krystal Biotech, Inc. (formerly Krystal Biotech, LLC)**  
**Notes to Financial Statements — Continued**

***Research and Development Expenses***

Research and development costs are charged to expense as incurred in performing research and development activities. The costs include employee compensation costs, facilities and overhead, preclinical activities and related clinical manufacturing costs, regulatory and other related costs.

The Company estimates contract research and clinical trials materials manufacturing expenses based on the services performed pursuant to contracts with research and manufacturing organizations that manufacture materials used in the Company's ongoing preclinical studies. Nonrefundable advanced payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

In accruing service fees, the Company estimates the time period over which services will be performed and the level of effort to be expended in each period. These estimates are based on communications with the third party service providers and the Company's estimates of accrued expenses using information available at each balance sheet date. If the actual timing of the performance of services or the level of effort varies from the estimate, the Company will adjust the accrual accordingly.

***Stock-Based Compensation Expense***

The Company accounts for its stock-based compensation awards to employees and directors in accordance with FASB ASC Topic 718, *Compensation-Stock Compensation* ("ASC 718"). ASC 718 requires all stock-based payments to employees, including grants of employee stock options and restricted stock, to be recognized in the statements of operations based on their grant-date fair values. Compensation expense related to awards to employees is recognized on a straight-line basis based on the grant-date fair value over the associated service period of the award, which is generally the vesting term. Share-based payments issued to non-employees are recorded at their fair values, and are periodically revalued as the equity instruments vest and are recognized as expense over the related service period in accordance with the provisions of ASC 718 and ASC Topic 505, *Equity*, and are expensed using an accelerated attribution model. The Company estimates the fair value of its stock options using the Black-Scholes option pricing model, which requires the input of subjective assumptions, including: (i) the expected stock price volatility; (ii) the expected term of the award; (iii) the risk-free interest rate; (iv) expected dividends; and (v) the estimated fair value of its common stock on the measurement date. Due to the lack of sufficient history and trading volume of its Common Stock 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. When selecting these public companies on which it has based its expected stock price volatility, the Company selected companies with comparable characteristics to it, including enterprise value, risk profiles, position within the industry, and with historical share price information sufficient to meet the expected term of the stock-based awards. The Company computes historical volatility data using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of the stock-based awards. The Company will continue to apply this process until a sufficient amount of historical information regarding the volatility of its own stock price becomes available. Due to the lack of Company-specific historical option activity, the Company has estimated the expected term of its employee stock options using the "simplified" method, whereby the expected term equals the arithmetic mean of the vesting term and the original contractual term of the option. The expected term for non-employee awards is the remaining contractual term of the option. The risk-free interest rates are based on the U.S. Treasury securities with a maturity date commensurate with the expected term of the associated award. The Company has never paid, and does not expect to pay dividends in the foreseeable future. The Company is also required to estimate forfeitures at the time of grant, and revise those estimates in subsequent periods if actual forfeitures differ from its estimates. The Company uses historical data to estimate forfeitures and records stock-based compensation expense only for those awards that are expected to vest. To the extent that actual forfeitures differ from the Company's estimates, the differences are recorded as a cumulative adjustment in the period the estimates were revised. Stock-based compensation expense recognized in the financial statements is based on awards that are ultimately expected to vest.

***Income Taxes***

For the year ended December 31, 2016, the Company was organized in the State of California as a LLC and was taxed as a partnership for United States income tax purposes and therefore filed federal and state flow-through income tax returns. As a result, no U.S. current or deferred income tax assets or liabilities are reflected in the December 31, 2016 financial statements. The Company's members are obligated to report that member's proportionate share of the Company's taxable income or loss.

**Krystal Biotech, Inc. (formerly Krystal Biotech, LLC)**  
**Notes to Financial Statements — Continued**

For the year ended December 31, 2017 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, we record deferred tax assets and liabilities for the expected future tax consequences of temporary differences between the financial statement carrying amounts and the tax basis of assets and liabilities using enacted tax rates expected to be in effect when the differences are expected to reverse. Valuation allowances are provided when necessary to reduce net deferred tax assets to the amount that is more likely than not to be realized. Based on the available evidence, we are unable, at this time, to support the determination that it is more likely than not that our deferred tax assets will be utilized in the future. Accordingly, we recorded a full valuation allowance as of December 31, 2017. We intend to maintain valuation allowances until sufficient evidence exists to support their reversal.

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, the Company did not have any significant uncertain tax positions.

The Company may recognize interest and penalties related to uncertain tax positions in income tax expense. As of December 31, 2017 and 2016, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in the Company’s statements of operations.

***Comprehensive Loss***

Comprehensive loss is defined as the change in equity during a period from transactions and other events and circumstances from non-owner sources. The Company is required to record all components of comprehensive loss in the financial statements in the period in which they are recognized. Net loss and other comprehensive loss are reported, net of their related tax effect, to arrive at a comprehensive loss. For the years ended December 31, 2017 and 2016, comprehensive loss was equal to the net loss.

***Recent Accounting Pronouncements***

In February 2016, the FASB issued *ASU 2016-02 Leases (Topic 842)* (“ASU 2016-02”), which replaces the existing lease accounting standards. The new standard requires a dual approach for lessee accounting under which a lessee would account for leases as finance (also referred to as capital) leases or operating leases. Both finance leases and operating leases will result in the lessee recognizing a right-of-use asset and corresponding lease liability. For finance leases the lessee would recognize interest expense and amortization of the right-of-use asset and for operating leases the lessee would recognize straight-line total lease expense. ASU 2016-02 is effective for fiscal years, and periods within those years, beginning after December 15, 2018. The Company generally does not finance purchases of equipment but it does lease office and lab facilities. The Company is in the process of evaluating the effect that this ASU will have on its financial statements and related disclosures.

**3. Net Loss Per Share Attributable to Common Stockholders and Members**

On March 31, 2017, the Company converted from an LLC to a C-corporation. Upon the conversion, each outstanding common unit and preferred unit (Note 8) was converted into one share of common stock and preferred stock, respectively. Common units had similar rights and characteristics of common stock issued upon the conversion. In calculating net loss per share, the Company retrospectively applied the effects of the conversion to the number of common units outstanding prior to the conversion. Net loss per share for periods prior to the conversion to a C-corporation refers to net loss per common unit.

Basic net loss per share attributable to common stockholders is calculated by dividing net loss attributable to common stockholders by the weighted average shares outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share attributable to common stockholders is computed by dividing the net loss by the weighted-average number of shares of common stock and common share equivalents outstanding for the period. Preferred stock and stock options are common share equivalents. There were 185,332 and 142,105 common stock equivalents outstanding as of December 31, 2017 and 2016, respectively, in the form of vested and unvested stock options that have been excluded from the calculation of diluted net loss per share attributable to common stockholders as their effect would be anti-dilutive for all periods presented. Therefore, basic and diluted net loss per share and per unit were the same for all periods presented.

**Krystal Biotech, Inc. (formerly Krystal Biotech, LLC)**  
**Notes to Financial Statements — Continued**

(In thousands, except shares, units, per share and per unit data)	Year Ended December 31,	
	2017	2016
<b>Numerator:</b>		
Net loss applicable to common stockholders and members	\$ (7,920)	\$ (1,150)
<b>Denominator:</b>		
Weighted-average basic and diluted common shares and common units	5,360,536	877,490
Basic and diluted net loss per common share and common unit	\$ (1.48)	\$ (1.31)

**4. Balance Sheet Components**

***Property and Equipment, Net***

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

	December 31,	
	2017	2016
Computer equipment and software	\$ 11	\$ 8
Laboratory equipment	214	7
Total property and equipment	225	15
Accumulated depreciation and amortization	(25)	(2)
Property and equipment, net	\$ 200	\$ 13

Depreciation expense was \$23 thousand and \$2 thousand for the years ended December 31, 2017 and 2016, respectively.

***Accrued Expenses and Other Current Liabilities***

Accrued expenses and other current liabilities consisted of the following (in thousands):

	December 31,	
	2017	2016
Accrued pre-clinical expenses	\$ 257	\$ —
Accrued Professional fees	77	—
Accrued payroll and benefits	10	—
Accrued taxes	103	1
Total	\$ 447	\$ 1

**5. Convertible Promissory Notes**

***General***

On November 16, 2016, the Company entered into a Note Purchase Agreement (the “Note Purchase Agreement”) for the issuance of convertible promissory notes (the “Notes”) due May 2018. The Notes bore interest at a rate of 6% per annum, which accrued based on a 365-day year. The Notes would have become immediately due and payable in the event of an occurrence of default by the Company. In accordance with their terms, as amended in July 2017, the principal and accrued interest under the Notes were converted into an aggregate of 968,053 shares of preferred stock upon the closing of the Sun Pharma Offering (as defined in Note 8) on August 8, 2017. These shares of preferred stock were then converted into shares of common stock on a 1-to-1 basis upon closing of the IPO.

***Conversion Features***

The terms of the Notes provided that, in the event the Company sells, merges, consolidates or reorganizes, where the equity owners of the Company own less than 50% of the voting shares post acquisition, then all the outstanding Notes, at the option of the Note holders, either: (i) become immediately due and payable, or (ii) convert into a number of shares of

**Krystal Biotech, Inc. (formerly Krystal Biotech, LLC)**  
**Notes to Financial Statements — Continued**

common stock or common units (rounded down to the nearest share), obtained by dividing the outstanding Notes converted by dividing the target valuation of \$16.0 million by the fully diluted shares.

Furthermore, in the event that the Company issued preferred units in the Company to investors for aggregate proceeds to the Company of not less than \$5.0 million, or if the Company converted into a corporation, shares of the preferred stock of the Company (in either case, the “Preferred Securities”), then the Notes would have automatically converted into a number of shares of Preferred Securities equal to the quotient arrived at by dividing the balance of the outstanding Notes so converted by a price per unit or share that is the lesser of: (i) 80% of the per unit or share price of the Preferred Securities issued upon the conversion; or (ii) the target valuation of \$16.0 million divided by the fully diluted units or shares immediately prior to closing of the offering which triggered the conversion.

In July 2017, the Notes were amended so that they would also automatically convert upon the closing of an IPO into shares of common stock.

On August 8, 2017, the Notes plus accrued interest were converted into 968,053 shares of preferred stock upon the closing of the Sun Pharma Offering.

On September 22, 2017, all outstanding shares of preferred stock converted into shares of common stock on a 1-to-1 basis upon the closing of the Company’s IPO.

As of December 31, 2017 and December 31, 2016, the Company had outstanding balances related to the Notes of \$0 and \$1.8 million, respectively. Additionally, as of December 31, 2017 and December 31, 2016, the Company had accrued interest related to the Notes of \$0 and \$7 thousand, respectively.

Interest expense related to the Notes was \$106 thousand and \$7 thousand for the years ended December 31, 2017 and 2016, respectively.

## **6 Related Party Convertible Promissory Notes**

On November 14, 2016, the Company issued a \$250 thousand convertible promissory note pursuant to the Note Purchase Agreement (Note 5) to a party related to a director of the Company. The terms of the Notes issued to the related party were negotiated at arm’s length and are identical to those of the Notes discussed in Note 5.

On December 27, 2016, the Company issued a \$448 thousand convertible promissory note pursuant to the Note Purchase Agreement (Note 5) to an affiliate of two executive officers and directors of the Company. The terms of the Notes issued to the related party were negotiated at arm’s-length and are identical to those of the Notes discussed in Note 5.

On May 17, 2017, the Company issued a \$250 thousand convertible promissory note pursuant to the Note Purchase Agreement (Note 5) to an affiliate of a director of the Company. The terms of the Notes issued to the related party were negotiated at arm’s length and are identical to those of the Notes discussed in Note 5.

On June 6, 2017, the Company executed a second Note Purchase Agreement (the “Second Note Purchase Agreement”) for the issuance of a \$750 thousand convertible promissory note to a director of the Company (the “June Note”) due May 2018. The June Note bore interest at a rate of 6% per annum, which is accrued based on a 365 day year. The June Note would have become immediately due and payable in the event of an occurrence of default by the Company.

### ***Conversion Features***

The June Note was convertible into shares of preferred stock automatically upon our closing of a preferred stock financing of at least \$5.0 million, or into shares of common stock upon the closing of an initial public offering. The conversion price of the June Note is 80% of the sales price of the preferred stock or 80% of the price at which our common stock is offered to the public in an initial public offering.

On August 8, 2017, upon the closing of the Sun Pharma Offering, the Notes and the June Note plus accrued interest thereon, consisting of \$40 thousand, were converted into 360,311 shares of preferred stock. On September 22, 2017, all outstanding shares of preferred stock converted into 2,061,773 shares of common stock on a 1-to-1 basis upon the closing of the IPO.



**Krystal Biotech, Inc. (formerly Krystal Biotech, LLC)**  
**Notes to Financial Statements — Continued**

As of December 31, 2017 and 2016, accrued interest on related party convertible promissory notes was \$0 and \$2 thousand, respectively.

Interest expense related to the related party convertible promissory notes was \$37 thousand and \$2 thousand for the years ended December 31, 2017 and 2016, respectively.

**7 Commitments and Contingencies**

***Significant Contracts and Agreements***

*Lease Agreement*

In May 2016, the Company signed an operating lease for laboratory and office space that commenced in June 2016 and expired on October 31, 2017 (the “2016 Lease”). In June 2016, the Company entered into an amendment to the 2016 Lease which amended the timing of the rent payment from one single payment to 17 equal monthly installments. On February 27, 2017, the Company entered into a second amendment to the 2016 Lease, which extended the expiration date of the 2016 Lease to October 31, 2018.

As of December 31, 2017, future minimum operating lease payments and future minimum payments to be received from non-cancelable subleases were as follows (in thousands):

	<u>Operating Leases</u>
2018	102
2019	—
2020	—
2021	—
2022	—
Thereafter	—
Future minimum operating lease payments	102
Less: minimum payments to be received from non-cancelable subleases	(18)
Total minimum lease payments, net	<u>\$ 84</u>

The Company recorded \$86 thousand and \$54 thousand in rent expense for the years ended December 31, 2017 and 2016, respectively.

*Clinical Supply Agreements*

The Company has entered into various product manufacturing and clinical supply agreements with Contract Manufacturing Organizations (the “CMOs”). The product manufacturing and clinical supply agreements provide the terms and conditions under which the CMOs will formulate, fill, inspect, package, label and test our products, KB103 and KB105 for clinical supply. The Company is obligated to make milestone payments. Additionally, certain raw materials, supplies, outsourced testing and other services for the purposes of batch production will be invoiced separately by the CMOs. The estimated remaining commitment as of December 31, 2017 under these agreements for the manufacturing of our drug product is approximately \$289 thousand. The Company is also responsible for the payment of a monthly service fee for project management services for the duration of the arrangement. The Company has incurred expenses under these agreements of \$1.5 million and \$11 thousand for the years ended December 31, 2017 and 2016, respectively.

**8. Capitalization**

***Conversion to C-Corporation***

On March 31, 2017, the Company converted from an LLC to a C-Corporation. Upon the conversion, all outstanding preferred units and common units were converted on a 1-to-1 basis into shares of preferred stock and common stock, respectively. Following the conversion, the Company had 450,000 authorized shares of preferred stock, \$0.00001 par value per share, of which 179,613 shares were issued and outstanding and 45,000,000 authorized shares of common stock, par value \$0.00001 per share, of which 3,490,884 shares were issued and outstanding.

**Krystal Biotech, Inc. (formerly Krystal Biotech, LLC)**  
**Notes to Financial Statements — Continued**

***Initial Public Offering***

On September 22, 2017, the Company completed its IPO of 4,554,000 shares of its common stock at a price to the public of \$10.00 per share, which includes the sale of 594,000 shares of the Company's common stock pursuant to the underwriters' full exercise of their option to purchase additional shares. The total proceeds from the offering to the Company, net of underwriting discounts and commissions of approximately \$3.2 million, were approximately \$42.3 million. After deducting offering expenses payable by the Company of approximately \$1.6 million, net proceeds to the Company were approximately \$40.7 million. Immediately prior to the closing of the IPO, all outstanding shares of the Company's preferred stock converted into 2,061,773 shares of common stock on a 1-to-1 basis.

***Sale of Common Stock***

On August 25, 2017, following the completion of the Sun Pharma Offering, Daniel S. Janney, a member of our board of directors, purchased 130,590 shares of our common stock at the same price per share paid by Sun Pharma, \$7.66 per share, through an investment entity owned and controlled by a board member for a total consideration of approximately \$1.0 million.

On November 1, 2017, the Company entered into a stock purchase agreement (the "Agreement") with the Epidermolysis Bullosa Medical Research Foundation, a California not-for-profit corporation ("EBMRF"), and EB Research Partnership, Inc., a New York not-for-profit corporation ("EBRP" and together with EBMRF, the "Purchasers"), pursuant to which the Company has agreed to issue and sell, and the Purchasers have agreed to purchase, an aggregate of 70,000 shares of the Company's common stock, par value \$0.00001 per share, for a purchase price of \$11.00 per share, resulting in aggregate gross proceeds to the Company of \$770,000 (the "Transaction"). The Company intends to commence work on or before September 1, 2018 and to use the proceeds exclusively to complete the research plan pursuant to the Agreement. There is a redemption feature whereby the Company shall repurchase all or a portion of the shares at a purchase price of \$11.00 per share or the closing trading price of the common stock on the redemption request date, whichever is higher, should the Company not commence work on or before September 1, 2018 or cease commercially reasonable efforts. As the redemption feature is within the control of the Company, the common stock issued pursuant to this Agreement is classified as permanent equity. The offer, sale and issuance of the shares of the Company are exempt from registration pursuant to Rule 506 of Regulation D and Section 4(a)(2) of the Securities Act of 1933, as amended. Pursuant to the Agreement, the Purchasers have agreed they are acquiring the securities for investment only and not with a view to or for sale in connection with any distribution thereof and appropriate legends are to be affixed to the securities to be issued in conjunction with the Agreement. The Purchasers are subject to a six month lock-up, and the shares purchased under the terms of the Agreement will be subject to restrictions on selling, transferring or otherwise disposing of such shares. The Transaction closed on November 2, 2017.

***Shares Outstanding***

As of December 31, 2017, 10,307,247 shares of common stock were outstanding. As of December 31, 2017, no shares of preferred stock were outstanding.

As of December 31, 2016, 3,490,884 common units and 179,613 preferred units were outstanding.

***Issuance of Preferred Stock and Conversion of Convertible Promissory Notes and Related Party Convertible Promissory Notes***

On August 4, 2017, the Company amended its articles of incorporation to authorize 1,500,000 shares of common stock, par value \$0.00001 per share, and 1,500,000 shares of preferred stock, par value \$0.00001 per share, of which 179,613 shares were designated as Series Seed preferred stock (the "Series Seed Preferred Stock"), 210,000 shares were designated as Series A preferred stock (the "Series A Preferred Stock"), 200,000 shares were designated as Series A-1 preferred stock (the "Series A-1 Preferred Stock") and 30,000 shares were designated as Series A-2 preferred stock (the "Series A-2 Preferred Stock"). The Series Seed Preferred Stock, Series A-1 Preferred Stock and Series A-2 Preferred Stock are collectively known as the preferred stock.

On August 8, 2017, the Company issued 914,107 shares of Series A Preferred Stock to a single investor ("Sun Pharma") at a purchase price of \$7.66 per share for aggregate proceeds of approximately \$7.0 million (the "Sun Pharma Offering"). Concurrently with the issuance of the Series A Preferred Stock, and in accordance with the conversion features of the Notes (Note 5), all outstanding Notes plus accrued interest thereon were automatically converted into shares of preferred stock. As the conversion price per share of preferred stock was lower than the market price of each share of preferred stock

**Krystal Biotech, Inc. (formerly Krystal Biotech, LLC)**  
**Notes to Financial Statements — Continued**

on the date of conversion, an interest expense of \$3.2 million was recorded upon conversion representing this beneficial conversion feature.

The following table outlines the conversion on August 8, 2017 of the Notes into shares of preferred stock (in thousands except share and per share amounts):

	Principal	Accrued Interest	Total	Conversion Price Per Share (1)		Shares of Series A-1	Shares of Series A-2	Fair Value Date of Conversion	Fair Value Series A-1	Fair Value Series A-2	Loss on Extinguishment of Convertible Promissory Notes
Convertible promissory notes	\$ 2,444	\$ 72	\$ 2,516	\$ 4.14	(1)	607,743	—	\$ 7.66	\$ 4,654	\$ —	\$ (2,138)
Related party convertible promissory notes	948	32	980	\$ 4.14	(1)	236,619	—	\$ 7.66	1,812	—	(832)
Related party convertible promissory notes—June Note	750	8	758	\$ 6.13	(2)	—	123,691	\$ 7.66	—	947	(189)
Total related party promissory notes	1,698	40	1,738			236,619	123,691		1,812	947	(1,021)
<b>Total</b>	<b>\$ 4,142</b>	<b>\$ 112</b>	<b>\$ 4,254</b>			<b>844,362</b>	<b>123,691</b>		<b>\$ 6,466</b>	<b>\$ 947</b>	<b>\$ (3,159)</b>

(1) The conversion price was determined by dividing the target valuation of \$16 million by the outstanding shares of 3,863,547 immediately prior to the issuance of the Series A on August 8, 2017 (Note 5).

(2) The conversion price was determined to be 80% of the \$7.66 sales price per share of the Series A shares issued on August 8, 2017 (Note 6).

***Preferred Units and Preferred Stock***

On April 15, 2016, the Company authorized 100 member units and issued 450 member units for aggregate proceeds of \$100 thousand. On December 31, 2017, the Company converted all of the member units into 12,771 preferred units at an issue price of \$7.83 (the “Original Issue Price”) per share plus 3,490,884 common units, and issued an additional 96,345 preferred units at the Original Issue Price for aggregate proceeds of \$754 thousand. On December 27, 2016, the Company issued an additional 70,497 preferred units at the Original Issue Price for aggregate proceeds of \$552 thousand. On March 31, 2017, all of the preferred units were converted into preferred stock on a 1-to-1 basis. As of September 22, 2017, all of the preferred stock was converted to common stock in connection with the Company’s IPO (Note 1). As of December 31, 2017 and December 31, 2016, the Company had balances of preferred units of \$0 and \$1.4 million, respectively.

The rights, preferences and privileges of the preferred stock consisted of the following:

**Conversion.** Each share of preferred stock shall be convertible at the option of the holder at any point in time into fully paid and non-assessable shares of common stock. Upon conversion, the preferred stock would be fully settled. Each share of preferred stock was convertible into that number of shares of common stock as determined by dividing the Original Issue Price of such share by the applicable conversion price. As of December 31, 2016, the conversion rate was 1-to-1, but was subject to future adjustments to the conversion price upon the occurrence of certain events including: (i) certain issuances of common stock at a price less than the conversion price in effect on the date of such issuance; and (ii) future stock splits, subdivisions, or combinations of outstanding common stock.

Each share of preferred stock shall automatically be converted into shares of common stock at the conversion price at the time in effect for such series of preferred upon the earlier of: (i) a qualified public offering, as defined in the Certificate of Incorporation; or (ii) the majority vote of the holders of preferred stock on a per share and as-converted to common stock basis.

**Voting Rights.** The holders of shares of preferred stock are entitled to one vote for each share of preferred stock held at all meetings of stockholders and written actions in lieu of meetings. The Board shall be elected by vote of the common stock and the preferred stock voting together as a single class on an as-converted basis.

**Dividends.** The holders of the preferred stock are entitled to receive dividends, if and when declared by the Board, and all dividends shall be paid pro rata on the common stock and the preferred stock, without preference, based on the number of shares of the common stock of the holders. From inception through December 31, 2017, no dividends have been declared or paid by the Company.

**Krystal Biotech, Inc. (formerly Krystal Biotech, LLC)**  
**Notes to Financial Statements — Continued**

*Liquidation Preference.* In the event of any liquidation, dissolution, winding up, consolidation or merger of the Company, the holders of the preferred stock shall be entitled to receive out of the assets of the Company, prior and in preference to any distribution to the holders of common stock, an amount equal to the Original Issue Price per share, plus all declared and unpaid dividends.

The preferred units have the same rights, preferences and privileges as the preferred stock with the exception of conversion rights or liquidation preferences in the event of a merger or consolidation.

**Common Units and Common Stock**

On December 31, 2016, in connection with the conversion of the member units into preferred units, the Company also issued 3,490,884 common units. On March 31, 2017, in connection with the conversion of the LLC to a C-Corporation, all of the common units were converted, on a 1-to-1 basis, into shares of common stock.

The voting, dividend and liquidation rights of the holders of the common stock are subject to and qualified by the rights, powers and privileges of the holders of the preferred stock and are as follows:

*Voting Rights.* The holders of shares of common stock are entitled to one vote for each share of common stock held at all meetings of stockholders and written actions in lieu of meetings. The Board shall be elected by vote of the Common Stock and the Preferred stock voting together as a single class on an as-converted basis.

*Dividends.* The holders of the common stock are entitled to receive dividends, if and when declared by the Board, and all dividends shall be paid pro rata on the common stock and the preferred stock, without preference, based on the number of shares of the common stock of the holders. From inception through December 31, 2017, no dividends have been declared or paid by the Company.

*Liquidation Preference.* After payment to the holders of shares of preferred stock of their liquidation preferences, the holders of the common stock are entitled to share ratably in the Company's assets available for distribution to stockholders, in the event of any voluntary or involuntary liquidation, dissolution, winding up, consolidation or merger of the Company or upon the occurrence of a deemed liquidation event.

**9. Stock-Based Compensation**

On October 1, 2016, the Board of Managers adopted the 2016 Equity Incentive Plan (the "2016 Plan"), which authorized the issuance of up to 189,472 incentive units to purchase common units.

The 2016 Plan provided for the issuance of incentive units to employees, members of the Board, and consultants of the Company. The incentive units generally expire ten years following the date of grant. The incentive units typically vest over a period of four years, however vesting provisions can vary by award based on the discretion of the Board. Incentive units to purchase common units carry an exercise price equal to the estimated fair value of the Company's common units on the date of grant. Generally, incentive units to purchase common units of the Company are exercised by payment of the exercise price in cash. Upon the termination of service, except by death or disability, of a holder of incentive units awarded under the 2016 Plan, all unvested units are forfeited and vested incentive units may be exercised within three months of termination by the holder. Common units issued as a result of awards under the 2016 Plan may be subject to repurchase provisions as designated in each individual award agreement.

On March 31, 2017, the Board adopted the 2017 Stock Incentive Plan (the "2017 Plan") which authorized the issuance of up to 193,050 shares of the Company's common stock under the plan. Commensurate with the opening of the 2017 Plan, all 113,683 outstanding incentive units granted under the 2016 Plan were converted into 113,683 options to purchase the Company's common stock under the 2017 Plan. Upon the adoption of the 2017 Plan, the 2016 Plan terminated and there were no incentive units outstanding.

The 2017 Plan provided for the issuance of stock options, restricted stock awards and unrestricted stock awards to employees, members of the Board, and consultants of the Company. The Company has not granted restricted or unrestricted stock awards under the 2017 Plan since its inception. Options generally expire ten years following the date of grant. Options typically vest over a period of four years, however vesting provisions can vary by award based on the discretion of the Board. Options to purchase common stock carry an exercise price equal to the estimated fair value of the Company's common stock

**Krystal Biotech, Inc. (formerly Krystal Biotech, LLC)**  
**Notes to Financial Statements — Continued**

on the date of grant. Generally, options to purchase shares of the Company's common stock are exercised by payment of the exercise price in cash. Upon the termination of service, except by death or disability, of a holder of stock options awarded under the 2017 Plan, all unvested options are forfeited and vested options may be exercised within three months of termination by the holder. Shares of common stock issued as a result of awards under the 2017 Plan may be subject to repurchase provisions as designated in each individual award agreement. The 2017 Plan terminated upon the adoption of the 2017 IPO Plan (as defined below).

On September 5, 2017, the Board approved the establishment of the Krystal Biotech, Inc. 2017 IPO Plan (the "2017 IPO Plan"), which was adopted prior to the effectiveness of our registration statement. Under the 2017 IPO Plan, the Company may grant incentive stock options, non-qualified stock options, stock appreciation rights, dividend equivalent rights, restricted stock, and stock grants to purchase up to 900,000 shares of the Company's Common Stock.

The Company granted 71,649 and 142,105 stock options during the years ended December 31, 2017 and 2016, respectively, to employees, consultants and member of the Board, which are included in the following table. The options vest ratably over a four-year period, and have a life of ten years. Stock options issued to non-employees are accounted for using the fair value method of accounting, and are periodically revalued as the options vest, and are recognized as expense over the related service period.

The following table summarizes the Company's stock option activity:

	Shares	Weighted- average Exercise Price	Weighted- average Remaining Contractual Life (Years)	Aggregate Intrinsic Value (In thousands) (1)
Outstanding at January 1, 2016	—			
Granted	142,105	\$ 2.46	9.7	
Exercised	—			
Cancelled or forfeited	—			
Outstanding at December 31, 2016	142,105	\$ 2.46	9.7	\$ 338
Granted	71,649	\$ 6.22		
Exercised	—			
Cancelled or forfeited	(28,422)	\$ 2.46		
Outstanding at December 31, 2017	<u>185,332</u>	<u>\$ 3.91</u>	<u>9.0</u>	<u>1,224</u>
Exercisable at December 31, 2017	<u>43,221</u>	<u>\$ 2.46</u>	<u>8.7</u>	<u>\$ 348</u>
Vested at December 31, 2017	<u>43,221</u>	<u>\$ 2.46</u>	<u>8.7</u>	<u>\$ 348</u>

- (1) The aggregate intrinsic value is calculated as the difference between the exercise price of the underlying options and the estimated fair value of the common stock for the options that were in the money at December 31, 2017 and December 31, 2016.

As of December 31, 2017, 900,000 shares of common stock were available for future grants under the 2017 IPO Plan.

The weighted-average grant-date fair value of options granted to employees during the year ended December 31, 2017 was \$6.42.

**Krystal Biotech, Inc. (formerly Krystal Biotech, LLC)**  
**Notes to Financial Statements — Continued**

Stock-based compensation expense for the years ended December 31, 2017 and 2016 relates solely to stock options granted under the 2017 Plan. The Company has recorded aggregate stock-based compensation expense related to the issuance of stock option awards to employees and non-employees in the statement of operations for the three and year ended December 31, 2017 and 2016 as follows (in thousands):

	Year Ended December 31,	
	2017	2016
Research and development	\$ 151	\$ 25
General and administrative	95	8
<b>Total stock-based compensation</b>	<b>\$ 246</b>	<b>\$ 33</b>

*Stock Options Granted to Employees.* For the and years ended December 31, 2017 and 2016, the Company recorded \$130 thousand and \$3 thousand, respectively, of stock-based compensation expense related to employees' stock options. For the year ended December 31, 2016, the Company had no employees. The fair value of options granted to employees was estimated at the date of grant using the Black-Scholes valuation model with the following weighted-average assumptions for the years ended December 31, 2017 and 2016:

	Year Ended December 31,	
	2017	2016
Expected stock price volatility	80%	—
Expected term of the award (years)	6.25	—
Risk-free interest rate	1.93%	—
Exercise price	\$ 6.22	—

There was \$623 thousand of unrecognized stock-based compensation expense related to employees' awards that is expected to be recognized over a weighted-average period of 3.0 years as of December 31, 2017.

*Stock Options Granted to Non-Employees.* Stock-based compensation expense related to stock options granted to non-employees is recognized as the stock options are earned. The Company believes that the estimated fair value of the stock options is more readily measurable than the fair value of the services rendered. For the year ended December 31, 2017 and 2016, the Company recorded \$116 thousand and \$30 thousand, respectively, of stock-based compensation expense related to non-employees' stock options.

The Company used the following weighted-average assumptions in estimating non-employee stock-based compensation expense:

The Company used the following weighted-average assumptions in estimating non-employee stock-based compensation expense:

	Year Ended December 31,	
	2017	2016
Expected stock price volatility	—	80%
Expected term of the award (years)	—	6.25
Risk-free interest rate	—	1.97%
Exercise price	— \$	2.46

There was \$93 thousand of unrecognized stock-based compensation expense related to non-employees' awards that is expected to be recognized over a weighted-average period of 2.9 years as of December 31, 2017.

There were no options granted to non-employees in the year ended December 31, 2017.

## 10. Income Taxes

From inception through December 31, 2016, the Company was a California LLC for federal and state income tax purposes, and therefore, all items of income or loss through December 31, 2016 flowed through to the members of the LLC. Effective January 1, 2017, the Company converted from an LLC to a C-corporation for federal and state income tax purposes. Prior to the conversion to a C-corporation, the Company did not record deferred tax assets or liabilities or have any net

**Krystal Biotech, Inc. (formerly Krystal Biotech, LLC)**  
**Notes to Financial Statements — Continued**

operating loss (“NOL”) carryforwards for federal income tax purposes. Effective upon the conversion to a C-corporation, the Company became subject to income tax at the federal and state levels.

We did not record a current or deferred income tax expense or benefit for the years ended December 31, 2017 and 2016. As we were an LLC for the year ended December 31, 2016, we were not subject to federal income tax. A reconciliation of income tax expense (benefit) computed at the statutory federal and state income tax rate of 28% for the year to income tax expense (benefit) as reflected in our financial statements for years ended December 31, 2017 and 2016 are as follows (in thousands):

	<b>December 31,</b>
	<b>2017</b>
Federal income tax expense (benefit) at statutory rate	\$ (2,693)
Change in valuation allowance	2,164
Impact of US tax reform	1,022
State income tax expense net of federal benefit	(514)
Other non-deductible expenses	21
Total tax expense (benefit)	\$ —

The significant components of the Company’s deferred tax assets as of December 31, 2017 are as follows (in thousands):

	<b>December 31,</b>
	<b>2017</b>
Deferred tax assets:	
Net operating loss carryforwards	\$ 2,029
Non-qualified option	29
Depreciation	(31)
Accrued expenses	137
Total deferred tax assets	2,164
Valuation allowance	(2,164)
Net deferred tax assets	\$ —

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, the Company has concluded that it is more likely than not that the benefit of its deferred tax assets will not be realized. Accordingly, the Company has provided a full valuation allowance for deferred tax assets as of December 31, 2017.

As of December 31, 2016, the Company had U.S. federal NOL carryforwards of approximately \$0 as the company was a flow-through entity. As of December 31, 2017, the Company had U.S. federal NOL carryforwards of approximately \$7.4 million which may be available to offset future income tax liabilities and expire at various dates through 2037.

Under the provisions of the Internal Revenue Code, the NOL carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. NOL carryforwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Internal Revenue Code, respectively, as well as similar state provisions. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. The Company has completed several financings since its inception which may have resulted in a change in control as defined by Sections 382 and 383 of the Internal Revenue Code, or could result in a change in control in the future.

Under 2017 Tax Cuts and Jobs Act, NOL deductions for NOLs arising in the tax years beginning after December 31, 2017 will be limited to 80% of taxable income and NOL carrybacks will be eliminated.

The Company files income tax returns in the United States at the federal level and in states in which the Company conducts business activities. The federal and state income tax returns are generally subject to tax examinations for the tax

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**Notes to Financial Statements — Continued**

year ended December 31, 2017. To the extent the Company has tax attribute carryforwards, the tax years in which the attribute was generated may still be adjusted upon examination by the Internal Revenue Service or state tax authorities to the extent utilized in a future period.

**11. Related Party Transactions**

*Convertible Promissory Notes*

As of December 31, 2017 and December 31, 2016, the Company had balances of \$0 and \$698 thousand in related party convertible promissory notes, respectively, as disclosed in Note 6.

*Preferred Units*

As of December 31, 2017 and December 31, 2016, the Company had outstanding balances of \$0 and \$1.4 million of preferred units, respectively. The preferred units (Note 8) as of December 31, 2016 were all held by the Chief Executive Officer and Chief Operating Officer of the Company.

*Sale of Common Stock*

On August 8, 2017, the Company issued 914,107 shares of Series A Preferred Stock to Sun Pharma at a purchase price of \$7.66 per share for aggregate proceeds of approximately \$7.0 million. Sun Pharma is affiliated with a member of the Board.

On August 25, 2017, the Company closed the sale of 130,590 shares of common stock with an affiliate of a member of the Board for aggregate proceeds of \$1.0 million.

In connection with our IPO, our Chief Executive Officer and Chief Operating Officer of the Company each purchased 100,000 shares of common stock at the offering price of \$10 per share.



**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***

Under the supervision of our Chief Executive Officer and Chief Financial Officer, we evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) of the Exchange Act as of December 31, 2017. Based on that evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that our disclosure controls and procedures were effective as of December 31, 2017 to ensure that information required to be disclosed by us in the reports we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate to allow timely discussion regarding required disclosures. In designing and evaluating our disclosure controls and procedures, management recognizes that any disclosure controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply its judgment in evaluating the benefits of possible controls and procedures relative to their costs.

***Management's Report on Internal Control over Financial Reporting***

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rules 13a-15(f) and 15d-15(f). Our management 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* (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission.

Based on the results of its evaluation, management concluded that our internal control over financial reporting was effective as of December 31, 2017.

***Inherent Limitations on Controls and Procedures***

Our management, including the Chief Executive Officer and Chief Financial Officer, do not expect that our disclosure controls and procedures and our internal controls will prevent all error and all fraud. A control system, no matter how well designed and operated, can only provide reasonable assurances that the objectives of the control system are met. The design of a control system reflects resource constraints; the benefits of controls must be considered relative to their costs. Because there are inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, within the Company have been or will be detected. As these inherent limitations are known features of the financial reporting process, it is possible to design into the process safeguards to reduce, though not eliminate, these risks. These inherent limitations include the realities that judgments in decision-making can be faulty and that breakdowns occur because of simple error or mistake. Controls can be circumvented by the individual acts of some persons, by collusion of two or more people, or by management override of the control. The design of any system of controls is based in part upon certain assumptions about the likelihood of future events. While our disclosure controls and procedures are designed to provide reasonable assurance of achieving their objectives, there can be no assurance that any design will succeed in achieving its stated goals under all future conditions. Over time, controls may become inadequate because of changes in conditions or deterioration in the degree of compliance with the policies or procedures. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

We intend to review and evaluate the design and effectiveness of our disclosure controls and procedures on an ongoing basis and to improve our controls and procedures over time and to correct any deficiencies that we may discover in the future. While our Chief Executive Officer and Chief Financial Officer have concluded that, as of December 31, 2017, the design of our disclosure controls and procedures, as defined in Rule 13a-15(e) under the Exchange Act, was effective, future events affecting our business may cause us to significantly modify our disclosure controls and procedures.

***Changes in Internal Control over Financial Reporting***

There was no change in our internal control over financial reporting identified in connection with the evaluation required by Rules 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the three months ended December 31, 2017 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

***Report of the Independent Registered Public Accounting Firm***

This Annual Report on 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.”

**Item 9B. Other Information.**

On March 8, 2018, Antony A. Riley was appointed Chief Financial Officer after serving in that position on an interim basis. Mr. Riley has over 20 years of financial management experience including as partner at the CFO Network LLC, a consulting firm, Acting Chief Financial Officer at Avanex Corporation and Corporate Controller at Kosan Biosciences. He received a B.Sc. from the University of Bristol and an M.B.A. from the University of Chicago Booth School of Business. Mr. Riley is a Certified Public Accountant (inactive) in the state of California.

Mr. Riley has entered into an “at-will” employment agreement with us, effective as of March 8, 2018, which provides for an annual base salary of \$120,000 and benefits made available by us to similarly-situated employees. In connection with his appointment, our board of directors approved a grant to Mr. Riley of an option to purchase 25,000 shares of common stock under the Krystal Biotech, Inc. 2017 IPO Plan and will vest ratably over four years. Mr. Riley’s employment agreement also provides that he will be bound by the terms of our Proprietary Information and Inventions Agreement and that he shall not disclose to us any third party proprietary information or trade secrets

There are no reportable family relationships between Mr. Riley and us and there have been no transactions between Mr. Riley and us that would require disclosure pursuant to Item 404(a) of Regulation S-K.

The foregoing description of Mr. Riley’s employment agreement does not purport to be complete and is qualified in its entirety by reference to the full text of the employment agreement, which is filed as Exhibit 10.1 to this Annual Report on Form 10-K and is incorporated herein by reference.

### PART III

#### **Item 10. Directors, Executive Officers and Corporate Governance.**

Information required by this Item is hereby incorporated by reference to our Definitive Proxy Statement.

We have adopted a Code of Conduct that applies to our officers, directors and employees which is available on our internet website at [www.krystalbio.com](http://www.krystalbio.com). The Code of Conduct contains general guidelines for conducting the business of our company consistent with the highest standards of business ethics, and is intended to qualify as a “code of ethics” within the meaning of Section 406 of the Sarbanes-Oxley Act of 2002 and Item 406 of Regulation S-K. In addition, we intend to promptly disclose (1) the nature of any amendment to our Code of Conduct that applies to our principal executive officer, principal financial officer, principal accounting officer or controller or persons performing similar functions and (2) the nature of any waiver, including an implicit waiver, from a provision of our code of ethics that is granted to one of these specified officers, the name of such person who is granted the waiver and the date of the waiver on our website in the future.

#### **Item 11. Executive Compensation.**

Information required by this Item is hereby incorporated by reference to our Definitive Proxy Statement.

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

Information required by this Item is hereby incorporated by reference to our Definitive Proxy Statement.

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

Information required by this Item is hereby incorporated by reference to our Definitive Proxy Statement.

#### **Item 14. Principal Accounting Fees and Services.**

Information required by this Item is hereby incorporated by reference to our Definitive Proxy Statement.

## PART IV

### Item 15. Exhibits, Financial Statement Schedules.

(a) List the following documents filed as a part of the report:

(1) Financial statements

The response to this portion of Item 15 is set forth under Item 8 above.

(2) Financial statement schedule.

All schedules have been omitted because they are not required or because the required information is given in the financial statements or notes thereto set forth under Item 8 above.

(3) Exhibits.

A list of exhibits filed with this report or incorporated herein by reference can be found in the Exhibit Index immediately following the signature page of this Report.

### Exhibit Index

Exhibit Number	Description
10.1*	<a href="#">Offer of employment to Antony Riley.</a>
23.1*	<a href="#">Consent of Mayer Hoffman McCann P.C.</a>
31.1*	<a href="#">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.</a>
31.2*	<a href="#">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.</a>
32.1*	<a href="#">Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.</a>
32.2*	<a href="#">Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.</a>
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.

### Item 16. Form 10-K Summary.

The Company has elected to not include a summary.

## 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, in the City of Pittsburgh, State of Pennsylvania, on March 12, 2018.

### KRYSTAL BIOTECH, INC.

By: /s/ Krish S. Krishnan  
Krish S. Krishnan  
President and Chief Executive Officer

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Krish S. Krishnan as his or her true and lawful attorney-in-fact and agent, with the full power of substitution, for him or her and in his or her name, place or stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this Annual Report on Form 10-K, and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent, or their, his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

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

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Krish S. Krishnan</u> Krish S. Krishnan	President and Chief Executive Officer and Director (Principal Executive Officer)	March 12, 2018
<u>/s/ Antony A. Riley</u> Antony A. Riley	Chief Financial Officer (Principal Financial Officer)	March 12, 2018
<u>/s/ Suma M. Krishnan</u> Suma M. Krishnan	Chief Operating Officer and Director	March 12, 2018
<u>/s/ Daniel S. Janney</u> Daniel S. Janney	Director	March 12, 2018
<u>/s/ R. Douglas Norby</u> R. Douglas Norby	Director	March 12, 2018
<u>/s/ Dino A. Rossi</u> Dino A. Rossi	Director	March 12, 2018
<u>/s/ Kirti Ganorkar</u> Kirti Ganorkar	Director	March 12, 2018



E M P L O Y M E N T A G R E E M E N T

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This Employment Agreement ("the Agreement"), dated March 8 2018, is between Krystal Biotech, Inc., a Delaware corporation (the "Company") and **Antony Riley**, ("Employee") and reflects the company's and Employee's desire to establish a full employment relationship.

1 . P O S I T I O N A N D R E S P O N S I B I L I T I E S

**a. Position.** Employee is employed by the Company to render services to the Company in the position of **Chief Financial Officer**, reporting to the Chief Executive Officer of the company beginning **March 8, 2018** ("Start Date"). Employee shall perform such duties and responsibilities as are normally related to such position in accordance with the standards of the industry and any additional duties now or hereafter assigned to Employee by the Company. Employee shall abide by the rules, regulations, and practices as adopted or modified from time to time in the Company's sole discretion. Employee's primary location shall be in Pittsburgh, PA. This employment offer is contingent upon the completion of a satisfactory background check.

**b. Other Activities.** Except upon the prior written consent of the Company, Employee will not, during the term of this Agreement, (i) accept any other employment, or (ii) engage, directly or indirectly, in any other business activity (whether or not pursued for pecuniary advantage) that might interfere with Employee's duties and responsibilities hereunder or create a conflict of interest with the Company.

**c. No Conflict.** Employee represents and warrants that Employee's execution of this Agreement, Employee's employment with the Company, and the performance of Employee's proposed duties under this Agreement shall not violate any obligations Employee may have to any other employer, person or entity, including any obligations with respect to proprietary or confidential information of any other person or entity.

2 . C O M P E N S A T I O N A N D B E N E F I T S

**a. Base Salary.** In consideration of the services to be rendered under this Agreement, the Company shall pay Employee a salary at the rate of **ONE HUNDRED TWENTY THOUSAND DOLLARS** (\$120,000) per year ("Base Salary"). The Base Salary shall be paid in accordance with the Company's regularly established payroll practice. Employee's Base Salary will be reviewed from time to time in accordance with the

established procedures of the Company for adjusting salaries for similarly situated employees and may be adjusted in the sole discretion of the Company.

**b. Stock Options.** The company shall recommend the Board of Directors that Employee be provided with an option to purchase 25,000 shares of the Common Stock of the Company, as adjusted by any stock splits that may occur before the options are granted. The price per share of any approved options will be the price to the public at which the Common Stock is offered in the initial public offering or, if an offering is not completed, at the fair market value of the shares as determined by the Board of Directors with the advice of a valuation consultant. Employee's entitlement to any stock options that may be approved is conditioned upon Employee's signing of an appropriate Equity Incentive Agreement and is subject to its terms and the terms of the Equity Incentive Plan under which the options are granted, including vesting requirements.

**c. Benefits.** Employee shall be eligible to participate in the benefits made generally available by the Company to similarly-situated employees, in accordance with the benefit plans established by the Company, and as may be amended from time to time in the Company's sole discretion.

**d. Expenses.** The Company shall reimburse Employee for reasonable business expenses incurred in the performance of Employee's duties hereunder in accordance with the Company's expense reimbursement guidelines.

**3 . A T - W I L L E M P L O Y M E N T ; T E R M I N A T I O N B**

**a. At-Will Termination by Company.** The employment of Employee shall be "at-will" at all times. The Company may terminate Employee's employment with the Company at any time, without any advance notice, for any reason or no reason at all, notwithstanding anything to the contrary contained in or arising from any statements, policies or practices of the Company relating to the employment, discipline or termination of its employees. Upon and after such termination, all obligations of the Company under this Agreement shall cease.

**4 . A T - W I L L E M P L O Y M E N T ; T E R M I N A T I O N B**

**a. At-Will Termination by Employee.** Employee may terminate employment with the Company at any time for any reason or no reason at all, upon thirty days' advance written notice. During such notice period Employee shall continue to diligently perform all of Employee's duties hereunder. The Company shall have the option, in its sole discretion, to make Employee's termination effective at any time prior to the end of such notice period as long as the Company pays Employee all compensation to which Employee is entitled up through the last day of the thirty-day notice period. Thereafter all obligations of the Company shall cease.

5 . T E R M I N A T I O N O B L I G A T I O N S

a. **Return of Property.** Employee agrees that all property (including without limitation all equipment, tangible proprietary information, documents, records, notes, contracts and computer-generated materials) furnished to or created or prepared by Employee incident to Employee's employment belongs to the Company and shall be promptly returned to the Company upon termination of Employee's employment.

b. **Resignation and Cooperation.** Following any termination of employment, Employee shall cooperate with the Company in the winding up of pending work on behalf of the Company and the orderly transfer of work to other employees. Employee shall also cooperate with the Company in the defense of any action brought by any third party against the Company that relates to Employee's employment by the Company.

c. **Continuing Obligations.** Employee understands and agrees that Employee's obligations under Sections 5 and 6 herein (including Exhibit A) shall survive the termination of Employee's employment for any reason and the termination of this Agreement.

6 . I N V E N T I O N S A N D P R O P R I E T A R Y I N F O R M

a. **Proprietary Information Agreement.** Employee agrees to sign and be bound by the terms of the Company's Proprietary Information and Inventions Agreement, which is attached as Exhibit A ("Proprietary Information Agreement").

b. **Non-Disclosure of Third Party Information.** Employee represents and warrants and covenants that Employee shall not disclose to the Company, or use, or induce the Company to use, any proprietary information or trade secrets of others at any time, including but not limited to any proprietary information or trade secrets of any former employer, if any; and Employee acknowledges and agrees that any violation of this provision shall be grounds for Employee's immediate termination and could subject Employee to substantial civil liabilities and criminal penalties. Employee further specifically and expressly acknowledges that no officer or other employee or representative of the Company has requested or instructed Employee to disclose or use any such third party proprietary information or trade secrets.

c. **Noncompetition.** In consideration of the Company's extension to Employee of full time employment with the Company, the Employee agrees that at no time during the Employee's employment with the Company, and for a period of one (1) year immediately following the termination of such employment (regardless of the reason for or the party initiating the termination), the Employee will not, directly or indirectly, on the Employee's own behalf or on behalf of any third party, in any capacity (whether as a proprietor, stockholder, partner, officer, employee, consultant,



contractor, or otherwise), work for, be a consultant for, be employed by, or provide strategic advice to any Competitor, where the services the Employee would render to the Competitor are similar to those which the Employee performed for the Company. As used herein, Competitor means any person or entity that (a) is engaged in the development of products or technologies which may compete with the products or technologies under development by the Company at the time of Employee's termination or within the twelve (12) month period immediately preceding such termination; and (b) is located within the territory of the United States. This provision does not apply to (1) the Employees' passive ownership of not more than 2% of the outstanding, publicly traded securities of another company; and (2) work in a capacity that is unrelated to development or of products or technologies which may compete with those under development by the Company.

**7 . A M E N D M E N T S ; W A I V E R S ; R E M E D I E S**

This Agreement may not be amended or waived except by a writing signed by Employee and by a duly authorized officer of the Company. Failure to exercise any right under this Agreement shall not constitute a waiver of such right. Any waiver of any breach of this Agreement shall not operate as a waiver of any subsequent breaches. All rights or remedies specified for a party herein shall be cumulative and in addition to all other rights and remedies of the party hereunder or under applicable law.

**8 . A S S I G N M E N T ; B I N D I N G E F F E C T**

**a. Assignment.** The performance of Employee is personal hereunder, and Employee agrees that Employee shall have no right to assign and shall not assign or purport to assign any rights or obligations under this Agreement. This Agreement may be assigned or transferred by the Company, including in connection with any conversion of the Company into corporate form; and nothing in this Agreement shall prevent the consolidation, merger or sale of the Company or a sale of any or all or substantially all of its assets.

**b. Binding Effect.** Subject to the foregoing restriction on assignment by Employee, this Agreement shall inure to the benefit of and be binding upon each of the parties; the affiliates, officers, directors, agents, successors and assigns of the Company; and the heirs, devisees, spouses, legal representatives and successors of Employee.

**9 . N O T I C E S**

All notices or other communications required or permitted hereunder shall be made in writing and shall be deemed to have been duly given if delivered: (a) by hand; (b) by a nationally recognized overnight courier service; or (c) by United States first class registered or certified mail, return receipt requested, to the principal address of the

other party, as set forth below. The date of notice shall be deemed to be the earlier of (i) actual receipt of notice by any permitted means, or (ii) five business days following dispatch by overnight delivery service or the United States Mail. Employee shall be obligated to notify the Company in writing of any change in Employee's address. Notice of change of address shall be effective only when done in accordance with this paragraph.

Company's Notice Address:

Krystal Biotech, Inc.  
2100 Wharton Street, Suite 701  
Pittsburgh, PA 15203

Employee's Notice Address:

Anthony Riley

#### **1 0 . S E V E R A B I L I T Y**

If any provision of this Agreement shall be held by a court or arbitrator to be invalid, unenforceable, or void, such provision shall be enforced to the fullest extent permitted by law, and the remainder of this Agreement shall remain in full force and effect. In the event that the time period or scope of any provision is declared by a court or arbitrator of competent jurisdiction to exceed the maximum time period or scope that such court or arbitrator deems enforceable, then such court or arbitrator shall reduce the time period or scope to the maximum time period or scope permitted by law.

#### **1 1 . T A X E S**

All amounts paid under this Agreement (including without limitation Base Salary) shall be paid less all applicable state and federal tax withholdings and any other withholdings required by any applicable jurisdiction or authorized by Employee.

#### **1 2 . G O V E R N I N G L A W**

This Agreement shall be governed by and construed in accordance with the laws of the State of California.

#### **1 3 . I N T E R P R E T A T I O N**

This Agreement shall be construed as a whole, according to its fair meaning, and not in favor of or against any party. Sections and section headings contained in this Agreement are for reference purposes only, and shall not affect in any manner the meaning or interpretation of this Agreement. Whenever the context requires, references to the singular shall include the plural and the plural the singular.

**1 4 . C O U N T E R P A R T S**

This Agreement may be executed in any number of counterparts, each of which shall be deemed an original of this Agreement, but all of which together shall constitute one and the same instrument.

**1 5 . A U T H O R I T Y**

Each party represents and warrants that such party has the right, power and authority to enter into and execute this Agreement and to perform and discharge all of the obligations hereunder; and that this Agreement constitutes the valid and legally binding agreement and obligation of such party and is enforceable in accordance with its terms.

**1 6 . E N T I R E A G R E E M E N T**

This Agreement is intended to be the final, complete, and exclusive statement of the terms of Employee's employment by the Company and may not be contradicted by evidence of any prior or contemporaneous statements or agreements, except for agreements specifically referenced herein (including the Employee Proprietary Information and Inventions Agreement attached as Exhibit A and the Company's Equity Incentive Plan and Equity Incentive Agreement). To the extent that the practices, policies or procedures of the Company, now or in the future, apply to Employee and are inconsistent with the terms of this Agreement, the provisions of this Agreement shall control. Any subsequent change in Employee's duties, position, or compensation will not affect the validity or scope of this Agreement.

**1 7 . E M P L O Y E E A C K N O W L E D G E M E N T**

**Employee acknowledges Employee has had the opportunity to consult legal counsel concerning this agreement, that Employee has read and understands the agreement, that Employee is fully aware of its legal effect, and that Employee has entered into it freely based on Employee's own judgment and not on any representations or promises other than those contained in this agreement.**

**In Witness Whereof**, the parties have duly executed this Agreement as of the date first written above.

**KRYSTAL BIOTECH, INC.**

**Antony Riley:**

By: /s/ Krish Krishnan

/s / Antony Riley

Title: CEO

**CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

We hereby consent to the incorporation by reference in Registration Statement No. 333-220589 on Form S-8 of Krystal Biotech, Inc., of our report dated March 12, 2018, relating to the financial statements, which appears in this Form 10-K.

/s/ Mayer Hoffman McCann P.C.  
San Diego, California  
March 12, 2018

**CERTIFICATION 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**

I, Krish S. Krishnan, certify that:

1. I have reviewed this Annual Report on Form 10-K of Krystal Biotech, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the small business issuer as of, and for, the periods presented in this report;
4. The small business issuer's other certifying officer(s) 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 small business issuer 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 small business issuer, including its 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 small business issuer'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 small business issuer's internal control over financial reporting that occurred during the small business issuer's most recent fiscal quarter (the small business issuer's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the small business issuer's internal control over financial reporting; and
5. The small business issuer's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the small business issuer's auditors and the audit committee of the small business issuer'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 small business issuer'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 small business issuer's internal control over financial reporting.

Date: March 12, 2018

By: \_\_\_\_\_ /s/ Krish S. Krishnan  
Krish S. Krishnan  
President and Chief Executive Officer  
(Principal Executive Officer)

**CERTIFICATION 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**

I, Antony A. Riley, certify that:

1. I have reviewed this Annual Report on Form 10-K of Krystal Biotech, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the small business issuer as of, and for, the periods presented in this report;
4. The small business issuer's other certifying officer(s) 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 small business issuer 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 small business issuer, including its 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 small business issuer'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 small business issuer's internal control over financial reporting that occurred during the small business issuer's most recent fiscal quarter (the small business issuer's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the small business issuer's internal control over financial reporting; and
5. The small business issuer's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the small business issuer's auditors and the audit committee of the small business issuer'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 small business issuer'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 small business issuer's internal control over financial reporting.

Date: March 12, 2018

By: \_\_\_\_\_  
/s/ Antony A. Riley  
Antony A. Riley  
Chief Financial Officer  
(Principal Financial and Accounting Officer)

**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 of Krystal Biotech, Inc. (the "Company") on Form 10-K for the period ending December 31, 2017 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

- (1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: March 12, 2018

By: \_\_\_\_\_  
/s/ Krish S. Krishnan  
Krish S. Krishnan  
President and Chief Executive Officer  
(Principal Executive Officer)



**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 of Krystal Biotech, Inc. (the "Company") on Form 10-K for the period ending December 31, 2017 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

- (1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: March 12, 2018

By: \_\_\_\_\_  
/s/ Antony A. Riley  
Antony A. Riley  
Chief Financial Officer  
(Principal Financial and Accounting Officer)

