Table of Contents

Filed Pursuant to Rule 424(b)5
Registration No. 333-227632

The information in this preliminary prospectus supplement is not complete and may be changed. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities, and we are not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to Completion
PRELIMINARY PROSPECTUS SUPPLEMENT

Dated October 17, 2018
(To prospectus dated October 12, 2018)

$60,000,000

Krystal Biotech, Inc.

Common Stock

We are offering $60,000,000 of shares of our common stock.

Our common stock is listed on The Nasdaq Capital Market under the symbol "KRYS." On October 16, 2018, the last reported sale price of our common stock on The Nasdaq Capital Market was $24.67 per share.

We are an "emerging growth company" under applicable Securities and Exchange Commission rules and will be subject to reduced public company reporting requirements for this prospectus and future filings.

Our business and an investment in our common stock involve significant risks. These risks are described under the caption "Risk Factors" beginning on page S-5 of this prospectus supplement and page 11 of the accompanying prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

	Per Share	*Total*
Public offering price	**$**	**$**
Underwriting discounts and commissions(1)	**$**	**$**
Proceeds, before expenses, to Krystal Biotech, Inc.	**$**	**$**

(1) See "Underwriting" beginning on page S-42 of this prospectus supplement for a description of the compensation payable to the underwriters.

The underwriters may also purchase up to an additional $9,000,000 of shares from us at the public offering price, less the underwriting discount, within 30 days from the date of this prospectus.

The underwriters expect to deliver the shares against payment in New York, New York on , 2018.

Cowen **William Blair** **Cantor**

Chardan **Ladenburg Thalmann**

, 2018

We have not authorized anyone to provide you with any information or to make any representation, other than those contained or incorporated by reference in this prospectus supplement and the accompanying prospectus, which together we sometimes refer to generally as the prospectus, or in any free writing prospectus prepared by us or on our behalf or to which we have referred you. We take no responsibility for, and provide no assurance as to the reliability of, any other information that others may give you. This prospectus supplement and the accompanying prospectus are an offer to sell only the shares offered hereby, but only in circumstances and in jurisdictions where it is lawful to so do. The information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus is accurate only as of its date, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or of any sale of our common stock.

Neither we nor any of the underwriters have done anything that would permit this offering or possession or distribution of this prospectus supplement and the accompanying prospectus in any jurisdiction where action for that purpose is required, other than the United States. You are required to inform yourself about, and to observe any restrictions relating to, this offering and the distribution of this prospectus supplement and the accompanying prospectus.

For investors outside the United States: we have not, and the underwriters have not, done anything that would permit this offering or possession or distribution of this prospectus supplement, the accompanying prospectus and in any free writing prospectus that we have authorized for use in connection with this offering in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus supplement, the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this prospectus supplement, the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering outside the United States.

TABLE OF CONTENTS

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus are part of a "shelf" registration statement on Form S-3 (File No. 333-227632) that we filed with the Securities and Exchange Commission, or the SEC, on October 1, 2018 and that was declared effective on October 12, 2018.

This document is in two parts. The first part is this prospectus supplement, which describes the terms of this offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part is the accompanying prospectus, which gives more general information about the shares of our common stock and other securities we may offer from time to time under our shelf registration statement, some of which does not apply to the securities offered by this prospectus supplement. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying prospectus or any document incorporated by reference herein or therein, on the other hand, you should rely on the information in this prospectus supplement.

You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering before making an investment decision. You should also read and consider the information in the documents referred to in the sections of this prospectus supplement entitled "Where You Can Find More Information" and "Information Incorporated by Reference."

You should rely only on the information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering. We have not authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it.

We are not making an offer to sell the securities covered by this prospectus supplement in any jurisdiction where the offer or sale is not permitted.

The information appearing in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering is accurate only as of its respective date, regardless of the time of delivery of the respective document or of any sale of securities covered by this prospectus supplement. You should not assume that the information contained in or incorporated by reference in this prospectus supplement or the accompanying prospectus, or in any free writing prospectus that we have authorized for use in connection with this offering, is accurate as of any date other than the respective dates thereof.

Unless the context indicates otherwise, as used in this prospectus supplement, the terms "Krystal," the "Company," "we," "us" and "our" refer to Krystal Biotech, Inc., a Delaware corporation, and its wholly-owned subsidiary, Krystal Australia Pty Ltd, an Australian proprietary limited company.

PROSPECTUS SUPPLEMENT SUMMARY

The following summary highlights certain information about us, this offering and selected information contained elsewhere or incorporated by reference in this prospectus supplement. This summary does not contain all of the information you should consider before investing in our common stock. Before making an investment decision, you should carefully read the entire prospectus supplement and the accompanying prospectus (including the documents incorporated by reference herein and therein), especially the risks of investing in our common stock discussed under the heading "Risk Factors" in this prospectus supplement and the accompanying prospectus and under similar headings in the other documents that are incorporated by reference into this prospectus supplement or the accompanying prospectus. You should also carefully read the information incorporated by reference into this prospectus supplement, including our financial statements, and the exhibits to the registration statement of which this prospectus supplement is a part.

In this prospectus supplement, unless we indicate otherwise or the context requires, references to the "Company," "Krystal," "we," "our," "ours," and "us" refer to Krystal Biotech, Inc. and its consolidated subsidiary. The following summary is qualified in its entirety by the more detailed information and financial statements and notes thereto included elsewhere in this prospectus supplement.

Overview

We are a gene therapy company dedicated to developing and commercializing novel treatments for patients suffering from skin diseases. We have developed a proprietary gene therapy platform, our STAR-D platform, that consists of an engineered, patented (issued and pending), viral vector based on modified herpes simplex virus 1, or HSV-1, and skin-optimized gene transfer technology, to develop off-the-shelf treatments for skin 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 and skin conditions.

Our lead product candidate, KB103, seeks to use topical gene therapy to treat dystrophic epidermolysis bullosa, or DEB, a rare and severe genetic disease, for which there is currently no approved treatment. In May 2018, we commenced a Phase 1/2 clinical study of KB103, a first-in-class topical gene therapy for the treatment of DEB, at Stanford University. We announced positive interim results from this clinical study on October 15, 2018. In particular, results to date on two patients met all primary efficacy (presence of functional protein type VII collagen expression, observation of NC1 and NC2 reactive anchoring fibrils and continued expression following repeat administration) and safety endpoints (no adverse events, inflammation or irritation) in topically administered KB103 wounds.

KB103 is the first topical HSV-1 based gene therapy engineered to deliver a human collagen protein to patients suffering from DEB. 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 European Union, United States, Japan and Canada.

Corporate Information

We commenced operations in April 2016. In March 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. On June 19, 2018, we incorporated Krystal Australia Pty Ltd, an Australian proprietary limited company, for the purposes of undertaking preclinical and clinical studies in Australia.

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 our Annual Report on Form 10-K for the fiscal year ended December 31, 2017;
- 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 total annual gross revenues, 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" in our Annual Report on Form 10-K for the fiscal year ended December 31, 2017, and have taken advantage of the exemption from auditor attestation on the effectiveness of our internal controls 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.

THE OFFERING

Common Stock Offered by Us	shares.
Common Stock to be Outstanding after this Offering	shares.
Option to Purchase Additional Shares	The underwriters have a 30-day option to purchase up to an additional shares of common stock.
Use of Proceeds	We currently intend to use the net proceeds from this offering, if any, together with our existing cash, cash equivalents and short-term investments: (i) to continue to advance KB103 through clinical trials; (ii) to advance the pre-clinical development of KB105 with clinical trials anticipated to commence in the first half of 2019; (iii) to complete development of a good manufacturing practices certified manufacturing facility for scale-up production of our pipeline compounds and commencement of operations of that facility; and (iv) the balance for working capital and general corporate purposes, including research and development expenses and capital expenditures. See "Use of Proceeds" on page S-40 of this prospectus supplement.
Risk Factors	Investing in our securities involves a high degree of risk. See "Risk Factors" beginning on page S-5 of this prospectus supplement and page 11 of the accompanying prospectus and other information included and incorporated by reference in this prospectus supplement and the accompanying prospectus for a discussion of factors that you should carefully consider before deciding to invest in our common stock.
Nasdaq Capital Market Symbol	"KRYS"

The number of shares of our common stock shown above to be outstanding immediately before and after this offering is based on 10,353,916 shares outstanding as of June 30, 2018, and excludes, as of such date:

- 54,118 shares of common stock issuable upon the exercise of outstanding stock options with a weighted-average exercise price of $3.29 per share;
- 726,574 shares of common stock reserved for future issuance under our 2017 IPO Stock Incentive Plan, as well as any automatic increases in the number of shares of common stock reserved for future issuance under this benefit plan; and

- 625,000 shares of common stock issued on August 17, 2018 to one investor at $16.00 per share in a private placement transaction.

Unless otherwise indicated, all information in this prospectus supplement assumes no exercise of the underwriters' option to purchase additional shares of common stock from us.

PRELIMINARY RESULTS OF OPERATIONS

We have not yet closed our books for our third quarter ended September 30, 2018, and our independent registered public accounting firm has not completed its review of our results for the third quarter. Set forth below are certain preliminary estimates that we expect to report for our third quarter. Our actual results may differ materially from these estimates due to the completion of our financial closing procedures, final adjustments and other developments that may arise between now and the time the financial results for our third quarter are finalized.

In light of the above, we estimate that our cash, cash equivalents and short-term investments are approximately $52.2 million as of September 30, 2018.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risk factors described below, together with the risks under the heading "Risk Factors" beginning on page 11 of the accompanying prospectus and under Part I, Item IA of our Annual Report on Form 10-K for the fiscal year ended December 31, 2017, filed with the SEC on March 12, 2018, and all other information contained or incorporated by reference into this prospectus supplement and the accompanying prospectus, including our financial statements and the related notes, as updated by our subsequent filings under the Securities Exchange Act of 1934, as amended, or the Exchange Act, and in any free writing prospectus that we have authorized for use in connection with this offering before acquiring any of our common stock. These risks could have a material and adverse impact on our business, results of operations, financial condition and growth prospects, which may cause the trading price of our common stock to decline and you could lose all or part of your investment.

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 June 30, 2018, we have an accumulated deficit of $13.5 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 date to research and development of our first 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 clinical development of KB103, including our current clinical trials and planned future trials;
- initiate additional clinical trials and preclinical studies for any additional product candidates that we may pursue in the future;
- prepare our Biologics License Application, or BLA, and marketing authorization application for KB103;
- establish and validate a commercial-scale cGMP manufacturing facility;
- manufacture current good manufacturing practices, or cGMP, material for clinical trials or potential commercial sales;
- 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 and additional product candidates 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 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, the European Medicines Agency, or the 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 current and planned clinical trials of KB103 and other product candidates;
- 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 studies and clinical trials of KB103. While we have commenced our first clinical trial 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. The successful commercialization of KB103 will require us to perform a variety of functions, including:

- further clinical development of KB103;
- obtaining required regulatory approvals;
- developing and operating a manufacturing facility or obtaining manufacturing services from third party manufacturers; 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. If we are unable to advance KB103 through 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 entered its first clinical trial in May 2018. The development and commercialization of KB103 (or any other product candidate we may develop) is subject to many uncertainties, including the following:

- successful enrollment and completion of clinical trials;
- positive results from our current and planned future 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.

KB103 is in early stage development, and there is no guarantee that the results from preclinical studies will be indicative of our ability to complete or the results to be obtained in the current or future studies and clinical trials.

We initiated our first clinical trial for KB103 in May 2018; however, there is no guarantee that results of this or any potential future clinical trials will be positive or that we will be able to complete this or any potential future clinical trials on the anticipated timelines or at all. The positive results we have observed for KB103 in preclinical studies may not be predictive of outcomes in our current and future

clinical trials, and the current and future 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. Furthermore, research and discoveries by us or others may identify serious adverse events, undesirable side effects or other unexpected properties of our current and future product candidates, including KB103, that could delay, prevent or cause the withdrawal of regulatory approval, limit the commercial potential, or result in significant negative consequences following marketing approval.

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 Tissues and Advanced 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 requirements and 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 KB103 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. We have experienced a period of significant expansion in headcount and expect to experience significant expansion of our facilities, infrastructure and overhead as we develop our own manufacturing facility and increase our research and development efforts. 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. Our current and each of our proposed clinical trials for KB103 includes a 5 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 and KB105, it may not effectively protect us from competition and we may be unable to obtain orphan drug designation 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. On April 16, 2018, the European Commission granted the Orphan Medicinal Product Designation, or OMPD, for KB103. On August 7, 2018, the FDA granted orphan drug designation to our second product candidate, KB105, currently in preclinical development for treatment of patients with transglutaminase 1 (TGM-1) deficient autosomal recessive congenital ichthyosis ("ARCI"). There are currently no treatments for ARCI, which affects approximately 20,000 patients

worldwide. 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 European Commission, upon a recommendation from 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 six 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 and KB105, 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, Regenerative Medicine Advanced Therapy 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.

On May 23, 2018, the FDA granted Fast Track designation in the United States for KB103. We have been granted rare pediatric disease designation for KB103. On August 23, 2018, the FDA granted rare pediatric disease designation for KB105. 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 after having received 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. We received the designation of “rare pediatric disease” for KB103 in December 2016 and for KB105 in August 2018 which could qualify us to receive a Rare Pediatric Priority Review Voucher.

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 or KB105, we may not experience a faster 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 and KB105, 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 pass a pre-approval inspection of our manufacturing facility by the FDA before KB103 can obtain marketing approval. 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 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 EMA 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 criminal and civil penalties or 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, criminal penalties, 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. On October 13, 2017, President Trump signed an Executive Order terminating the cost-sharing subsidies that reimburse insurers under the ACA. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in ACA risk corridor payments to third-party payors who argued were owed to them. In addition, CMS has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. Further, each chamber of Congress has put forth multiple bills this year designed to repeal or repeal and replace portions of the ACA. While Congress has not passed repeal legislation, the Tax Reform Act includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." Further, the Bipartisan Budget Act of 2018, or the BBA, among other things, amends the ACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." Congress may consider other legislation to repeal and replace elements of the ACA. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

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 2027 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 time for Medicare contractors to recoup Medicare 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.

Further, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which have resulted in several recent Congressional inquiries and proposed and enacted bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. In addition, the United States 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 for branded prescription drugs to limit the growth of government paid health care costs. For example, the United States government has passed legislation requiring pharmaceutical manufacturers to provide rebates and discounts to certain entities and governmental payors to participate in federal healthcare programs. Further, Congress and the current administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs, and the current administration recently released a "Blueprint", or plan, to reduce the cost of drugs. The current administration's Blueprint contains certain measures that the U.S. Department of Health and Human Services is already working to implement. Individual states in the United States have also been increasingly passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

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 Anti-Kickback Statute, federal civil and criminal false claim laws and the 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 as well as other jurisdictions. The laws that will affect our operations include, but are not limited to:

- the federal 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 to clarify that a person or entity does not have 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 that a claim for items or services resulting from an Anti-Kickback Statute violation is a false claim under the federal False Claims Act. Cases against pharmaceutical manufacturers support the view that 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 Nondiscrimitation 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 product candidates, KB103 and KB105, 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.

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 KB103, KB105, any future innovations related to our STAR-D platform, and our institutional knowledge, including our manufacturing processes. 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 currently have one issued patent in the United States, U.S. Patent No. 9,877,990, covering, in part, pharmaceutical formulations and methods of treating dystrophic epidermolysis bullosa, or DEB, using our KB103 product, which we refer to as the ’990 patent. A corresponding international application has been filed in accordance with the Paris Cooperation treaty, and a number of patent applications are on file in foreign jurisdictions stemming from this international application. We are actively prosecuting a continuing patent application in front of the U.S. Patent and Trademark Office, or USPTO, directed to further aspects of our KB103 product candidate. In addition, we are seeking patent protection for other key aspects of our business, including our product KB105, through additional patent applications 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. For example, there is no assurance that the ’990 patent, or any other patent we are granted, will prevent third parties from developing competing technologies. Moreover, our patent estate, including the ’990 patent, does not preclude third parties from having intellectual property rights that could interfere with our freedom to use our platform for dermatological indications. 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 our own. 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, KB105 or related technologies, including, for example, interference proceedings, post grant review challenges, and inter partes review before the USPTO. For example, a third party may bring an inter partes review challenging the ’990 patent and any future patent that may be granted to us. 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 or other unauthorized use of intellectual property. 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 interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, or distribution activities.

We may not have sufficient financial or other resources to 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 we, our employees or our advisors have wrongfully used or disclosed alleged trade secrets of other parties, including 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, and we have and may in the future enter into agreements providing us with rights to intellectual property of third parties for limited purposes. Although we try to observe the terms of agreements under which we obtain access to third party intellectual property and 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 third parties or the current or former employers of employees or advisors. For instance, a third party has asserted that we referred to an HSV-1 vector it provided to us in one of our patent applications in breach of agreements between us and such third party. We believe this assertion is without merit, but litigation may be necessary to defend against this claim, or claims from others that may be asserted in the future. If we fail in defending any such claims, in addition to paying monetary damages, we may be subject to an injunction and 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 this Offering and 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 September 30, 2018, 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 37.3% 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.

If securities analysts publish negative evaluations of our stock, the price of our stock could decline.

The trading market for our common stock relies in part on the research and reports that industry or financial analysts publish about us or our business. If securities 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 has been and is likely to continue 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 this offering, and may not use them effectively.

Our management will have broad discretion in the application of our cash, including the net proceeds from this offering, and could spend the proceeds in ways that do not improve our business, financial condition or results of operations or enhance the value of our common stock. You may not agree with our decisions, and our use of the proceeds may not yield any return on your investment. Because of the number and variability of factors that will determine our use of the net proceeds from this offering, their ultimate use may vary substantially from their currently intended use. Our failure to apply the net proceeds of this offering effectively could compromise our ability to pursue our growth strategy and we might not be able to yield a significant return, if any, on our investment of these net proceeds. You will not have the opportunity to influence our decisions on how to use the net proceeds from this offering. The failure by our management to apply these funds effectively could result in financial losses that could harm 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 this offering, in a manner that does not produce income or that loses value. See "Use of Proceeds."

If you purchase shares of common stock in this offering, you will suffer immediate and substantial dilution of your investment.

The public offering price of our common stock will be substantially higher than the net tangible book value per share of our common stock. Therefore, if you purchase shares of our common stock in this offering, you will pay a price per share that substantially exceeds our net tangible book value per share after this offering. To the extent outstanding options are exercised, you will incur further dilution. Based on the public offering price of $ per share, you will experience immediate dilution of $ per share, representing the difference between the price paid by the purchasers of the shares of common stock sold in the offering and our as adjusted net tangible book value per share of $ after giving effect to this offering. See "Dilution."

In addition, we have a significant number of stock awards outstanding. To the extent that outstanding stock options have been or may be exercised or other shares issued, you may experience further dilution. Further, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans.

We may sell shares or other securities in any other offering at a price per share that is less than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock, or securities convertible or exchangeable into common stock, in future transactions may be higher or lower than the price per share paid by investors in this offering.

If additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to investors purchasing our common stock in this offering or result in downward pressure on the price of our common stock.

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

We are an "emerging growth company," as defined in the 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.

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.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and any accompanying prospectus, as well as the documents incorporated by reference herein and therein, contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and releases issued by the SEC and within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Exchange Act. Forward-looking statements include, among others, information concerning our strategy, future operations, future financial position, future revenue, projected expenses, business prospects, and plans and objectives of management. Forward-looking statements include all statements that are not historical facts and can be identified by terms such as “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict, “project,” “seek,” “should,” “target,” “will,” “would,” or similar expressions and the negatives of those terms. These statements relate to future events or to our future operating or financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements.

Forward-looking statements contained in this prospectus include, but are not limited to, statements about the following:

- the initiation, timing, progress and results of preclinical studies and clinical trials for KB103 and any other product candidates, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the trials will become available and our research and development programs;
- the timing, scope or results of regulatory filings and approvals, including timing of final U.S. Food and Drug Administration, or FDA, marketing and other regulatory approval of KB103;
- our ability to achieve certain accelerated or orphan drug designations from the FDA;
- our estimates regarding the potential market opportunity for KB103 and any other product candidates;
- our research and development programs for our product candidates;
- our plans and ability to successfully develop and commercialize our product candidates, including KB103 and KB105;
- our ability to identify and develop new product candidates;
- our ability to identify, recruit and retain key personnel;
- our commercialization, marketing and manufacturing capabilities and strategy;
- the implementation of our business model, strategic plans for our business, product candidates and technology;
- the scalability and commercial viability of our proprietary manufacturing methods and processes;
- the rate and degree of market acceptance and clinical utility of our product candidates and gene therapy, in general;
- our competitive position;
- our intellectual property position and our ability to protect and enforce our intellectual property;
- our financial performance;
- developments and projections relating to our competitors and our industry;
- our ability to establish and maintain collaborations or obtain additional funding;
- our expectations related to the use of proceeds from this offering;
- our estimates regarding expenses, future revenue, capital requirements and needs for or ability to obtain additional financing;

- our ability to successfully resolve any intellectual property or other claims that may be brought against us;
- any statements regarding compliance with the listing standards of The Nasdaq Capital Market;
- the impact of laws and regulations;
- the effects of recent accounting pronouncements on our financial statements and other future events;
- our expectations regarding the time during which we will be an emerging growth company under the JOBS Act; and
- any statements regarding future economic conditions or performance and any statement of assumptions underlying any of the foregoing.

Forward-looking statements are subject to a number of risks, uncertainties and assumptions, including those described in “Risk Factors” and elsewhere in this prospectus supplement and the accompanying prospectus. Moreover, we operate in a very competitive and rapidly changing environment, and new risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this prospectus supplement and/or the accompanying prospectus may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Also, forward-looking statements represent our management’s beliefs and assumptions only as of the date of this prospectus supplement or the accompanying prospectus, as applicable. You should read this prospectus supplement, the accompanying prospectus, and the documents that we have filed as exhibits to the registration statement, of which this prospectus supplement is a part, completely and with the understanding that our actual future results may be materially different from what we expect.

Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future.

USE OF PROCEEDS

We estimate that the net proceeds from our issuance and sale of shares of our common stock in this offering will be approximately $ million (or $ million if the underwriters exercise in full their option to purchase additional shares), after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

As of September 30, 2018, we had cash, cash equivalents and short-term investments of approximately $52.2 million. We intend to use the net proceeds from this offering together with our existing cash, cash equivalents and short-term investments as follows:

- to continue to advance KB103 through clinical trials;
- to advance the pre-clinical development of KB105 with clinical trials anticipated to commence in the first half of 2019;
- to complete development of a good manufacturing practices certified manufacturing facility for scale-up production of our pipeline compounds and commencement of operations of that facility; and
- the balance for working capital and general corporate purposes, including research and development expenses and capital expenditures.

The expected net proceeds of this offering will not be sufficient for us to fund our product candidates through regulatory approval, and we will need to raise additional capital in order to complete the development and commercialization of our product candidates.

The amounts and timing of our use of the net proceeds from this offering will depend on a number of factors, including the timing and progress of our research and development efforts, the timing and progress of any partnering and commercialization efforts, technological advances and the competitive environment for our products, as well as the amount of cash used in our operations. Although we have no present intention or commitment to do so, we may use a portion of the net proceeds for the acquisition of, or investment in, technologies, intellectual property or businesses that complement our business.

Our expected use of net proceeds from this offering represents our current intentions based upon our present plans and business condition. As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses for the net proceeds to be received upon the completion of this offering or the actual amounts that we will spend on the uses set forth above. We may find it necessary or advisable to use the net proceeds for other purposes, and our management will retain broad discretion over the allocation of the net proceeds of this offering. Pending the uses described above, we intend to temporarily invest the proceeds in short-term, interest-bearing instruments or other investment-grade securities, certificates of deposits or short-term U.S. government securities.

DILUTION

Dilution is the amount by which the price paid by the purchasers of the shares of common stock sold in the offering exceeds the net tangible book value per share of common stock after the offering. Net tangible book value per share is determined by subtracting our total liabilities from the total book value of our tangible assets and dividing the difference by the number of shares of common stock deemed to be outstanding at that date.

Our historical net tangible book value as of June 30, 2018 was $45.3 million, or $4.37 per share.

After giving effect to the sale of $ of shares of common stock in this offering at the public offering price of $ per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of June 30, 2018 would have been $ million, or $ per share. This represents an immediate increase in as adjusted net tangible book value of $ per share to our existing stockholders and immediate dilution of $ per share to new investors purchasing common stock in this offering.

The following table illustrates this dilution on a per share basis to new investors:

Public offering price per share		$
Historical net tangible book value per share as of June 30, 2018	$4.37	
Increase per share attributable to new investors	$	
As adjusted net tangible book value per share after giving effect to this offering		$
Dilution in adjusted net tangible book value per share to new investors		$

If the underwriters exercise in full their option to purchase of additional shares of our common stock, the as adjusted net tangible book value per share after giving effect to this offering would be $ per share, representing an immediate increase to existing stockholders of $ per share, and immediate dilution to new investors in this offering of $ per share.

The number of shares of our common stock shown above to be outstanding immediately before and after this offering is based on 10,353,916 shares outstanding as of June 30, 2018, and excludes, as of such date:

- 54,118 shares of common stock issuable upon the exercise of outstanding stock options with a weighted-average exercise price of $3.29 per share;
- 726,574 shares of common stock reserved for future issuance under our 2017 IPO Plan, as well as any automatic increases in the number of shares of common stock reserved for future issuance under this benefit plan; and
- 625,000 shares of common stock issued on August 17, 2018 to one investor at $16.00 per share in a private placement transaction.

Unless otherwise indicated, all information in this prospectus supplement assumes no exercise of the underwriters' option to purchase additional shares of common stock from us.

To the extent that options are exercised, new options are issued under our equity incentive plans, or we issue additional shares of common stock in the future, there will be further dilution to investors participating in this offering.

UNDERWRITING

We and the underwriters for the offering named below have entered into an underwriting agreement with respect to the common stock being offered. Subject to the terms and conditions of the underwriting agreement, each underwriter has severally agreed to purchase from us the number of shares of our common stock set forth opposite its name below. Cowen and Company, LLC, William Blair & Company, L.L.C. and Cantor Fitzgerald & Co. are the representatives of the underwriters.

Underwriter	Number of Shares
Cowen and Company, LLC	
William Blair & Company, L.L.C.	
Cantor Fitzgerald & Co.	
Chardan Capital Markets LLC	
Ladenburg Thalmann & Co. Inc.	
Total	

The underwriting agreement provides that the obligations of the underwriters are subject to certain conditions precedent and that the underwriters have agreed, severally and not jointly, to purchase all of the shares sold under the underwriting agreement if any of these shares are purchased, other than those shares covered by the option described below. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against specified liabilities, including liabilities under the Securities Act of 1933, and to contribute to payments the underwriters may be required to make in respect thereof.

The underwriters are offering the shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel and other conditions specified in the underwriting agreement. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Option to Purchase Additional Shares. We have granted to the underwriters an option to purchase up to additional shares of common stock at the public offering price, less the underwriting discount. This option is exercisable for a period of 30 days. To the extent that the underwriters exercise this option, the underwriters will purchase additional shares from us in approximately the same proportion as shown in the table above.

Discounts and Commissions. The following table shows the public offering price, underwriting discount and proceeds, before expenses to us. These amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

We estimate that the total expenses of the offering, excluding underwriting discount, will be approximately $ and are payable by us. We have also agreed to reimburse the underwriters for up to $25,000 for their FINRA counsel fees and expenses, which reimbursed fee is deemed underwriting compensation for this offering by FINRA.

		Total	
	Per Share	Without Over-Allotment	With Over Allotment
Public offering price			
Underwriting discount			
Proceeds, before expenses, to Krystal Biotech, Inc.			

The underwriters propose to offer the shares of common stock to the public at the public offering price set forth on the cover of this prospectus. The underwriters may offer the shares of common stock to securities dealers at the public offering price less a concession not in excess of $ per share. If all of the shares are not sold at the public offering price, the underwriters may change the offering price and other selling terms.

Stabilization. In connection with this offering, the underwriters may engage in stabilizing transactions, overallotment transactions, syndicate covering transactions, penalty bids and purchases to cover positions created by short sales.

- Stabilizing transactions permit bids to purchase shares of common stock so long as the stabilizing bids do not exceed a specified maximum, and are engaged in for the purpose of preventing or retarding a decline in the market price of the common stock while the offering is in progress.
- Overallotment transactions involve sales by the underwriters of shares of common stock in excess of the number of shares the underwriters are obligated to purchase. This creates a syndicate short position which may be either a covered short position or a naked short position. In a covered short position, the number of shares over-allotted by the underwriters is not greater than the number of shares that they may purchase in the overallotment option. In a naked short position, the number of shares involved is greater than the number of shares in the overallotment option. The underwriters may close out any short position by exercising their overallotment option and/or purchasing shares in the open market.
- Syndicate covering transactions involve purchases of common stock in the open market after the distribution has been completed in order to cover syndicate short positions. In determining the source of shares to close out the short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared with the price at which they may purchase shares through exercise of the overallotment option. If the underwriters sell more shares than could be covered by exercise of the overallotment option and, therefore, have a naked short position, the position can be closed out only by buying shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that after pricing there could be downward pressure on the price of the shares in the open market that could adversely affect investors who purchase in the offering.
- Penalty bids permit the representatives to reclaim a selling concession from a syndicate member when the common stock originally sold by that syndicate member is purchased in stabilizing or syndicate covering transactions to cover syndicate short positions.

These stabilizing transactions, syndicate covering transactions and penalty bids may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock in the open market may be higher than it would otherwise be in the absence of these transactions. Neither we nor the underwriters make any representation or prediction as to the effect that the transactions described above may have on the price of our common stock. These transactions may be effected on the Nasdaq Stock Market, in the over-the-counter market or otherwise and, if commenced, may be discontinued at any time.

Passive Market Making. In connection with this offering, underwriters and selling group members may engage in passive market making transactions in our common stock on the Nasdaq Stock Market in accordance with Rule 103 of Regulation M under the Exchange Act during a period before the commencement of offers or sales of common stock and extending through the completion of the distribution. A passive market maker must display its bid at a price not in excess of the highest

independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, such bid must then be lowered when specified purchase limits are exceeded.

Lock-Up Agreements. Pursuant to certain "lock-up" agreements, we and our executive officers and directors, have agreed, subject to certain exceptions, not to, for a period of 90 days, offer for sale, contract to sell, sell, distribute, grant any option, right or warrant to purchase, pledge, hypothecate or otherwise dispose of, directly or indirectly, any shares of our common stock or any securities convertible into, or exercisable or exchangeable for, shares of our common stock.

In addition, we and each such person agrees that, without the prior written consent of Cowen and Company, LLC and William Blair & Company, L.L.C., we or such other person will not make any demand for, or exercise any right with respect to the registration of any of the common stock or any securities convertible into or exchangeable or exercisable for common stock, or the filing of any registration statement under the Securities Act relating to, any common stock or securities convertible into or exchangeable or exercisable for any common stock for a period of 90 days after the date of the pricing of the offering.

This lock-up provision applies to common stock and to securities convertible into or exchangeable or exercisable for common stock. The exceptions permit us, among other things and subject to restrictions, to: (a) issue common stock, options or restricted stock units pursuant to employee benefit plans, (b) issue common stock upon exercise of outstanding options or warrants, (c) issue securities in connection with acquisitions or similar transactions or (d) file registration statements on Form S-8. The exceptions permit parties to the "lock-up" agreements, among other things and subject to restrictions, to: (a) make certain gifts, (b) transfer common stock acquired in open market transactions after this offering and (c) pursuant to a change of control of our company after the offering, that has been approved by the independent members of our board of directors. In addition, the lock-up provision will not restrict broker-dealers from engaging in market making and similar activities conducted in the ordinary course of their business.

Cowen and Company, LLC and William Blair & Company, L.L.C., in their sole discretion, may release our common stock and other securities subject to the lock-up agreements described above in whole or in part at any time before the termination of the 90-day period. When determining whether or not to release our common stock and other securities from lock-up agreements, Cowen and Company, LLC and William Blair & Company, L.L.C. will consider, among other factors, the holder's reasons for requesting the release, the number of shares for which the release is being requested and market conditions at the time of the request.

Canada. The common stock may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 *Prospectus Exemptions* or subsection 73.3(1) of the *Securities Act* (Ontario), and are permitted clients, as defined in National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*. Any resale of the common stock must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus supplement (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 *Underwriting Conflicts* (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

United Kingdom. Each of the underwriters has represented and agreed that:

- it has not made or will not make an offer of the securities to the public in the United Kingdom within the meaning of section 102B of the Financial Services and Markets Act 2000 (as amended) (FSMA) except to legal entities which are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities or otherwise in circumstances which do not require the publication by us of a prospectus pursuant to the Prospectus Rules of the Financial Services Authority (FSA);
- it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of section 21 of FSMA) to persons who have professional experience in matters relating to investments falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 or in circumstances in which section 21 of FSMA does not apply to us; and
- it has complied with and will comply with all applicable provisions of FSMA with respect to anything done by it in relation to the securities in, from or otherwise involving the United Kingdom.

Switzerland. The securities will not be offered, directly or indirectly, to the public in Switzerland and this prospectus does not constitute a public offering prospectus as that term is understood pursuant to article 652a or 1156 of the Swiss Federal Code of Obligations.

European Economic Area. In relation to each Member State of the European Economic Area (the "EEA") which has implemented the European Prospectus Directive (each, a "Relevant Member State"), an offer of our shares may not be made to the public in a Relevant Member State other than:

- to any legal entity which is a qualified investor, as defined in the European Prospectus Directive;
- to fewer 150 natural or legal persons (other than qualified investors as defined in the European Prospectus Directive), subject to obtaining the prior consent of the relevant dealer or dealers nominated by us for any such offer; or
- in any other circumstances falling within Article 3(2) of the European Prospectus Directive,

provided that no such offer of our shares shall require us or any underwriter to publish a prospectus pursuant to Article 3 of the European Prospectus Directive or supplement prospectus pursuant to Article 16 of the European Prospectus Directive and each person who initially acquires any shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed to and with each of the underwriters and with us that it is a "qualified investor" within the meaning of the law in that Relevant Member State implementing Article 2(1)(e) of the European Prospectus Directive.

In the case of any shares being offered to a financial intermediary as that term is used in Article 3(2) of the European Prospectus Directive, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer or any shares to the public other than their offer or resale in a Relevant Member State to qualified investors as so defined or in circumstances in which the prior consent of the representatives has been obtained to each such proposed offer or resale.

For the purposes of this description, the expression an "offer to the public" in relation to the securities in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the securities to be offered so as to enable an investor to decide to purchase or subscribe for the securities, as the expression may be varied in that Relevant Member State by any measure implementing the European Prospectus Directive in that member state, and the expression "European Prospectus Directive" means Directive 2003/71/EC (and amendments hereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State) and includes any relevant implementing measure in each Relevant Member State. The expression 2010 PD Amending Directive means Directive 2010/73/EU.

Israel. In the State of Israel this prospectus shall not be regarded as an offer to the public to purchase shares of common stock under the Israeli Securities Law, 5728—1968, which requires a prospectus to be published and authorized by the Israel Securities Authority, if it complies with certain provisions of Section 15 of the Israeli Securities Law, 5728—1968, including, inter alia, if: (i) the offer is made, distributed or directed to not more than 35 investors, subject to certain conditions (the "Addressed Investors"); or (ii) the offer is made, distributed or directed to certain qualified investors defined in the First Addendum of the Israeli Securities Law, 5728—1968, subject to certain conditions (the "Qualified Investors"). The Qualified Investors shall not be taken into account in the count of the Addressed Investors and may be offered to purchase securities in addition to the 35 Addressed Investors. The company has not and will not take any action that would require it to publish a prospectus in accordance with and subject to the Israeli Securities Law, 5728—1968. We have not and will not distribute this prospectus or make, distribute or direct an offer to subscribe for our common stock to any person within the State of Israel, other than to Qualified Investors and up to 35 Addressed Investors.

Qualified Investors may have to submit written evidence that they meet the definitions set out in of the First Addendum to the Israeli Securities Law, 5728—1968. In particular, we may request, as a condition to be offered common stock, that Qualified Investors will each represent, warrant and certify to us and/or to anyone acting on our behalf: (i) that it is an investor falling within one of the categories listed in the First Addendum to the Israeli Securities Law, 5728—1968; (ii) which of the categories listed in the First Addendum to the Israeli Securities Law, 5728—1968 regarding Qualified Investors is applicable to it; (iii) that it will abide by all provisions set forth in the Israeli Securities Law, 5728—1968 and the regulations promulgated thereunder in connection with the offer to be issued common stock; (iv) that the shares of common stock that it will be issued are, subject to exemptions available under the Israeli Securities Law, 5728—1968: (a) for its own account; (b) for investment purposes only; and (c) not issued with a view to resale within the State of Israel, other than in accordance with the provisions of the Israeli Securities Law, 5728—1968; and (v) that it is willing to provide further evidence of its Qualified Investor status. Addressed Investors may have to submit written evidence in respect of their identity and may have to sign and submit a declaration containing, inter alia, the Addressed Investor's name, address and passport number or Israeli identification number.

We have not authorized and do not authorize the making of any offer of securities through any financial intermediary on our behalf, other than offers made by the underwriters and their respective affiliates, with a view to the final placement of the securities as contemplated in this document. Accordingly, no purchaser of the shares, other than the underwriters, is authorized to make any further offer of shares on our behalf or on behalf of the underwriters.

Electronic Offer, Sale and Distribution of Shares. A prospectus in electronic format may be made available on the websites maintained by one or more of the underwriters or selling group members, if any, participating in this offering and one or more of the underwriters participating in this offering may distribute prospectuses electronically. The representatives may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account

holders. Internet distributions will be allocated by the underwriters and selling group members that will make internet distributions on the same basis as other allocations. Other than the prospectus in electronic format, the information on these websites is not part of this prospectus or the registration statement of which this prospectus forms a part, has not been approved or endorsed by us or any underwriter in its capacity as underwriter, and should not be relied upon by investors.

Other Relationships. Certain of the underwriters and their affiliates have provided, and may in the future provide, various investment banking, commercial banking and other financial services for us and our affiliates for which they have received, and may in the future receive, customary fees.

LEGAL MATTERS

The validity of the shares of our common stock being offered hereby will be passed upon by Morrison & Foerster LLP, San Francisco, California. Goodwin Procter LLP, New York, New York is acting as counsel for the underwriters in connection with certain legal matters related to this offering.

EXPERTS

Mayer Hoffman McCann P.C., an independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the years ended December 31, 2017 and 2016, as set forth in its report, which is incorporated by reference in this prospectus supplement. Our financial statements are incorporated by reference in reliance on Mayer Hoffman McCann P.C.'s report, given on the authority of said firm as experts in accounting and auditing.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We are subject to the information requirements of the Exchange Act. In accordance with the Exchange Act, we file annual, quarterly and current reports, proxy statements and other information with the SEC. Such reports, proxy statements and other information filed by us are available to the public free of charge at www.sec.gov. You may also read and copy any document we file with the SEC at the public reference facilities maintained by the SEC at 100 F Street, N.E., Washington, D.C. 20549. You may obtain information on the operation of the public reference facilities by calling the SEC at 1-800-SEC-0330. Copies of certain information filed by us with the SEC are also available on our website at www.krystalbio.com. The information available on or through our website is not part of this prospectus supplement or the accompanying prospectus.

This prospectus is part of a registration statement on Form S-3 that we filed with the SEC and does not contain all the information set forth or incorporated by reference in the registration statement. You should review the information and exhibits in the registration statement for further information about us and the securities being offered hereby. Statements in this prospectus supplement concerning any document we filed as an exhibit to the registration statement or that we otherwise filed with the SEC are not intended to be comprehensive and are qualified by reference to the filings. You should review the complete document to evaluate these statements.

INFORMATION INCORPORATED BY REFERENCE

The SEC rules allow us to "incorporate by reference" into this prospectus supplement information that we file with the SEC. Incorporation by reference allows us to disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference into this prospectus supplement is considered to be part of this prospectus supplement. These documents may include Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, as well as proxy statements. You should read the information incorporated by reference because it is an important part of this prospectus supplement.

This prospectus and the registration statement of which this prospectus is a part incorporate by reference the information or documents listed below, other than those documents or the portions of those documents deemed to be furnished and not filed in accordance with the SEC rules:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2017 filed with the SEC on March 12, 2018;
- our Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2018 and June 30, 2018, filed with the SEC on May 7, 2018 and August 6, 2018, respectively;
- our Current Reports on Form 8-K filed with the SEC on May 9, 2018, June 1, 2018, August 17, 2018 and October 15, 2018;
- our Definitive Proxy Statement on Schedule 14A filed with the SEC on April 20, 2018; and
- the description of our common stock contained in our Registration Statement on Form 8-A filed with the SEC on September 19, 2017, pursuant to Section 12(b) of the Exchange Act, including any amendment or report filed for the purpose of updating such description.

Any statement contained in any document incorporated by reference herein shall be deemed to be modified or superseded for purposes of this prospectus supplement to the extent that a statement contained in this prospectus supplement or any prospectus modifies or supersedes such statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus supplement.

We also incorporate by reference any future filings, other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items, made with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, in each case, other than those documents or the portions of those documents deemed to be furnished and not filed in accordance with SEC rules, until the offering of the securities under the registration statement of which this prospectus supplement forms a part is terminated or completed. Information in such future filings updates and supplements the information provided in this prospectus supplement. Any statements in any such future filings will be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

Because we are incorporating by reference future filings with the SEC, this prospectus supplement is continually updated and later information filed with the SEC may update and supersede some of the information included or incorporated by reference in this prospectus supplement. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus supplement or in any document previously incorporated by reference have been modified or superseded.

We will provide without charge to each person, including any beneficial owners, to whom this prospectus supplement is delivered, upon his or her written or oral request, a copy of any or all reports

or documents referred to above which have been or may be incorporated by reference into this prospectus supplement but not delivered with this prospectus supplement, excluding exhibits to those reports or documents unless they are specifically incorporated by reference into those documents. You may request a copy of these documents by writing or telephoning us at the following address:

Krystal Biotech, Inc.
2100 Wharton Street, Suite 701
Pittsburgh, Pennsylvania 15203
(412) 586-5830
Attention: Antony A. Riley
Chief Financial Officer

Table of Contents

PROSPECTUS

$200,000,000

Krystal Biotech, Inc.

Common Stock
Preferred Stock
Debt Securities
Warrants
Rights
Units
and
625,000 Shares of Common Stock
Offered by the Selling Stockholder

This prospectus relates to a primary offering by the Company and a secondary offering by the selling stockholder.

In the primary offering, from time to time, we may offer or sell, together or separately, in one or more offerings:

- common stock;
- preferred stock;
- debt securities;
- warrants to purchase common stock or preferred stock;
- rights to purchase common stock or preferred stock; and
- units comprised of two or more of the foregoing securities.

We may sell any combination of these securities in one or more offerings, up to a maximum aggregate offering price of $200,000,000, in amounts, at prices and on terms to be determined at the time of each offering thereof. This prospectus provides you with a general description of the securities we may offer. Each time we offer securities using this prospectus, we will provide the specific terms of the securities and the offering in one or more supplements to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplement and any related free writing prospectus may also add to, update or change the information contained in this prospectus and will also describe the specific manner in which we will offer the securities.

The securities may be sold directly by us to investors, through agents designated from time to time or to or through underwriters or dealers, on a continuous or delayed basis. For additional information on the methods of sale, you should refer to the section titled "Plan of Distribution" in this prospectus. If any agents, underwriters or dealers are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such agents, underwriters or dealers and any applicable fees, commissions, discounts and over-allotment options will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds that we expect to receive from such sale will also be set forth in a prospectus supplement.

This prospectus may not be used to sell any securities unless accompanied by a prospectus supplement. You should carefully read this prospectus, any accompanying prospectus supplement and any related free writing prospectus, as well as any documents incorporated by reference, prior to investing in any of our securities.

This prospectus also relates to the resale, from time to time, by the selling stockholder identified in this prospectus under the caption "Selling Stockholder," of up to 625,000 shares of our common stock, par value $0.00001 per share, on the terms described in this prospectus or in an applicable prospectus supplement. We will not receive any proceeds from the sale of shares of common stock by the selling stockholder. The selling stockholder will bear all commissions and discounts, if any, attributable to the sale of the shares.

The selling stockholder may sell the shares of our common stock offered by this prospectus from time to time on terms to be determined at the time of sale through ordinary brokerage transactions or through any other means described in this prospectus under the caption "Plan of Distribution." The shares of common stock may be sold at fixed prices, at market prices prevailing at the time of sale, at prices related to prevailing market price or at negotiated prices.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading "Risk Factors" beginning on page 11 of this prospectus, in any accompanying prospectus supplement and in any related free writing prospectus, and under similar headings in the documents incorporated by reference into this prospectus, any accompanying prospectus supplement and any related free writing prospectus.

Our common stock is traded on The NASDAQ Capital Market under the symbol "KRYS." On September 28, 2018, the last reported sale price of our common stock on The NASDAQ Capital Market was $17.58 per share. We do not expect our preferred stock, debt securities, warrants, rights or units to be listed on any securities exchange or over-the-counter market unless otherwise described in the applicable prospectus supplement.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is October 12, 2018

TABLE OF CONTENTS

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the U.S. Securities and Exchange Commission (the "SEC") utilizing a "shelf" registration process. Under this shelf registration process, we may, from time to time, offer shares of our common stock, shares of our preferred stock, debt securities, warrants, rights or units comprised of two or more of the foregoing securities, together or separately, in one or more offerings, for a maximum aggregate offering price not to exceed $200,000,000.

In addition, this prospectus relates to the resale, from time to time, by the selling stockholder identified in this prospectus under the caption "Selling Stockholder," of up to 625,000 shares of our common stock, par value $0.00001 per share. Throughout this prospectus, when we refer to the shares of our common stock being registered on behalf of the selling stockholder, we are referring to the shares of our common stock issued to the selling stockholder pursuant to the stock purchase agreement we entered into with the selling stockholders on August 16, 2018.

This prospectus provides you with a general description of the securities we may offer. Each time we sell any securities under this prospectus, we will provide a prospectus supplement that will contain more specific information about the terms of that specific offering, including the specific amounts, prices and terms of the securities offered. Any prospectus supplement may include a discussion of risks or other special considerations applicable to us or the offered securities. Any prospectus supplement may also add to, update or change information contained in this prospectus. To the extent there is a conflict between the information contained in this prospectus, on the one hand, and the information contained in any prospectus supplement, on the other hand, you should rely on the information in the prospectus supplement. If any statement in one of these documents is inconsistent with a statement in another document having a later date-for example, a document incorporated by reference in the accompanying prospectus-the statement in the document having the later date modifies or supersedes the earlier statement.

This prospectus and any applicable prospectus supplement contain and incorporate by reference market data, industry statistics and other data that have been obtained or compiled from information made available by third parties. These data, to the extent they contain estimates or projections, involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates or projections. Industry publications and other reports we have obtained from independent parties generally state that the data contained in these publications or other reports have been obtained in good faith or from sources considered to be reliable, but they do not guarantee the accuracy or completeness of such data.

We urge you to carefully read this prospectus, any applicable prospectus supplement and any related free writing prospectus, any documents that we incorporate by reference in this prospectus, any applicable prospectus supplement and any related free writing prospectus, and the additional information described below under "Where You Can Find More Information" and "Incorporation of Certain Documents by Reference" before making an investment decision. You should rely only on the information contained or incorporated by reference in this prospectus, any applicable prospectus supplement and any related free writing prospectus. We have not authorized anyone to provide you with different information. If anyone provides you with additional, different or inconsistent information, you should not rely on it. You should not assume that the information we have included in this prospectus, any applicable prospectus supplement, any related free writing prospectus or any documents incorporated by reference herein or therein is accurate as of any date other than the dates of those documents. Our business, financial condition, results of operations and prospects may have changed since those dates.

This document may only be used where it is legal to sell these securities. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any jurisdiction whether the offer or sale is not permitted.

Unless the context indicates otherwise, as used in this prospectus, the terms "Krystal," the "Company," "we," "us" and "our" refer to Krystal Biotech, Inc., a Delaware corporation, and its wholly-owned subsidiary, Krystal Australia Pty Ltd, an Australian proprietary limited company.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We are subject to the information requirements of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). In accordance with the Exchange Act, we file annual, quarterly and current reports, proxy statements and other information with the SEC. Such reports, proxy statements and other information filed by us are available to the public free of charge at www.sec.gov. You may also read and copy any document we file with the SEC at the public reference facilities maintained by the SEC at 100 F Street, N.E., Washington, D.C. 20549. You may obtain information on the operation of the public reference facilities by calling the SEC at 1-800-SEC-0330. Copies of certain information filed by us with the SEC are also available on our website at www.krystalbio.com. The information available on or through our website is not part of this prospectus or any accompanying prospectus supplement or related free writing prospectus and should not be relied upon.

This prospectus is part of a registration statement on Form S-3 that we filed with the SEC and does not contain all the information set forth or incorporated by reference in the registration statement. You should review the information and exhibits in the registration statement for further information about us and the securities being offered hereby. Statements in this prospectus concerning any document we filed as an exhibit to the registration statement or that we otherwise filed with the SEC are not intended to be comprehensive and are qualified by reference to the filings. You should review the complete document to evaluate these statements.

INFORMATION INCORPORATED BY REFERENCE

The SEC rules allow us to "incorporate by reference" into this prospectus information that we file with the SEC. Incorporation by reference allows us to disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference into this prospectus is considered to be part of this prospectus. These documents may include Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, as well as proxy statements. You should read the information incorporated by reference because it is an important part of this prospectus.

This prospectus and the registration statement of which this prospectus is a part incorporate by reference the information or documents listed below, other than those documents or the portions of those documents deemed to be furnished and not filed in accordance with the SEC rules:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2017 filed with the SEC on March 12, 2018;
- our Quarterly Reports on Form 10-Q for the fiscal quarter ended March 31, 2018 and June 30, 2018, filed with the SEC on May 7, 2018 and August 6, 2018, respectively;
- our Current Reports on Form 8-K filed with the SEC on May 9, 2018, June 1, 2018, and August 17, 2018;
- our Definitive Proxy Statement on Schedule 14A filed with the SEC on April 20, 2018; and
- the description of our common stock contained in our Registration Statement on Form 8-A filed with the SEC on September 19, 2017, pursuant to Section 12(b) of the Exchange Act, including any amendment or report filed for the purpose of updating such description.

Any statement contained in any document incorporated by reference herein shall be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or any prospectus supplement modifies or supersedes such statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

We also incorporate by reference any future filings, other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items, made with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, in each case, other than those documents or the portions of those documents deemed to be furnished and not filed in accordance with SEC rules, until the offering of the securities under the registration statement of which this prospectus forms a part is terminated or completed. Information in such future filings updates and supplements the information provided in this prospectus. Any statements in any such future filings will be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

Because we are incorporating by reference future filings with the SEC, this prospectus is continually updated and later information filed with the SEC may update and supersede some of the information included or incorporated by reference in this prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus or in any document previously incorporated by reference have been modified or superseded.

We will provide without charge to each person, including any beneficial owners, to whom this prospectus is delivered, upon his or her written or oral request, a copy of any or all documents referred to above which have been or may be incorporated by reference into this prospectus but not delivered with this prospectus, excluding

exhibits to those documents unless they are specifically incorporated by reference into those documents. You may request a copy of these documents by writing or telephoning us at the following address.

Krystal Biotech, Inc.
2100 Wharton Street, Suite 701
Pittsburgh, Pennsylvania 15203
(412) 586-5830
Attention: Antony A. Riley
Chief Financial Officer

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and any accompanying prospectus supplement, as well as the documents incorporated by reference therein, contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and releases issued by the SEC and within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Exchange Act. Forward-looking statements include, among others, information concerning our strategy, future operations, future financial position, future revenue, projected expenses, business prospects, and plans and objectives of management. Forward-looking statements include all statements that are not historical facts and can be identified by terms such as "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict, "project," "seek," "should," "target," "will," "would," or similar expressions and the negatives of those terms. These statements relate to future events or to our future operating or financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements.

Forward-looking statements contained in this prospectus include, but are not limited to, statements about the following:

- the initiation, timing, progress and results of preclinical and clinical trials for KB103 and any other product candidates, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the trials will become available and our research and development programs;
- the timing, scope or results of regulatory filings and approvals, including timing of final U.S. Food and Drug Administration (the "FDA") marketing and other regulatory approval of KB103;
- our ability to achieve certain accelerated or orphan drug designations from the FDA;
- our estimates regarding the potential market opportunity for KB103 and any other product candidates;
- our research and development programs for our product candidates;
- our plans and ability to successfully develop and commercialize our product candidates, including KB103 and KB105;
- our ability to identify and develop new product candidates;
- our ability to identify, recruit and retain key personnel;
- our commercialization, marketing and manufacturing capabilities and strategy;
- the implementation of our business model, strategic plans for our business, product candidates and technology;
- the scalability and commercial viability of our proprietary manufacturing methods and processes;
- the rate and degree of market acceptance and clinical utility of our product candidates and gene therapy, in general;
- our competitive position;
- our intellectual property position and our ability to protect and enforce our intellectual property;
- our financial performance;
- developments and projections relating to our competitors and our industry;
- our ability to establish and maintain collaborations or obtain additional funding;
- our expectations related to the use of proceeds from this offering;

- our estimates regarding expenses, future revenue, capital requirements and needs for or ability to obtain additional financing;
- our ability to successfully resolve any intellectual property or other claims that may be brought against us;
- any statements regarding compliance with the listing standards of The NASDAQ Capital Market;
- the impact of laws and regulations;
- our expectations regarding the time during which we will be an emerging growth company under the JOBS Act; and
- any statements regarding future economic conditions or performance and any statement of assumptions underlying any of the foregoing.

Forward-looking statements are subject to a number of risks, uncertainties and assumptions, including those described in "Risk Factors" and elsewhere in this prospectus. Moreover, we operate in a very competitive and rapidly changing environment, and new risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this prospectus may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Also, forward-looking statements represent our management's beliefs and assumptions only as of the date of this prospectus. You should read this prospectus and the documents that we have filed as exhibits to the registration statement, of which this prospectus is a part, completely and with the understanding that our actual future results may be materially different from what we expect.

Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future.

PROSPECTUS SUMMARY

The following summary highlights selected information contained elsewhere or incorporated by reference in this prospectus. This summary does not contain all of the information you should consider before investing in the securities. Before making an investment decision, you should carefully read the entire prospectus, the applicable prospectus supplement and any related free writing prospectus, including the risks of investing in our securities discussed under the heading "Risk Factors" in this prospectus, the applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus. You should also carefully read the information incorporated by reference into this prospectus, including our financial statements, and the exhibits to the registration statement of which this prospectus is a part.

In this prospectus, unless we indicate otherwise or the context requires, references to the "Company," "Krystal," "we," "our," "ours," and "us" refer to Krystal Biotech, Inc. and its consolidated subsidiary. The following summary is qualified in its entirety by the more detailed information and financial statements and notes thereto included elsewhere in this prospectus.

Krystal Biotech, Inc.

We are a gene therapy company dedicated to developing and commercializing novel treatments for patients suffering from skin diseases. We have developed a proprietary gene therapy platform, our STAR-D platform, that consists of an engineered, patented (issued and pending), viral vector based on modified herpes simplex virus 1, or HSV-1, and skin-optimized gene transfer technology, to develop off-the-shelf treatments for skin 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 and skin conditions.

Our lead product candidate, KB103, seeks to use topical gene therapy to treat dystrophic epidermolysis bullosa ("DEB"), a rare and severe genetic disease, for which there is currently no approved treatment. In May 2018, the first two patients were enrolled in Phase 1/2 clinical study of KB103 at Stanford University, a first-in-class topical gene therapy for the treatment of DEB.

KB103 is the first-ever topical HSV-1 based gene therapy engineered to deliver a human collagen protein to patients suffering from DEB. 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 European Union (the "EU"), United States, Japan and Canada.

We commenced operations in April 2016. In March 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. On June 19, 2018, we incorporated Krystal Australia, a proprietary limited company, for the purposes of undertaking preclinical and clinical studies in Australia.

Description of Securities

We may offer shares of our common stock or preferred stock, various series of debt securities, warrants or other rights to purchase common stock or preferred stock, or units consisting of combinations of the foregoing, either individually or in combination with other securities, in each case from time to time under this prospectus, together with the applicable prospectus supplement or any related free writing prospectus, at prices and on terms to be determined by market conditions at the time of offering. This prospectus provides you with a general description of the securities we may offer. At the time we offer a type or series of securities, we will provide a prospectus supplement describing the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

- designation or classification;
- aggregate principal amount or aggregate offering price;
- voting or other rights;
- rates and times of payment of interest, dividends or other payments;
- original issue discount;
- maturity;
- ranking;
- restrictive covenants;
- redemption, conversion, exercise, exchange, settlement or sinking fund terms, including prices or rates, and any provisions for changes to or adjustments in such prices or rates and in the securities or other property receivable upon conversion, exercise, exchange or settlement;
- any securities exchange or market listing arrangements; and
- important U.S. federal income tax considerations.

The applicable prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change any of the information contained in this prospectus or in the documents incorporated by reference in this prospectus.

We may sell the securities directly to investors or to or through underwriters, dealers or agents. We and our underwriters, dealers or agents reserve the right to accept or reject all or part of any proposed purchase of securities. If we do offer securities to or through underwriters or agents, we will include in the applicable prospectus supplement (a) the names of the underwriters or agents and applicable fees, discounts and commissions to be paid to them, (b) details regarding over-allotment options, if any, and (c) net proceeds to us, if any.

Common Stock. We may issue shares of our common stock from time to time. Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders. The holders of our common stock are entitled to receive dividends out of funds legally available if our board of directors, in its discretion, determines to issue dividends and then only at the times and in the amounts that our board of directors may determine. Upon our liquidation, dissolution or winding-up, the assets legally available for distribution to our stockholders would be distributable ratably among the holders of our common stock at that time, subject to prior satisfaction of all outstanding debt and liabilities. Our common stock is not entitled to preemptive rights, and is not subject to conversion, redemption or sinking fund provisions. In this prospectus, we have summarized certain general features of the common stock under the heading "Description of Capital Stock—Common Stock." We urge you, however, to read the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) related to any common stock being offered.

Preferred Stock. We may issue shares of our preferred stock from time to time, in one or more series. Our board of directors will determine the designation, powers, preferences and rights of the shares of each series and any of their qualifications, limitations or restrictions, in each case without further vote or action by our stockholders.

If we sell any series of preferred stock under this prospectus, we will fix the designations, voting powers, preferences and rights of the preferred stock of each series we issue under this prospectus, as well as the qualifications, limitations or restrictions thereof, in the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that contains the terms of the series of preferred stock we are offering. In this prospectus, we have summarized certain general features of the preferred stock under "Description of Capital Stock—Preferred Stock." We urge you, however, to read the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) related to the series of preferred stock being offered, as well as the complete certificate of designation that contains the terms of the applicable series of preferred stock.

Debt Securities. We may issue debt securities from time to time, in one or more series, as senior, subordinated or junior subordinated, convertible or non-convertible and secured or unsecured debt. Any senior debt securities will rank equally with any unsubordinated debt. Subordinated debt securities will rank equally with any other subordinated debt of the same ranking we may issue. Convertible debt securities will be convertible into or exchangeable for our common stock or other securities at predetermined conversion rates, and conversion may be mandatory or at the holder's option.

Debt securities will be issued under one or more indentures-contracts between us and a national banking association or other eligible party acting as trustee. In this prospectus, we have summarized certain general features of the debt securities under the heading "Description of Debt Securities." You should read the prospectus supplements, any free writing prospectus we may authorize and the indentures, supplemental indentures and forms of debt securities relating to any series of debt securities we may offer. We have filed the form of indenture as an exhibit to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

Warrants, Other Rights and Units. We may, from time to time issue warrants or other rights (together, "Rights"), in one or more series, for the purchase of common stock or preferred stock. We may issue such Rights independently or together with such securities, and such Rights may be attached to or separate from them. We may issue securities in units ("Units"), each consisting of two or more types of securities. For example, we might issue Units consisting of a combination of common stock and warrants to purchase common stock. In this prospectus, we have summarized certain general features of the Rights and Units under the heading "Description of Warrants, Other Rights and Units." We urge you, however, to read the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) related to the particular series of Rights and/or Units being offered, as well as the form of Rights and/or Rights agreement and Rights certificate, as applicable, that contain the terms of the warrants. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of Rights and/or Rights agreement and Rights certificate, as applicable, that contain the terms of the particular series of Rights we are offering, and any supplemental agreements, before the issuance of such Rights.

Rights may be issued under a Rights agreement that we enter into with a Rights agent. We will indicate the name and address of the Rights agent, if any, in the applicable prospectus supplement relating to a particular series of Rights.

NASDAQ Capital Market Listing

Our common stock is listed on The NASDAQ Capital Market under the symbol "KRYS." The applicable prospectus supplement will contain information, where applicable, as to other listings, if any, on The NASDAQ Capital Market or any other securities market or other exchange of the securities covered by the applicable prospectus supplement.

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 our Annual Report on Form 10-K for the fiscal year ended December 31, 2017;
- 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 total annual gross revenues, 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" in our Annual Report on Form 10-K for the fiscal year ended December 31, 2017, and have taken advantage of the exemption from auditor attestation on the effectiveness of our internal controls 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.

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 June 30, 2018, we have an accumulated deficit of $13.5 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 date to research and development of our first 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 clinical development of KB103, including our current clinical trials and planned future trials;
- initiate additional clinical trials and preclinical studies for any additional product candidates that we may pursue in the future;
- prepare our Biologics License Application, or BLA, and marketing authorization application for KB103;
- establish and validate a commercial-scale cGMP manufacturing facility;
- manufacture current good manufacturing practices, or cGMP, material for clinical trials or potential commercial sales;
- 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 and additional product candidates 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 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, the European Medicines Agency (the "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 current and planned clinical trials of KB103 and other product candidates;
- 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 and clinical trials of KB103. While we have commenced our first clinical trial 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. The successful commercialization of KB103 will require us to perform a variety of functions, including:

- further clinical development of KB103;
- obtaining required regulatory approvals;
- developing and operating a manufacturing facility or obtaining manufacturing services from third party manufacturers; 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. If we are unable to advance KB103 through 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 entered its first clinical trial in May 2018. The development and commercialization of KB103 (or any other product candidate we may develop) is subject to many uncertainties, including the following:

- successful enrollment and completion of clinical trials;
- positive results from our current and planned future 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.

KB103 is in early stage development, and there is no guarantee that the results from preclinical studies will be indicative of our ability to complete or the results to be obtained in the current or future studies and clinical trials.

We initiated our first clinical trial for KB103 in May 2018; however, there is no guarantee that results of this or any potential future clinical trials will be positive or that we will be able to complete this or any potential future clinical trials on the anticipated timelines or at all. The positive results we have observed for KB103 in preclinical trials may not be predictive of outcomes in our current and future clinical trials, and the current and future 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. Furthermore, research and discoveries by us or others may identify serious adverse events, undesirable side effects or other unexpected properties of our current and future product candidates, including KB103, that could delay, prevent or cause the withdrawal of regulatory approval, limit the commercial potential, or result in significant negative consequences following marketing approval.

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 KB103 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. We have experienced a period of significant expansion in headcount and expect to experience significant expansion of our facilities, infrastructure and overhead as we develop our own manufacturing facility and increase our research and development efforts. 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 and KB105, 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. On April 19, 2018, the EMA granted the Orphan Medicinal Product Designation, or OMPD, for KB103. On August 9, 2018, the FDA granted orphan drug designation to our second product candidate, KB105, currently in preclinical development for treatment of patients with transglutaminase 1 (TGM-1) deficient autosomal recessive congenital ichthyosis ("ARCI"). There are currently no treatments for ARCI, which affects approximately 20,000 patients worldwide. 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 and KB105, 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, Regenerative Medicine Advanced Therapy 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.

On May 27, 2018, the FDA granted Fast Track designation in the United States for KB103. We have been granted rare pediatric disease designation for KB103. On August 23, 2018, the FDA granted rare pediatric disease designation for KB105. 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 after having received 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. We received the designation of "rare pediatric disease" for KB103 in December 2016 and for KB105 in August 2018 which 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 or KB105, 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 and KB105, 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 product candidates, KB103 and KB105, 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.

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 KB103, KB105, any future innovations related to our STAR-D platform, and our institutional knowledge, including our manufacturing processes. 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 currently have one issued patent in the United States covering, in part, pharmaceutical formulations

and methods of treating dystrophic epidermolysis bullosa ("DEB") using our KB103 product. A corresponding international application has been filed in accordance with the Paris Cooperation treaty, and a number of patent applications are on file in foreign jurisdictions stemming from this international application. We are actively prosecuting a continuing patent application in front of the U.S. Patent and Trademark Office, or USPTO, directed to further aspects of our KB103 product candidate. In addition, we are seeking patent protection for other key aspects of our business, including our product KB105, through additional patent applications 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 our own. 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, KB105 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 or other unauthorized use of intellectual property. 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 interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, or distribution activities.

We may not have sufficient financial or other resources to 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 we, our employees or our advisors have wrongfully used or disclosed alleged trade secrets of other parties, including 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, and we have and may in the future enter into agreements providing us with rights to intellectual property of third parties for limited purposes. Although we try to observe the terms of agreements under which we obtain access to third party intellectual property and 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 third parties or the current or former employers of employees or advisors. 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 this 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 September 28, 2018, 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 37.3% 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.

If securities analysts publish negative evaluations of our stock, the price of our stock could decline.

The trading market for our common stock relies in part on the research and reports that industry or financial analysts publish about us or our business. If securities 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 has been and is likely to continue 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 any offering, and may not use them effectively.

Our management will have broad discretion in the application of our cash, including the net proceeds from any offering, 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 any offering, 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 product candidates, including 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 product candidates, including 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.

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.

USE OF PROCEEDS

Except as described in any applicable prospectus supplement or in any free writing prospectuses we have authorized for use in connection with a specific offering, we currently intend to use the net proceeds from the sale of the securities offered by us hereunder, if any, for working capital and general corporate purposes, including research and development expenses and capital expenditures.

The amounts and timing of our use of the net proceeds from this offering will depend on a number of factors, such as our funding requirements and the availability and cost of other funds at the time of sale, the timing and progress of our research and development efforts, the timing and progress of any partnering and commercialization efforts, technological advances and the competitive environment for our products. As of the date of this prospectus, we cannot specify with certainty all of the particular uses for the net proceeds to us from the sale of the securities offered by us hereunder. Accordingly, our management will have broad discretion in the timing and application of these proceeds. Pending application of the net proceeds as described above, we intend to temporarily invest the proceeds in short-term, interest-bearing instruments or other investment-grade securities, certificates of deposits or short-term U.S. government securities.

We will not receive any proceeds from the resale of shares of our common stock by the selling stockholder.

RATIO OF EARNINGS TO FIXED CHARGES

Any time debt securities are offered pursuant to this prospectus, we will provide a table setting forth our ratio of earnings to fixed charges on a historical basis in the applicable prospectus supplement, if required.

	Year Ended December 31,		Six Months Ended June 30,
	2016	2017	2018
Ratio of earnings to fixed charges	*	*	*

(*) We did not record earnings for the years ended December 31, 2016 or 2017 or the six months ended June 30, 2018. Accordingly, our earnings were insufficient to cover fixed charges for such periods and we are unable to disclose a ratio of earnings to fixed charges for such periods. The dollar amount of the deficiency in earnings available for fixed charges for the years ended December 31, 2016 and 2017 and the six months ended June 30, 2018 was $1.2 million, $7.9 million and $4.4 million, respectively.

DIVIDEND POLICY

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings for use in the operation of our business and do not anticipate paying any dividends on our common stock in the foreseeable future. Any future determination to declare dividends will be made at the discretion of our board of directors and will depend on our financial condition, operating results, capital requirements, general business conditions and other factors that our board of directors may deem relevant.

GENERAL DESCRIPTION OF SECURITIES

We may offer shares of our common stock or preferred stock, various series of debt securities, warrants or other rights to purchase common stock or preferred stock, or units consisting of combinations of the foregoing, either individually or in combination with other securities, in each case from time to time under this prospectus, together with the applicable prospectus supplement or any related free writing prospectus, at prices and on terms to be determined by market conditions at the time of offering. This prospectus provides you with a general description of the securities we may offer. At the time we offer a type or series of securities, we will provide a prospectus supplement describing the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

- designation or classification;
- aggregate principal amount or aggregate offering price;
- voting or other rights;
- rates and times of payment of interest, dividends or other payments;
- original issue discount;
- maturity;
- ranking;
- restrictive covenants;
- redemption, conversion, exercise, exchange, settlement or sinking fund terms, including prices or rates, and any provisions for changes to or adjustments in such prices or rates and in the securities or other property receivable upon conversion, exercise, exchange or settlement;
- any securities exchange or market listing arrangements; and
- important U.S. federal income tax considerations.

This prospectus may not be used to offer or sell securities unless accompanied by a prospectus supplement. The prospectus supplement may add, update or change any of the information contained in this prospectus or in the documents incorporated by reference in this prospectus. We urge you to read the prospectus supplement related to any securities being offered.

We may sell the securities directly to investors or to or through underwriters, dealers or agents. We and our underwriters, dealers or agents reserve the right to accept or reject all or part of any proposed purchase of securities. If we do offer securities to or through underwriters or agents, we will include in the applicable prospectus supplement (a) the names of the underwriters or agents and applicable fees, discounts and commissions to be paid to them, (b) details regarding over-allotment options, if any, and (c) net proceeds to us, if any.

The following descriptions are not complete and may not contain all the information you should consider before investing in any securities we may offer hereunder; they are summarized from, and qualified by reference to, our Certificate of Incorporation, Bylaws and the other documents referred to in the descriptions, all of which are or will be publicly filed with the SEC, as applicable. See “Where You Can Find More Information.”

DESCRIPTION OF CAPITAL STOCK

General

Our authorized capital stock consists of 80,000,000 shares of common stock, $0.00001 par value per share, and 20,000,000 shares of preferred stock, $0.00001 par value per share. As of September 28, 2018, there were 10,978,916 shares of our common stock outstanding and no shares of preferred stock outstanding.

The following description summarizes the most important terms of our capital stock. Because it is only a summary, it does not contain all the information that may be important to you. The description is intended as a summary, and is qualified in its entirety by reference to our second amended and restated certificate of incorporation (our "Certificate of Incorporation") and our amended and restated bylaws (our "Bylaws"). For a complete description, you should refer to our Certificate of Incorporation and Bylaws.

Common Stock

Dividend Rights

The holders of our common stock are entitled to receive dividends out of funds legally available if our board of directors, in its discretion, determines to issue dividends and then only at the times and in the amounts that our board of directors may determine. See "Dividend Policy" above.

Voting Rights

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders. We have not provided for cumulative voting for the election of directors in our Certificate of Incorporation. Accordingly, holders of a majority of the shares of our common stock will be able to elect all of our directors. Our Certificate of Incorporation has established a classified board of directors, divided into three classes with staggered three-year terms. Only one class of directors will be elected at each annual meeting of our stockholders, with the other classes continuing for the remainder of their respective three-year terms.

No Preemptive or Similar Rights

Our common stock is not entitled to preemptive rights, and is not subject to conversion, redemption or sinking fund provisions.

Right to Receive Liquidation Distributions

Upon our liquidation, dissolution or winding-up, the assets legally available for distribution to our stockholders would be distributable ratably among the holders of our common stock at that time, subject to prior satisfaction of all outstanding debt and liabilities.

Preferred Stock

Pursuant to our Certificate of Incorporation, our board of directors is authorized, subject to limitations prescribed by Delaware law, to issue from time to time up to 20,000,000 shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each series and to fix the designation, powers, preferences and rights of the shares of each series and any of their qualifications, limitations or restrictions, in each case without further vote or action by our stockholders. Our board of directors may increase or decrease the number of shares of any series of preferred stock, but not below the number of shares of that series then outstanding, without any further vote or action by our stockholders. Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of our common stock. The issuance of preferred stock, while providing

flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in control of our company and might adversely affect the market price of our common stock and the voting and other rights of the holders of our common stock. We have no current plan to issue any shares of preferred stock.

The General Corporation Law of the State of Delaware (the "DGCL"), the state of our incorporation, provides that the holders of preferred stock will have the right to vote separately as a class on any proposal involving fundamental changes in the rights of holders of that preferred stock. This right is in addition to any voting rights that may be provided for in the applicable certificate of designation.

Anti-Takeover Provisions

The provisions of Delaware law, our Certificate of Incorporation and our Bylaws could have the effect of delaying, deferring or discouraging another person from acquiring control of our company. These provisions, which are summarized below, may have the effect of discouraging takeover bids. They are also designed, in part, to encourage persons seeking to acquire control of us to negotiate first with our board of directors. We believe that the benefits of increased protection of our potential ability to negotiate with an unfriendly or unsolicited acquirer outweigh the disadvantages of discouraging a proposal to acquire us because negotiation of these proposals could result in an improvement of their terms.

Delaware Law

We are subject to the provisions of Section 203 of the DGCL, regulating corporate takeovers. In general, Section 203 of the DGCL prohibits a publicly held Delaware corporation from engaging in a business combination with an interested stockholder for a period of three years following the date on which the person became an interested stockholder unless:

- prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, but not the outstanding voting stock owned by the interested stockholder: (i) shares owned by persons who are directors and also officers; and (ii) shares owned by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or
- at or subsequent to the date of the transaction, the business combination is approved by the board of directors of the corporation and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66.67% of the outstanding voting stock that is not owned by the interested stockholder.

Generally, a business combination includes a merger, asset or stock sale, or other transaction or series of transactions together resulting in a financial benefit to the interested stockholder. An interested stockholder is a person who, together with affiliates and associates, owns or, within three years prior to the determination of interested stockholder status, did own 15% or more of a corporation's outstanding voting stock. We expect the existence of this provision to have an anti-takeover effect with respect to transactions our board of directors does not approve in advance. We also anticipate that Section 203 of the DGCL may also discourage attempts that might result in a premium over the market price for the shares of common stock held by stockholders.

Second Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws Provisions

Our Certificate of Incorporation and our Bylaws include a number of provisions that could deter hostile takeovers or delay or prevent changes in control of our company, including the following:

- *Board of Directors Vacancies.* Our Certificate of Incorporation and Bylaws authorizes only our board of directors to fill vacant directorships, including newly created seats. In addition, the number of directors constituting our board of directors may only be set by a resolution adopted by a majority vote of our entire board of directors. These provisions would prevent a stockholder from increasing the size of our board of directors and then gaining control of our board of directors by filling the resulting vacancies with its own nominees. This makes it more difficult to change the composition of our board of directors but promotes continuity of management.
- *Classified Board.* Our Certificate of Incorporation and Bylaws provide that our board of directors will be classified into three classes of directors, each with staggered three-year terms. A third party may be discouraged from making a tender offer or otherwise attempting to obtain control of us as it is more difficult and time consuming for stockholders to replace a majority of the directors on a classified board of directors.
- *Stockholder Action; Special Meetings of Stockholders.* Our Certificate of Incorporation provides that our stockholders may not take action by written consent, but may only take action at annual or special meetings of our stockholders. As a result, a holder controlling a majority of our capital stock may not amend our restated bylaws or remove directors without holding a meeting of our stockholders called in accordance with our restated bylaws. Further, our Certificate of Incorporation and Bylaws provide that special meetings of our stockholders may be called only by a majority of our board of directors, the chairman of our board of directors, or our Chief Executive Officer, thus prohibiting a stockholder from calling a special meeting. These provisions might delay the ability of our stockholders to force consideration of a proposal or for stockholders controlling a majority of our capital stock to take any action, including the removal of directors.
- *Advance Notice Requirements for Stockholder Proposals and Director Nominations.* Our Bylaws provides advance notice procedures for stockholders seeking to bring business before our annual meeting of stockholders or to nominate candidates for election as directors at our annual meeting of stockholders. Our Bylaws also specifies certain requirements regarding the form and content of a stockholder's notice. These provisions may preclude our stockholders from bringing matters before our annual meeting of stockholders or from making nominations for directors at our annual meeting of stockholders if the proper procedures are not followed. We expect that these provisions may also discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of our company.
- *No Cumulative Voting.* The DGCL provides that stockholders are not entitled to the right to cumulate votes in the election of directors unless a corporation's certificate of incorporation provides otherwise. Our Certificate of Incorporation does not provide for cumulative voting.
- *Directors Removed Only for Cause.* Our Certificate of Incorporation provides that stockholders may remove directors only for cause and only by the affirmative vote of the holders of at least two-thirds of our outstanding common stock.
- *Amendment of Charter Provisions.* Any amendment of the above expected provisions in our Certificate of Incorporation requires approval by holders of at least two-thirds of our outstanding common stock.
- *Issuance of Undesignated Preferred Stock.* Our board of directors has the authority, without further action by the stockholders, to issue up to 20,000,000 shares of undesignated preferred stock with rights and preferences, including voting rights, designated from time to time by our board of directors. The existence of authorized but unissued shares of preferred stock will enable our board of directors to

render more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or other means.

- *Choice of Forum.* Our Certificate of Incorporation provides that the Court of Chancery of the State of Delaware will be the exclusive forum for: any derivative action or proceeding brought on our behalf; any action asserting a breach of fiduciary duty; any action asserting a claim against us arising pursuant to the DGCL, our Certificate of Incorporation or our Bylaws; any action to interpret, apply, enforce or determine the validity of our Certificate of Incorporation or our Bylaws; or any action asserting a claim against us that is governed by the internal affairs doctrine. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that a court could find these types of provisions to be inapplicable or unenforceable.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A. The transfer agent's address is 250 Royall Street Canton, Massachusetts 02021, and its telephone number is 1-800-962-4284. Our shares of common stock were issued in uncertificated form only, subject to limited circumstances.

NASDAQ Capital Market Listing

Our common stock is listed on The NASDAQ Capital Market under the symbol "KRYS."

DESCRIPTION OF DEBT SECURITIES

We may issue debt securities from time to time, in one or more series, as senior, subordinated or junior subordinated, convertible or non-convertible and secured or unsecured debt. Any senior debt securities will rank equally with any unsubordinated debt. Subordinated debt securities will rank equally with any other subordinated debt of the same ranking we may issue. Convertible debt securities will be convertible into or exchangeable for our common stock or other securities at predetermined conversion rates, and conversion may be mandatory or at the holder's option.

Debt securities will be issued under one or more indentures-contracts between us and a national banking association or other eligible party acting as trustee. Following is a summary of certain general features of debt securities we may issue; we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement, which may differ from the terms we describe below. You should read the prospectus supplements, any free writing prospectus we may authorize and the indentures, supplemental indentures and forms of debt securities relating to any series of debt securities we may offer.

General

Except as we may otherwise provide in a prospectus supplement, the relevant indenture will provide that debt securities may be issued from time to time in one or more series. The indenture will not limit the amount of debt securities that may be issued thereunder and will provide that the specific terms of any series of debt securities shall be set forth in, or determined pursuant to, an authorizing resolution, an officers' certificate or a supplemental indenture, if any, relating to such series.

We will describe in each prospectus supplement the following terms relating to any series of debt securities:

- the title or designation;
- whether they will be secured or unsecured, and the terms of any security;
- whether the debt securities will be subject to subordination, and any terms thereof;
- any limit upon the aggregate principal amount;
- the date or dates on which the debt securities may be issued and on which we will pay the principal;
- the interest rate, which may be fixed or variable, or the method for determining the rate, the date interest will begin to accrue, the date or dates interest will be payable and the record dates for interest payment dates or the method for determining them;
- the manner in which the amounts of payment of principal of, premium or interest on the debt securities will be determined, if these amounts may be determined by reference to an index based on a currency or currencies other than that in which the debt securities are denominated or designated to be payable or by reference to a commodity, commodity index, stock exchange index or financial index;
- the currency of denomination;
- if payments of principal of, premium or interest will be made in one or more currencies or currency units other than that or those in which the debt securities are denominated, the manner in which the exchange rate with respect to these payments will be determined;
- the place or places where the principal of, premium, and interest will be payable, where debt securities of any series may be presented for registration of transfer, exchange or conversion, and where notices and demands to or upon the Company in respect of the debt securities may be made;
- the form of consideration in which principal of, premium or interest will be paid;
- the terms and conditions upon which we may redeem the debt securities;

- any obligation we have to redeem or purchase the debt securities pursuant to any sinking fund, amortization or analogous provisions or at the option of a holder;
- the dates on which and the price or prices at which we will repurchase the debt securities at the option of holders and other detailed terms and provisions of these obligations;
- the denominations in which the debt securities will be issued, if other than denominations of $1,000 and any integral multiple thereof;
- the portion of principal amount payable upon declaration of acceleration of the maturity date, if other than the principal amount;
- whether the debt securities are to be issued at any original issuance discount and the amount of discount with which they may be issued;
- whether the debt securities will be issued in certificated or global form and, in such case, the depositary and the terms and conditions, if any, upon which interests in such global security or securities may be exchanged in whole or in part for the individual securities represented thereby;
- provisions, if any, for defeasance in whole or in part and any addition or change to provisions related to satisfaction and discharge;
- the form of the debt securities;
- the terms and conditions upon which convertible debt securities will be convertible or exchangeable into securities or property of the Company or another person, if at all, and any additions or changes, if any, to permit or facilitate the same;
- provisions, if any, granting special rights to holders upon the occurrence of specified events;
- any restriction or condition on transferability;
- any addition or change in the provisions related to compensation and reimbursement of the trustee;
- any addition to or change in the events of default described in this prospectus or in the indenture and any change in the acceleration provisions so described;
- whether the debt securities will restrict our ability to pay dividends, or will require us to maintain any asset ratios or reserves;
- whether we will be restricted from incurring any additional indebtedness;
- any addition to or change in the covenants described in this prospectus or in the indenture, including terms of any restrictive covenants; and
- any other terms which may modify or delete any provision of the indenture.

We may issue debt securities that provide for an amount less than their stated principal amount to be due and payable upon declaration of acceleration of their maturity pursuant to the terms of the indenture. We will provide you with information on the U.S. federal income tax considerations and other special considerations applicable to any debt securities in the applicable prospectus supplement.

Conversion or Exchange Rights

We will set forth in the applicable prospectus supplement the terms, if any, on which a series of debt securities may be convertible into or exchangeable for our common stock or other securities. We will include provisions as to settlement upon conversion or exchange and whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock or other securities that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Merger or Sale; No Protection in Event of a Change of Control or Highly Leveraged Transaction

Except as we may otherwise provide in a prospectus supplement, the indenture will provide that we may not merge or consolidate with or into another entity, or sell other than for cash or lease all or substantially all our assets to another entity, or purchase all or substantially all the assets of another entity unless we are the surviving entity or, if we are not the surviving entity, the successor, transferee or lessee entity expressly assumes all of our obligations under the indenture or the debt securities, as appropriate.

Unless we state otherwise in the applicable prospectus supplement, the debt securities will not contain any provisions that may afford holders additional protection in the event we have a change of control or in the event of a highly leveraged transaction (whether or not such transaction results in a change of control), which could adversely affect them.

Events of Default under the Indenture

Except as we may otherwise provide in a prospectus supplement, the following will be events of default under the indenture with respect to any series of debt securities that we may issue:

- if we fail to pay interest when due and our failure continues for 90 days and the time for payment has not been extended or deferred;
- if we fail to pay the principal, or premium, if any, when due whether by maturity or called for redemption;
- if we fail to pay a sinking fund installment, if any, when due and our failure continues for 30 days;
- if we fail to observe or perform any other covenant relating to the debt securities, other than a covenant specifically relating to and for the benefit of holders of another series of debt securities, and our failure continues for 90 days after we receive written notice from the debenture trustee or holders of not less than a majority in aggregate principal amount of the outstanding series; and
- if specified events of bankruptcy, insolvency or reorganization occur as to the Company.

No event of default with respect to a particular series of debt securities (except as to certain events of bankruptcy, insolvency or reorganization) will necessarily constitute an event of default with respect to any other series. The occurrence of an event of default may constitute an event of default under any bank credit agreements we may have in existence from time to time. In addition, the occurrence of certain events of default or an acceleration under the indenture may constitute an event of default under certain of our other indebtedness outstanding from time to time.

Except as we may otherwise provide in a prospectus supplement, if an event of default with respect to debt securities of any series at the time outstanding occurs and is continuing, then the trustee or the holders of not less than a majority in principal amount of the outstanding series may, by a notice in writing to us (and to the debenture trustee if given by the holders), declare to be due and payable immediately the principal (or, if the debt securities are discount securities, that portion of the principal amount as may be specified in the terms of such securities) of and premium and accrued and unpaid interest, if any, on all such debt securities. Before a judgment or decree for payment of the money due has been obtained with respect to any series, the holders of a majority in principal amount of that series (or, at a meeting of holders at which a quorum is present, the holders of a majority in principal amount represented at such meeting) may rescind and annul the acceleration if all events of default, other than the non-payment of accelerated principal, premium, if any, and interest, if any, have been cured or waived as provided in the applicable indenture (including payments or deposits in respect of principal, premium or interest that had become due other than as a result of such acceleration) and the Company has deposited with the indenture trustee or paying agent a sum sufficient to pay all amounts owed to the indenture trustee under the

indenture, all arrears of interest, if any, and the principal and premium, if any, on the debt securities that have become due other than by such acceleration. We refer you to the relevant prospectus supplement relating to any discount securities for the particular provisions relating to acceleration of a portion of the principal amount thereof upon the occurrence of an event of default.

Subject to the terms of the indenture, and except as we may otherwise provide in a prospectus supplement, if an event of default under the indenture shall occur and be continuing, the debenture trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series, unless such holders have offered the debenture trustee reasonable indemnity. The holders of a majority in principal amount of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the debenture trustee, or exercising any trust or power conferred on the debenture trustee, with respect to that series, provided that, subject to the terms of the indenture, the debenture trustee need not take any action that it believes, upon the advice of counsel, might involve it in personal liability or might be unduly prejudicial to holders not involved in the proceeding.

Except as we may otherwise provide in a prospectus supplement, a holder of the debt securities of any series will only have the right to institute a proceeding under the indenture or to appoint a receiver or trustee, or to seek other remedies if:

- the holder previously has given written notice to the debenture trustee of a continuing event of default with respect to that series;
- the holders of at least a majority in aggregate principal amount outstanding of that series have made written request, and such holders have offered reasonable indemnity to the debenture trustee to institute the proceeding as trustee; and
- the debenture trustee does not institute the proceeding and does not receive from the holders of a majority in aggregate principal amount outstanding of that series (or at a meeting of holders at which a quorum is present, the holders of a majority in principal amount of such series represented at such meeting) other conflicting directions within 60 days after the notice, request and offer.

Except as we may otherwise provide in a prospectus supplement, these limitations will not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, them.

We will periodically file statements with the applicable debenture trustee regarding our compliance with specified covenants in the applicable indenture.

Modification of Indenture; Waiver

Except as we may otherwise provide in a prospectus supplement, the debenture trustee and the Company may, without the consent of any holders, execute a supplemental indenture to change the applicable indenture with respect to specific matters, including, among other things:

- to surrender any right or power conferred upon the Company;
- to provide, change or eliminate any restrictions on payment of principal of or premium, if any; provided that any such action shall not adversely affect the interests of the holders of debt securities of any series in any material respect;
- to change or eliminate any of the provisions of the indenture; provided that any such change or elimination shall become effective only when there is no outstanding debt security created prior to the execution of such supplemental indenture that is entitled to the benefit of such provision and as to which such supplemental indenture would apply;
- to evidence the succession of another entity to the Company;

- to evidence and provide for the acceptance of appointment by a successor trustee with respect to one or more series of debt securities and to add or change provisions of the indenture to facilitate the administration of the trusts thereunder by more than one trustee;
- to cure any ambiguity, mistake, manifest error, omission, defect or inconsistency in the indenture or to conform the text of any provision in the indenture or in any supplemental indenture to any description thereof in the applicable section of a prospectus, prospectus supplement or other offering document that was intended to be a verbatim recitation of a provision of the indenture or of any supplemental indenture;
- to add to or change or eliminate any provision of the indenture as shall be necessary or desirable in accordance with any amendments to the U.S. Trust Indenture Act of 1939;
- to make any change in any series of debt securities that does not adversely affect in any material respect the interests of the holders thereof; and
- to supplement any of the provisions of the indenture to such extent as shall be necessary to permit or facilitate the defeasance and discharge of any series of debt securities; provided that any such action shall not adversely affect the interests of holders of any debt securities.

In addition, and except as we may otherwise provide in a prospectus supplement, under the indenture the rights of holders of a series of debt securities may be changed by us and the debenture trustee with the written consent of the holders of at least a majority in aggregate principal amount outstanding (or, at a meeting of holders of such series at which a quorum is present, the holders of a majority in principal amount represented at such meeting) that is affected. The debenture trustee and the Company may, however, make the following changes only with the consent of each holder of any outstanding debt securities affected:

- extending the fixed maturity;
- reducing the principal amount, reducing the rate of or extending the time of payment of interest, or any premium payable upon redemption;
- reducing the principal amount of discount securities payable upon acceleration of maturity;
- making the principal of or premium or interest payable in currency other than that stated;
- impairing the right to institute suit for the enforcement of any payment on or after the fixed maturity date;
- materially adversely affecting the economic terms of any right to convert or exchange; and
- reducing the percentage of debt securities, the holders of which are required to consent to any amendment or waiver; or modifying, without the written consent of the trustee, the rights, duties or immunities of the trustee.

Except for certain specified provisions, and except as we may otherwise provide in a prospectus supplement, the holders of at least a majority in principal amount of any series (or, at a meeting of holders of such series at which a quorum is present, the holders of a majority in principal amount represented at such meeting) may, on behalf of the holders of all debt securities of that series, waive our compliance with provisions of the indenture. The holders of a majority in principal amount of the outstanding debt securities of any series may, on behalf of all such holders, waive any past default under the indenture with respect to that series and its consequences, other than a default in the payment of the principal of, premium or any interest; provided, however, that the holders of a majority in principal amount of the outstanding debt securities of any series may rescind an acceleration and its consequences, including any related payment default that resulted from the acceleration.

Discharge

Except as we may otherwise provide in a prospectus supplement, the indenture will provide that we can elect to be discharged from our obligations with respect to one or more series of debt securities. In order to

exercise our rights to be discharged, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, the premium, if any, and interest on, the debt securities of the affected series on the dates payments are due.

Form, Exchange and Transfer

Except as we may otherwise provide in a prospectus supplement, we will issue debt securities only in fully registered form without coupons and, unless we otherwise specify in the applicable prospectus supplement, in denominations of $1,000 and any integral multiple thereof. Except as we may otherwise provide in a prospectus supplement, the indenture will provide that we may issue debt securities in temporary or permanent global form and as book-entry securities that will be deposited with a depositary named by us and identified in a prospectus supplement with respect to that series.

At the option of the holder, subject to the terms of the indenture and the limitations applicable to global securities described in the applicable prospectus supplement, the holder will be able to exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indenture and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities or the indenture, we will impose no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

Except as we may otherwise provide in a prospectus supplement, if we elect to redeem the debt securities of any series, we will not be required to:

- issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or
- register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Debenture Trustee

The debenture trustee, other than during the occurrence and continuance of an event of default under the indenture, will undertake to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default, the debenture trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs. Subject to this provision, the debenture trustee will be under no obligation to exercise any of the powers given it by the indenture at the request of any holder unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of interest on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

Unless we otherwise indicate in the applicable prospectus supplement, we will pay principal of and any premium and interest at the office of the indenture trustee or, at the option of the Company, by check payable to the holder. Unless we otherwise indicate in a prospectus supplement, we will designate the corporate trust office of the debenture trustee as our sole paying agent for payments. We will name in the applicable prospectus supplement any other paying agents that we initially designate. We will maintain a paying agent in each place of payment.

All money we pay to a paying agent or the debenture trustee for the payment of principal or any premium or interest which remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the debt security thereafter may look only to us for payment thereof.

Governing Law

The indenture and the debt securities will be governed and construed in accordance with the laws of the State of New York.

No Personal Liability of Directors, Officers, Employees and Stockholders

No incorporator, stockholder, employee, agent, officer, director or subsidiary of ours will have any liability for any obligations of ours or, due to the creation of any indebtedness under the debt securities, the indentures or supplemental indentures. The indentures provide that all such liability is expressly waived and released as a condition of, and as consideration for, the execution of such indentures and the issuance of the debt securities.

DESCRIPTION OF WARRANTS, OTHER RIGHTS AND UNITS

We may, from time to time, issue warrants or other rights (together, "Rights"), in one or more series, for the purchase of common stock or preferred stock. We may issue Rights independently or together with such securities, and such Rights may be attached to or separate from them. Rights will be evidenced by a Rights certificate issued under one or more Rights agreements between us and a Rights agent which will act solely as our agent in connection with the Rights and will not have any obligation or relationship of agency or trust for or with any holders or beneficial owners of Rights. We may issue securities in units ("Units"), each consisting of two or more types of securities. For example, we might issue Units consisting of a combination of common stock and warrants to purchase common stock. If we issue Units, the prospectus supplement relating to the Units will contain the information described above with regard to each of the securities that is a component of the Units. In addition, the prospectus supplement relating to the Units will describe the terms of any Units we issue. The forms of any such certificates and agreements will be filed as exhibits to the registration statement of which this prospectus is a part by amendment thereof or as exhibits to a Current Report on Form 8-K incorporated herein by reference, and the accompanying prospectus supplement and such forms may add, update or change the terms and conditions of the Rights or Units described in this prospectus.

The following description of material terms and provisions of Rights and Units will generally apply to the Rights and/or Units offered by this prospectus unless we provide otherwise in the applicable prospectus supplement, which may specify different or additional terms. The following summaries are subject to, and qualified in their entirety by reference to, all the provisions of the form of Rights and/or the Rights agreement and Rights certificate, as applicable, and any supplemental agreements applicable to a particular series of Rights and/or Units that we may offer under this prospectus. We urge you to read the applicable prospectus supplement related to the particular series of Rights or Units that we may offer under this prospectus, as well as any related free writing prospectus, and the complete form of Rights and/or the Rights agreement and Right certificates, as applicable, and any supplemental agreements, that contain the terms of the Rights.

The particular terms of each issue of Rights or Units will be described in the applicable prospectus supplement, including, as applicable:

- the title of the Rights or Units;
- any initial offering price;
- the title, aggregate principal amount or number and terms of the securities purchasable upon exercise of the Rights;
- the principal amount or number of securities purchasable upon exercise of each Right and the price at which that principal amount or number may be purchased upon exercise of each Right;
- the currency or currency units in which any offering price and any exercise price are payable;
- the title and terms of any related securities with which the Rights are issued and the number of the Rights issued with each security;
- any date on and after which the Rights or Units and the related securities will be separately transferable;
- any minimum or maximum number of Rights that may be exercised at any one time;
- the date on which the right to exercise the Rights will commence and the date on which the right will expire;
- a discussion of U.S. federal income tax, accounting or other considerations applicable to the Rights or Units;
- whether the Rights represented by the Rights certificates, if applicable, will be issued in registered or bearer form and, if registered, where they may be transferred and registered;

- any anti-dilution provisions of the Rights or Units;
- any redemption or call provisions applicable to the Rights;
- any provisions for changes to or adjustments in the exercise price of any Rights; and
- any additional terms of the Rights or Units, including terms, procedures and limitations relating to exchange and exercise of the Rights or Units.

Rights certificates will be exchangeable for new Rights certificates of different denominations and, if in registered form, may be presented for registration of transfer, and Rights may be exercised, at the corporate trust office of the Rights agent or any other office indicated in the related prospectus supplement. Before the exercise of Rights, holders of Rights will not be entitled to payments of any dividends, principal, premium or interest on securities purchasable upon exercise of the Rights, to vote, consent or receive any notice as a holder of and in respect of any such securities or to enforce any covenants in any indenture, or to exercise any other rights whatsoever as a holder of securities purchasable upon exercise of the Rights.

SELLING STOCKHOLDER

The selling stockholder may, from time to time, offer and sell, or otherwise disposed of, up to 625,000 shares of our common stock under this prospectus. The 625,000 shares of our common stock held by the selling stockholder were issued and sold to the selling stockholder in a private placement (the "Private Placement") pursuant to a stock purchase agreement, dated August 16, 2018 (the "Purchase Agreement"), between us and the selling stockholder. Pursuant to the Purchase Agreement, the Company agreed to file a registration statement with the SEC registering the resale of the shares issued and sold in the Private Placement, to have such registration statement declared effective within the time period set forth in the Purchase Agreement, and to keep such registration statement effective for up to three years. The 625,000 shares of our common stock held by the selling stockholder are being registered by the registration statement of which this prospectus forms a part pursuant to such registration rights granted to the selling stockholder pursuant to the Purchase Agreement.

The following table sets forth certain information with respect to the selling stockholder, including (i) the shares of our common stock beneficially owned by the selling stockholder prior to this offering, (ii) the number of shares being offered by the selling stockholder pursuant to this prospectus and (iii) the selling stockholder's beneficial ownership after completion of this offering, assuming that all of the shares covered hereby (but none of the other shares, if any, held by the selling stockholder) are sold.

The table is based on information supplied to us by the selling stockholder, with beneficial ownership and percentage ownership determined in accordance with the rules and regulations of the SEC and includes voting or investment power with respect to shares of stock. This information does not necessarily indicate beneficial ownership for any other purpose. The percentage of beneficial ownership after this offering is based on 10,978,916 shares outstanding on September 28, 2018.

The registration of these shares of common stock does not mean that the selling stockholder will sell or otherwise dispose of all or any of those securities. The selling stockholder may sell or otherwise dispose of all, a portion or none of such shares from time to time. We do not know the number of shares, if any, that will be offered for sale or other disposition by any of the selling stockholder under this prospectus. Furthermore, the selling stockholder may have sold, transferred or disposed of the shares of common stock covered hereby in transactions exempt from the registration requirements of the Securities Act since the date on which we filed this prospectus.

To our knowledge and except as noted below, the selling stockholder has not, or within the past three years has not, any position, office or other material relationship with us or any of our predecessors or affiliates.

	Beneficial Ownership Before This Offering		Beneficial Ownership After This Offering	
Selling Stockholder(1)	Number of Shares Owned	Shared Offered Hereby	Number of Shares Owned	Percentage of Outstanding Shares
Frazier Life Sciences IX, L.P.(2)	625,000	625,000	—	—

(1) This table and the information in the notes below are based upon information supplied by the selling stockholder, including reports and amendments thereto filed with the SEC on Schedule 13G.

(2) Consists of 625,000 shares of Common Stock held directly by Frazier Life Sciences IX, L.P. FHMLS IX, L.P. is the general partner of Frazier Life Sciences IX, L.P. and FHMLS IX, L.L.C. is the general partner of FHMLS IX, L.P. Patrick Heron and James Topper are the members of FHMLS IX, L.L.C. Each of FHMLS IX, L.P., FHMLS IX, L.L.C., Patrick Heron and James Topper disclaims beneficial ownership of these shares, except to the extent of its or his pecuniary interest in such shares, if any. The address of the principal business office of Frazier Life Sciences IX, L.P. is c/o Frazier Healthcare Partners, 601 Union Street, Suite 3200, Seattle, Washington 98101.

PLAN OF DISTRIBUTION

Our Plan of Distribution

We may sell the securities, from time to time, to or through underwriters or dealers, through agents or remarketing firms, or directly to one or more purchasers pursuant to:

- underwritten public offerings;
- negotiated transactions;
- block trades;
- "At the Market Offerings," within the meaning of Rule 415(a)(4) of the Securities Act, into an existing trading market, at prevailing market prices; or
- through a combination of these methods.

We may sell the securities to or through one or more underwriters or dealers (acting as principal or agent), through agents, or directly to one or more purchasers.

We may distribute securities from time to time in one or more transactions:

- at a fixed price or prices, which may be changed;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

A prospectus supplement or supplements (and any related free writing prospectus that we may authorize to be provided to you) will describe the terms of the offering of the securities, including, to the extent applicable:

- the name or names of the underwriters, dealers or agents, if any;
- if the securities are to be offered through the selling efforts of brokers or dealers, the plan of distribution and the terms of any agreement, arrangement, or understanding entered into with broker(s) or dealer(s) prior to the effective date of the registration statement, and, if known, the identity of any broker(s) or dealer(s) who will participate in the offering and the amount to be offered through each;
- the purchase price of the securities or other consideration therefor, and the proceeds, if any, we will receive from the sale;
- if any of the securities being registered are to be offered otherwise than for cash, the general purposes of the distribution, the basis upon which the securities are to be offered, the amount of compensation and other expenses of distribution, and by whom they are to be borne;
- any delayed delivery arrangements;
- any over-allotment or other options under which underwriters may purchase additional securities from us;
- any agency fees or underwriting discounts and other items constituting agents' or underwriters' compensation;
- any public offering price;
- any discounts, commissions or commissions allowed or reallowed or paid to dealers;
- the identity and relationships of any finders, if applicable; and
- any securities exchange or market on which the securities may be listed.

Only underwriters named in the prospectus supplement will be underwriters of the securities offered by the prospectus supplement.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Unless otherwise indicated in the prospectus supplement, subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement, other than securities covered by any over-allotment option. Any public offering price and any discounts or concessions allowed or reallowed or paid to dealers may change from time to time. We may use underwriters, dealers or agents with whom we have a material relationship. We will describe in the prospectus supplement, naming the underwriter, dealer or agent, the nature of any such relationship.

We may use a remarketing firm to offer the securities in connection with a remarketing arrangement upon their purchase. Remarketing firms will act as principals for their own account or as agents for us. These remarketing firms will offer or sell the securities pursuant to the terms of the securities. A prospectus supplement will identify any remarketing firm and the terms of its agreement, if any, with us and will describe the remarketing firm's compensation. Remarketing firms may be deemed to be underwriters in connection the securities they remarket.

If we offer and sell securities through a dealer, we or an underwriter will sell the securities to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale. The name of the dealer and the terms of the transaction will be set forth in the applicable prospectus supplement.

We may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities and we will describe any commissions payable to the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, the agent will act on a best-efforts basis for the period of its appointment.

Dealers and agents participating in the distribution of the securities may be deemed to be underwriters, and compensation received by them on resale of the securities may be deemed to be underwriting discounts. If such dealers or agents were deemed to be underwriters, they may be subject to statutory liabilities under the Securities Act.

We may sell securities directly to one or more purchasers without using underwriters or agents. Underwriters, dealers and agents that participate in the distribution of the securities may be underwriters as defined in the Securities Act, and any discounts or commissions they receive from us and any profit on their resale of the securities may be treated as underwriting discounts and commissions under the Securities Act.

We may authorize agents or underwriters to solicit offers by certain types of institutional investors to purchase securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the prospectus supplement.

We may provide agents, underwriters and dealers with indemnification against civil liabilities, including liabilities under the Securities Act, or contribution with respect to payments that the agents, underwriters or dealers may make with respect to these liabilities. Agents, underwriters and dealers, or their respective affiliates, may engage in transactions with, or perform services for, us in the ordinary course of business.

All securities we may offer, other than common stock, will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities.

Any underwriter may engage in over-allotment, stabilizing transactions, short-covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Over-allotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum price. Syndicate-covering or other short-covering transactions involve purchases of the securities, either through exercise of the over-allotment option or in the open market after the distribution is completed, to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a stabilizing or covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

Any underwriters that are qualified market makers on The NASDAQ Capital Market may engage in passive market making transactions in the common stock on The NASDAQ Capital Market in accordance with Regulation M under the Exchange Act, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the common stock. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded. Passive market making may stabilize the market price of the securities at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

Selling Stockholder's Plan of Distribution

The selling stockholder, including its transferees, donees, pledgees, assignees and successors-in-interest, may sell, transfer or otherwise dispose of any or all of the shares of common stock offered by this prospectus from time to time on The Nasdaq Capital Market or any other stock exchange, market or trading facility on which the shares are traded or in private transactions. These dispositions may be at fixed prices, at market prices prevailing at the time of sale, at prices related to prevailing market price or at negotiated prices. The selling stockholder may use any one or more of the following methods when selling shares:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- "at the market" or through market makers or into an existing market for shares:
- short sales;
- broker-dealers may agree with the selling stockholder to sell a specified number of such shares at a stipulated price per share;
- through one or more underwritten offerings on a firm commitment or best efforts basis;
- a combination of any such methods of sale;

- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise; or
- any other method permitted pursuant to applicable law.

The selling stockholder may also sell shares under Rule 144 under the Securities Act, if available, rather than under this prospectus.

Broker-dealers engaged by the selling stockholder may arrange for other brokers-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the selling stockholder or, if any broker-dealer acts as agent for the purchaser of shares, from the purchaser in amounts to be negotiated. The selling stockholder does not expect these commissions and discounts relating to its sales of shares to exceed what is customary in the types of transactions involved.

The selling stockholder may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the common stock in the course of hedging the positions they assume. The selling stockholder may also sell shares of our common stock short and deliver these securities to close out its short positions, or loan or pledge the common stock to broker-dealers that in turn may sell these securities. The selling stockholder may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus, as supplemented or amended to reflect such transaction.

The selling stockholder and any broker-dealers or agents that are involved in selling the shares may be deemed to be "underwriters" within the meaning of the Securities Act in connection with such sales. In such event, any commissions received by such broker-dealers or agents and any profit on the resale of the shares purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. The selling stockholder has advised us that it has not entered into any agreements, understandings or arrangements with any underwriters or broker-dealers regarding the sale of its shares of common stock, nor is there an underwriter or coordinating broker acting in connection with a proposed sale of shares of common stock by the selling stockholder.

Because the selling stockholder may be deemed to be an "underwriter" within the meaning of the Securities Act, it will be subject to the prospectus delivery requirements of the Securities Act. In addition, any securities covered by this prospectus which qualify for sale pursuant to Rule 144 under the Securities Act may be sold under Rule 144 rather than under this prospectus. The selling stockholder had advised us that there is no underwriter or coordinating broker acting in connection with the proposed sale of the resale securities by the selling stockholder.

The shares will be sold only through registered or licensed brokers or dealers if required under applicable state securities laws. In addition, in certain states, the shares may not be sold unless they have been registered or qualified for sale in the applicable state or an exemption from the registration or qualification requirement is available and is complied with.

Under applicable rules and regulations under the Exchange Act, any person engaged in the distribution of the resale shares may not simultaneously engage in market making activities with respect to our common stock for the applicable restricted period, as defined in Regulation M, prior to the commencement of the distribution. In addition, the selling stockholder will be subject to applicable provisions of the Exchange Act and the rules and regulations thereunder, including Regulation M, which may limit the timing of purchases and sales of shares of our common stock by the selling stockholder or any other person. We will make copies of this prospectus available to the selling stockholder and have informed the selling stockholder of the need to deliver a copy of this prospectus to each purchaser at or prior to the time of the sale (including by compliance with Rule 172 under the Securities Act).

We have agreed to indemnify the selling stockholder against certain losses, claims, damages and liabilities, including liabilities under the Securities Act.

We will not receive any proceeds from the sale of the shares by the selling stockholder.

LEGAL MATTERS

The validity of the securities being offered hereby will be passed upon by Morrison & Foerster LLP, San Francisco, California. Additional legal matters may be passed upon for us or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

Mayer Hoffman McCann P.C., an independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the years ended December 31, 2017 and 2016, as set forth in its report, which is incorporated by reference in this prospectus and the registration statement. Our financial statements are incorporated by reference in reliance on Mayer Hoffman McCann P.C.'s report, given on the authority of said firm as experts in accounting and auditing.

$60,000,000

Krystal Biotech, Inc.

Common Stock

PROSPECTUS SUPPLEMENT

Cowen

William Blair

Cantor

Chardan

Ladenburg Thalmann

, 2018