UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2021

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 FOR THE TRANSITION PERIOD FROM TO**

Commission File Number 001-38210

Krystal Biotech, Inc.

(Exact name of Registrant as specified in its Charter)

Delaware	**82-1080209**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
2100 Wharton Street **Suite 701** **Pittsburgh** **Pennsylvania**	**15203**
(Address of principal executive offices)	**(Zip Code)**

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

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock	KRYS	NASDAQ Capital Market

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

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

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

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

Indicate by check mark whether the Registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the Registrant was required to submit such files). Yes ☒ No ☐

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

Large accelerated filer	☒	Accelerated filer	☐
Non-accelerated filer	☐	Smaller reporting company	☒
Emerging growth company	☐		

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

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. Yes ☒ No ☐

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

The aggregate market value of common stock held by non-affiliates of the Registrant, based on the closing sales price for such stock on June 30, 2021 as reported by The Nasdaq Stock Market, was $1.2 billion. This calculation excludes 5,327,648 shares held by executive officers, directors and stockholders that the Registrant has concluded are affiliates of the Registrant. Exclusion of such shares should not be construed to indicate that any such person possesses the power, direct or indirect, to direct or cause the direction of the management or policies of the registrant or that such person is controlled by or under common control with the Registrant.

The number of shares of Registrant's common stock outstanding as of February 18, 2022 was 25,208,085.

Portions of the Registrant's definitive proxy statement relating to its 2022 Annual Meeting of Stockholders are incorporated by reference into Part III of this Report where indicated. Such proxy statement will be filed with the U.S. Securities and Exchange Commission within 120 days after the end of the fiscal year to which this report relates.

EXPLANATORY NOTE

The registrant met the "large accelerated filer" requirements as of the end of its 2021 fiscal year pursuant to Rule 12b-2 of the Securities Exchange Act of 1934, as amended. However, the registrant (as a smaller reporting company transitioning to the larger reporting company system based on its public float as of June 30, 2021) is not required to satisfy the larger reporting company disclosure requirements until its first quarterly report on Form 10-Q for the 2022 fiscal year and thus is eligible to check the "Smaller Reporting Company" box on the cover of this Form 10-K."

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FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. 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 appearing in a number of places throughout this Annual Report on Form 10-K include, but are not limited to, statements about the following, among other things:

- the initiation, timing, progress and results of preclinical and clinical trials for Vyjuvek™ (beremagene geperpavec also known as "B-VEC" and previously “KB103”), KB105, KB301, KB104, KB407, KB408 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 impact that the coronavirus disease 2019 ("COVID-19") pandemic and measures to prevent its spread may have on our business operations, access to capital, research and development activities, and preclinical and clinical trials for our product candidates;
- the timing, scope or results of regulatory filings and approvals, including timing of final U.S. Food and Drug Administration ("FDA"), marketing and other regulatory approval of our product candidates;
- our ability to achieve certain accelerated or orphan drug designations from the FDA;
- our estimates regarding the potential market opportunity for Vyjuvek, KB105, KB301, KB104, KB407, KB408 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;
- 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 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; and

- any statements regarding economic conditions, including statements related to the economic fallout from the COVID-19 pandemic and the impact on our business, 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,” "Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere in this Annual Report. 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 Annual Report 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 Annual Report. You should read this Annual Report 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.

Throughout this Annual Report, unless the context requires otherwise, all references to "Krystal," "the Company,", "we," "our," "us" or similar terms refer to Krystal Biotech, Inc., together with its consolidated subsidiaries.

Summary Risk Factors

Our business is subject to a number of risks, including risks that may prevent us from achieving our business objectives or may adversely affect our business, financial condition, results of operations, cash flows and prospects. These summary risks provide an overview of many of the risks we are exposed to in the normal course of our business and are discussed more fully in “Risk Factors” herein. These risks include, but are not limited to, the following:

- We have incurred net losses since inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.
- We may need to raise additional funding in order to receive approval for our product candidates. 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.
- 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.
- Business interruptions resulting from the COVID-19 pandemic or similar public health crises could cause a disruption of the development efforts of our product candidates and adversely impact our business.
- We are a development-stage company. If we are unable to advance our product candidates through clinical trials, obtain regulatory approval and ultimately commercialize our product candidates, or if we experience significant delays in doing so, our business will be materially harmed.
- Our lead candidate, Vyjuvek, has not been submitted to or reviewed by regulatory agencies, and we cannot predict when, or if, we will obtain regulatory approval to commercialize Vyjuvek and the approval may be for a narrower indication than we seek.
- Vyjuvek 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.
- 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.
- We have a limited number of employees and limited corporate infrastructure and may experience difficulties in managing growth.
- Even if we obtain regulatory approval for a product candidate, our product candidates will remain subject to regulatory oversight. We will continue to incur costs related to regulatory compliance and are subject to risks related to non-compliance with or changes to applicable laws and regulations, which could cause our product candidates to lose approval.

- 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.
- 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 our lead product candidate, Vyjuvek or any future product candidate.
- Delays in obtaining regulatory approvals of the process and facilities needed to manufacture our product candidates or disruptions in our manufacturing process may delay or disrupt our product development and commercialization efforts.
- Although we have established our own manufacturing facility for our product candidates, we may need to continue to utilize third parties for the manufacturing of sterile gel that is mixed with our in-house produced vectors for the near future. Therefore, we are subject to the risk that these third parties may not perform satisfactorily.
- If we are unable to expand our market development capabilities or enter into agreements with third parties to market and sell our product candidates, we may be unable to generate any product revenue.
- We may not be successful in our efforts to identify or discover additional product candidates and may fail to capitalize on programs or product candidates that may be a greater commercial opportunity or for which there is a greater likelihood of success.
- If we are unable to manage expected growth in the scale and complexity of our operations, our performance may suffer.
- If we are unable to obtain and maintain adequate U.S. and foreign patent protection for our product candidates, and/or our vector platform, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technologies similar or identical to ours, and our ability to successfully commercialize our current product candidates, any future product candidates we may develop, and our platform technologies may be adversely affected.
- 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.
- Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.
- We are subject to claims asserting that we, our employees or our advisors have wrongfully used or disclosed alleged trade secrets of other parties or claims asserting ownership of what we regard as our own intellectual property and we may face other such claims in the future.
- Our Chief Executive Officer and Chairman of the Board of Directors and our founder, Chief Operating Officer and director will have the ability to substantially influence all matters submitted to stockholders for approval.

Item 1. Business.

Overview

Krystal Biotech, Inc. (the “Company,” “Krystal,” “we,” or “us,” or other similar pronouns) is a clinical-stage biotechnology company focused on the development of easy to use, redosable gene therapies to dramatically improve the lives of patients living with debilitating diseases. We have developed a proprietary gene delivery platform that presently enables off-the-shelf treatments for serious dermatology and respiratory diseases. Our platform consists of a patented, engineered viral vector derived from the herpes simplex virus type 1 (“HSV-1”) that we have optimized for local and repeat gene transfer to epithelial cells. We are initially using our platform to develop treatments for rare or orphan monogenic diseases caused by the absence of or a mutation in a single gene and novel therapies to treat more prevalent conditions. Further, we have incorporated a wholly owned subsidiary, Jeune Aesthetics, Inc., under which we are developing treatments for use in the setting of aesthetic skin conditions.

Our Redosable Gene Therapy Platform

We believe that certain inherent features of HSV-1 virus, combined with the modifications we have made to the viral backbone provides our proprietary gene therapy platform with specific advantages over other viral and non-viral vector platforms including the following:

- **Repeat Administration**: One of the major challenges with many viral vector platforms is that the host immune system may recognize them as foreign agents and launch a robust immune response, resulting in toxicity and rapid removal of the virus. Wild type HSV-1 is known to persist in the body by becoming latent and hiding from the immune system. We have harnessed the natural ability of HSV-1 to evade host-mediated immunogenicity, while removing specific viral elements that exacerbate the host immunity, thus making our viral vector safer for repeat administration as needed to achieve durability of effect. The immune evasive properties of our vector also enable us to treat patients who may have baseline antibodies to HSV-1, ensuring that prior exposure to the wildtype virus will not limit the number of patients who may be amenable to treatment with our product candidates.
- **Non-Integrating Nature**: Upon entry into cells, the HSV-1 vector persists as an episomal unit in the nucleus, meaning it remains physically separate from the host cell chromosome. Certain other viral vectors currently being used in the development of gene therapy treatments, such as the lentiviral and retroviral vectors, integrate into the host cell DNA to achieve gene expression. Integration into the host cell DNA carries the risk of disrupting host genes. In contrast, a non-integrating vector such as our HSV-1 vector does not carry the same risk of disrupting the expression of host cell genes.
- **Payload Capacity**: HSV-1 is a large virus, approximately 150 kilobases, or Kb, of DNA in size. We have made strategic deletions within this genome to remove critical “immediate early”, or IE, genes. These IE genes are required for expression of most of the downstream genes that allow the HSV-1 virus to replicate and destroy host cells. Deletion of these IE genes inhibits expression of most of the viral proteins, making the resulting viral vector replication-deficient and non-toxic. These deletions also enable the vector to easily accommodate a payload of 35Kb or greater without any significant impact on yield or titer. In our lead product candidate, Vyjuvek, we have successfully inserted two functional copies of the complete ~9Kb human COL7A1 gene. In contrast, packaging capacity for most other vectors being used is at or under ~10Kb, which limits their ability to deliver large transgenes. In addition, we believe the high payload capacity of our viral vector will allow us to insert multiple and/or combinations of genes or effectors that could enable the treatment of non-monogenic conditions.
- **High Transduction Efficiency**: Poor transduction efficiency has remained a major hurdle for direct delivery of most vectors particularly in the epithelia of the skin and lung. HSV-1 has a natural affinity, or tropism, for epithelial cells, consequently our vector penetrates and delivers its payload much more efficiently than other vectors, resulting in transduction efficiencies or cell penetration as high as 95% in cell-based studies. The greater payload capacity of our vector and the high transduction efficiencies achieved allow us to deliver a full gene (or genes) directly to any patient’s tissues for off-the-shelf, in vivo gene expression without additional manipulation.
- **Direct Delivery**: Our engineered HSV-1 vector allows for noninvasive or minimally invasive local gene delivery. The advantages of direct delivery are that our products can be administered in a doctor’s office or potentially the patient’s home, requiring no hospitalization or expensive, invasive, and time-consuming procedures or sophisticated medical teams. Taking gene therapy to the patient minimizes patient travel and circumvents upfront logistical burdens typical of other gene therapy approaches.
- **Stability**: HSV-1 is extremely stable and resistant to degradation by physical shearing, solvents, and enzymes, facilitating purification and flexibility with final formulation of our product candidates. Our vectors are stable frozen for long-term storage, under refrigerated conditions for short-term storage and shipment, in addition to being stable over several freeze-thaw cycles. This should facilitate our ability to ship our products globally from our manufacturing facilities in Pennsylvania.
- **Reproducible and Scalable Manufacturing**: Successful production of viral vectors involves two steps: (i) the ‘upstream’ process, which yields a bulk virus harvest; and (ii) the ‘downstream’ process, which involves purification and concentration of the clinical product. Successful and reproducible execution of both processes is critical for clinical manufacturing and scale-up. Our scientific team collectively has decades of experience and expertise in HSV engineering and purification that has allowed us to successfully optimize our HSV-1 vector production process and develop in-house Chemistry, Manufacturing and Control ("CMC") capabilities.
- **Existing Regulatory Precedent**: The first FDA- and European Medicines Agency (“EMA”)-approved oncolytic virus product, Imlygic® by Amgen, for treatment of melanoma, a skin cancer, is based on a genetically engineered HSV-1 virus. Because this product also employs an HSV-1 backbone, it has created a regulatory precedent for approval of an HSV-1-based therapy. In addition, Imlygic® is a chronic

therapy, given bi-weekly, which provides support for the use of an HSV-1 backbone in chronic gene therapy of the type we are developing.

The above listed benefits of our innovative platform make it the ideal choice for topical and intradermal applications to treat skin diseases, skin conditions and inhaled formulations to treat respiratory diseases.

Our Product Candidates

The following table summarizes information regarding our product candidates in various stages of clinical and preclinical development:

Krystal Biotech Pipeline

	Product	Protein	Indication	Discovery	Preclinical	Phase 1/2	Phase 3	Key Upcoming Milestone	Ownership
Dermatology	VYJUVEK†¤•Δ‡§	Type VII collagen	Dystrophic EB					File BLA in 1H22; MAA in 2H22	Krystal
Dermatology	KB105†¤•‡	Transglutaminase 1 (TGM1)	TGM1-deficient ARCI					Resume dosing in Phase 2 study in 2022	Krystal
Dermatology	KB104¤	Serine Peptidase Inhibitor Kazal Type 5 (SPINK5)	Netherton Syndrome					File IND in 2022	Krystal
Dermatology	KB1XX	Undisclosed programs							Krystal
Dermatology	KB5XX	Vector encoded antibodies	Chronic skin conditions						Krystal
Respiratory	KB407†¤‡	Cystic fibrosis transmembrane conductance regulator (CFTR)	Cystic fibrosis					Initiate Phase 1 Australian study in 1H22; Initiate Phase 1 US study in 2H22	Krystal
Respiratory	KB408	Alpha-1 antitrypsin (AAT)	alpha-1 antitrypsin deficiency						Krystal
Respiratory	KB4XX	Undisclosed programs							Krystal

All pipeline compounds are investigational, being evaluated in clinical or pre-clinical studies.

†: FDA Orphan Drug Designation;
¤: FDA Rare Pediatric Disease Designation;
•: Fast-track Designation;
Δ: FDA RMAT designation;
‡: EMA Orphan Drug Designation;
§: EMA PRIME Designation.

Rare disease

More prevalent conditions

Jeune Aesthetics Pipeline

	Product	Protein	Indication	Discovery	Preclinical	Phase 1/2	Phase 3	Key Upcoming Milestone	Ownership
Aesthetics	KB301	Type III collagen	Aesthetic skin conditions					Announce Ph1 Cohort 2 data in 1Q22	JEUNE
Aesthetics	KB302	Type I collagen	Aesthetic skin conditions						JEUNE
Aesthetics	KB303	Elastin	Aesthetic skin conditions						JEUNE
Aesthetics	KB304	Type III collagen & Elastin	Aesthetic skin conditions						JEUNE
Aesthetics	KB305	Type IV collagen	Aesthetic skin conditions						JEUNE

Rare Skin Programs

Investigational Vyjuvek (beremagene geperpavec) for dystrophic epidermolysis bullosa ("Dystrophic EB")

Disease Background

Dystrophic epidermolysis bullosa, or dystrophic EB, is a rare and severe monogenic skin disease. Dystrophic EB 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 the protein type VII collagen ("COL7") that forms anchoring fibrils that bind the dermis (inner layer of the skin) to the epidermis (outer layer of the skin). In dystrophic EB 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 dystrophic EB are sometimes called "butterfly children," because their skin is likened to be as fragile as the wings of a butterfly. Dystrophic EB 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. We believe that there are, at present, approximately 3,000 diagnosed dystrophic EB patients in the United States and approximately 9,000 worldwide. The current standard of care for dystrophic EB patients is limited to palliative measures that seek to provide relief from some of the symptoms of dystrophic EB but do not meaningfully impact disease outcomes. While not disease-modifying, current treatment is estimated to cost between $200,000 and $400,000 annually per patient in the United States.

Vyjuvek

Vyjuvek is a redosable, off-the-shelf gene therapy designed to deliver two copies of the *COL7A1* gene when applied topically, directly onto an open wound. Unlike the current standard of care, Vyjuvek seeks to treat dystrophic EB at the molecular level by providing the patient's skin cells the template to make normal COL7 protein, thereby addressing the fundamental disease-causing mechanism. Vyjuvek was specifically designed to be easily administered by a healthcare professional in a doctor's office or potentially at the patient's home. The FDA and the EMA have each granted Vyjuvek orphan drug designation for the treatment of dystrophic EB, and the FDA has granted Vyjuvek fast track designation and rare pediatric designation for the treatment of dystrophic EB. In addition, in 2019, the FDA granted Regenerative Medicine Advanced Therapy ("RMAT") to Vyjuvek for the treatment of dystrophic EB and the EMA granted PRIority MEdicines ("PRIME"), eligibility for Vyjuvek to treat dystrophic EB.

We believe our approach to treating dystrophic EB is positively differentiated relative to other known efforts to develop corrective treatments that employ autologous approaches. Autologous treatments use a patient's own tissues and cells to manufacture an individualized therapy. Such therapies tend to be expensive, invasive and time consuming to use, and require extensive patient travel, extended hospital stays, highly sophisticated medical teams and procedures.

Clinical Development of Vyjuvek

We initiated Phase 1 testing of Vyjuvek in May 2018 at Stanford University, and we announced positive interim results from this clinical study on two patients in October 2018. The Phase 2 portion of the trial commenced in December 2018 at Stanford University, and we announced positive interim results from this clinical study on June 24, 2019. Complete Phase 1/2 was initially presented at the Society of Investigational Dermatology ("SID") meeting in May 2020.

We initiated Phase 3 testing of Vyjuvek in July of 2020. The pivotal GEM-3 trial of Vyjuvek for the treatment of dystrophic EB was a randomized, double-blind, intra-patient placebo-controlled multicenter study designed to evaluate the efficacy and safety of Vyjuvek for patients suffering from both recessive and dominant forms of dystrophic EB. The trial enrolled 31 participants with dystrophic EB, aged 6 months or older at time of consent. In each patient, a primary wound pair was identified by the investigator; one wound was randomized to receive a weekly topical application of Vyjuvek and the other to receive placebo. These primary wounds were treated once weekly for six months until wound closure. If a wound re-opened at any point during the study, weekly dosage resumed until closure. The dose administered to each wound was dependent on the size of the wound and ranged from 4x10^8 to 1.2x10^9 PFU per wound. A maximum vector dose per patient per week was defined on the basis of preclinical and clinical safety data. In the event that the maximum dose per patient had not been reached based on dosing of the primary wounds, the study investigators and patients had the opportunity to select additional "secondary" wounds across which the remaining weekly dose was applied.

The primary outcome measure was complete wound healing determined by the Investigator in the primary Vyjuvek treated wounds versus placebo treated at the six-month timepoints, meaning week 22 and Week 24 or Week 24 and Week 26.

Secondary endpoints included investigator assessed complete wound healing at the three-month timepoints, meaning weeks 8 and 10 or 10 and 12 and mean change in pain severity using either a VAS or FLACC-R Scale at weeks 22, 24 and 26.

In November 2021 we announced positive topline results from the GEM-3 trial:

- 31 patients (31 primary matched-wound pairs) were enrolled and evaluable for safety and efficacy per the primary intent-to-treat ("ITT") analysis
- 67% of wounds treated with Vyjuvek achieved the primary endpoint of investigator assessed complete wound healing at the six-month timepoints as compared to 22% of wounds treated with placebo (absolute difference (95% CI): 45.8% (23.6%-68.0%); p<0.005
- 71% of wounds treated with Vyjuvek achieved the secondary endpoint of investigator assessed complete wound healing at the three-month timepoints as compared to 20% of wounds treated with placebo (absolute difference (95% CI): 51.0% (29.3%-72.6%); p<0.005)
- In an ad-hoc analysis, the trial also demonstrated a statistical difference between the active and placebo groups for wounds that demonstrated complete wound healing at both the three- and six-month timepoints (p<0.005)
- Vyjuvek was well tolerated. No drug-related serious adverse events or discontinuations due to treatment were reported. One mild drug-related adverse event was reported during the trial
- The immunogenicity profile of Vyjuvek (as measured by anti-HSV-1 and anti-COL7 antibodies) was consistent with the prior GEM-1/2 study where we observed no meaningful change in anti-HSV-1 or anti-COL7 antibodies

We expect to file a Biologics License Application ("BLA") with the FDA in the first half of 2022. We are aligned with the EMA that data from GEM-3 is sufficient to form the basis of a Marketing Authorisation Application ("MAA"), which we expect to submit to the EMA in the second half of 2022.

KB105 for TGM1-deficient autosomal recessive congenital ichthyosis ("ARCI")

Disease Background

ARCI is a life-long, severe monogenic skin disease. While a number of genetic mutations have been associated with the development of ARCI, the most common cause of ARCI is an inactivating mutation in the human transglutaminase-1 ("*TGM1*") gene encoding the enzyme transglutaminase-1, a protein that is essential for the proper formation of the skin barrier. Mutations in the *TGM1* gene, and the subsequent disruption to the epidermal barrier, leads to pronounced dehydration, trans-epidermal exposure to unwanted toxins and surface microorganisms, and a greatly increased risk of infection. Transglutaminase-1 deficiency is associated with increased mortality in the neonatal period and has a dramatic impact on quality of life.

Patients suffering from ARCI often exhibit life-long pronounced plate-like scaling of the skin, which is often of a dark color and can cover the whole body. Such patients frequently suffer from exposure of the inner eyelid surface due to turning away of the eyelids from the eye (ectropion), the turning outwards of the lips (eclabium), deformities of joint and nasal cartilage (hypoplasia), scarring alopecia (especially at the edge of the scalp) and a thickening of the skin on the palms of the hands and soles of the feet (palmoplantar keratoderma). Additional complications experienced by ARCI patients include episodes of sepsis, fluid and electrolyte imbalances due to impaired skin barrier function, and failure to thrive, especially during the neonatal period and infancy. Severe heat intolerance and nail dystrophy are also frequently observed. There are currently no treatments targeting molecular correction of this disease. There are approximately 20,000 cases of TGM1-deficient ARCI worldwide and about 400 new cases per year globally.

KB105

KB105 is a redosable, off the-shelf gene therapy designed to deliver two copies of the *TGM1* gene when applied topically, directly to a patient's exfoliated skin. The goal of direct supplementation of TGM1 protein at the site of administration is local correction and phenotypic improvement. Like Vyjuvek, KB105 was designed to be easily administered by a healthcare professional in the doctor's office or, potentially, at the patient's home.

The FDA and the EMA have each granted KB105 orphan drug designation for the treatment of TGM1-ARCI, and the FDA has granted KB105 fast track designation and rare pediatric designation for the treatment of TGM1-ARCI.

Clinical Development of KB105

In September 2019 we initiated a Phase 1/2 trial in TGM1-ARCI patients. In May 2020, initial clinical data from the Phase 1 portion of the study which enrolled adult patients were presented at the SID meeting. In August 2020, we initiated the second phase of our Phase 2 portion of the clinical trial of KB105 to treat ARCI. We enrolled one patient in whom four rectangular 100cm2 (4-inch x 4-inch) areas of skin were selected as Target Areas. Each treatment area was assigned to receive repeat doses of 4.0x109 PFU (n=2 treatment areas) or 1.0x1010 PFU (n=2 treatment areas). Each area was dosed on Day 1 and 3, after which dosing continued either every 3 days (n=2 treatment areas) or every 6 days (n=2 treatment areas) up to day 30. Treatment areas were clinically evaluated at pre- and post-KB105 application timepoints, using a 5-point IGA scale (0 = clear; 1 = almost clear; 2 = mild; 3 = moderate; 4 = very severe). In July 2021, we announced initial Phase 2 data.

Repeated topical doses of KB105 were well tolerated, and no drug-related adverse effects were reported. No vector shedding or systemic viral exposure was detected at any time point. Improvement on the IGA scale was observed in each treatment area, with the maximum effect observed in TA3 and TA4 that received the highest dose; at day 27, the investigator assigned an IGA score of 2, which was improved as compared to baseline score of 4 in each area. Variable 1-point improvements were observed at other time points and in the treatment areas that received the lowest dose. As in the Phase 1 portion of the trial, TGM1 turnover was observed to be variable but relatively rapid, and the observed IGA improvements were not sustained through day 60.

We plan to resume enrollment in the Phase 2 portion of this trial in 2022.

KB104 for Netherton Syndrome

Disease Background

Netherton Syndrome is a debilitating monogenic autosomal recessive skin disorder. The disease arises due to mutations in the Serine Protease Inhibitor Kazal-type 5 (“*SPINK5*”) gene, resulting in loss of activity of its encoded serine protease inhibitor protein SPINK5 (also known as Lympho-Epithelial Kazal type-related Inhibitor (“LEKTI”)). In healthy individuals, SPINK5 is one of the serine protease inhibitors expressed in the outermost layers of the skin, and it plays a critical role in the regulation of serine proteases which hydrolyze extracellular proteins that hold corneocytes together. In patients suffering from Netherton Syndrome, the suppressive effects of SPINK5 on these serine proteases is abolished due to underlying genetic mutations in the *SPINK5* gene. Consequently, hyperactivated serine proteases in the skin cause uncontrolled desquamation, leading to a defective skin barrier.

In infants, severe Netherton Syndrome can be associated with failure to thrive, hypernatremic dehydration secondary to excess fluid loss, delayed growth, short stature, and recurrent infections. Clinically, Netherton Syndrome is characterized by congenital ichthyosiform erythroderma, hair shaft defects, recurrent infections, and a defective skin barrier. A predisposition to allergies, asthma, and eczema is also characteristic of Netherton Syndrome. Ultimately, those afflicted by Netherton Syndrome often experience chronic skin inflammation, severe dehydration, and stunted growth.

There are approximately 38,000 cases of patients worldwide and about 700 new cases per year globally. There are no current approved treatments for Netherton Syndrome. Existing approaches are limited to palliative treatments, including topical moisturizers, repair formulas and steroids.

KB104

KB104 is a redoseable gene therapy designed to deliver two copies of the *SPINK5* gene to relevant skin cells when applied topically. By directly supplementing the skin with functional SPINK5, the goal of therapy is to locally correct the desquamation and improve the barrier function of the skin. In preclinical testing a properly localized human *SPINK5* gene was detected 48 hours after topical KB104 application in mice without toxicity. KB104-mediated human SPINK5 was expressed in the correct layer of skin at the transcript and protein levels.

The FDA has granted KB104 rare pediatric designation for the treatment of Netherton Syndrome.

We plan to file an IND with the FDA and initiate a clinical trial of KB104 in Netherton Syndrome in 2022.

Rare Pulmonary Programs

KB407 for Cystic Fibrosis (“CF”)

Disease Background

CF is the most common inherited genetic disorder in the United States and is caused by mutations in the cystic fibrosis transmembrane conductance regulator (“*CFTR*”) gene. Lack of functional CFTR protein in secretory airway epithelia results in defective Cl-, bicarbonate, and thiocyanate secretion, coupled with enhanced Na+ absorption and mucus production, leading to dehydration and acidification of the airway surface liquid. CF is characterized by recurrent chest infections, increased airway secretions, and eventually, respiratory failure. While CF comprises a multiorgan pathology affecting the upper and lower airways, gastrointestinal and reproductive tracts, and the endocrine system, the primary cause of morbidity and mortality in CF is due to progressive lung destruction.

According to the U.S. Cystic Fibrosis Foundation (“CFF”), the median age at death for patients with CF in the United States was 30.8 years in 2018. Currently approved CFTR modulating therapies are limited to patients with specific genetic mutations and there is a significant unmet medical need for the approximately 10% of patients with CF who have genetic mutations non-amenable to currently approved CFTR small molecule “modulators”. According to the CFF, approximately 30,000 patients in the United States and more than 70,000 patients worldwide are living with CF, and approximately 850 new cases of CF were diagnosed in 2018.

KB407

KB407 is a redosable off the-shelf gene therapy designed to deliver two copies of the *CFTR* gene directly to the airway epithelia via inhaled (nebulized) administration. By inducing expression of full length, normal CFTR protein in the lung, treatment with KB407 has potential to restore ion and water flow into and out of lung cells to correct the lung manifestations of the disease in patients regardless of their underlying genetic mutation. Preclinical efforts to date have shown that KB407 successfully transduces patient-derived epithelial cells and delivers functional CFTR in vitro in 2D and 3D organotypic systems, and is amendable to non-invasive inhaled administration in vivo, as indicated by successful delivery to the lungs through the use of a clinically relevant nebulizer in small animal models. Successful delivery and distribution throughout the lung also was observed in a nonhuman primate.

The FDA and the EMA have each granted KB407 orphan drug designation for the treatment of cystic fibrosis, and the FDA has granted KB407 rare pediatric designation for the treatment of cystic fibrosis.

Clinical Development of KB407

In September 2021, we announced that we were granted approval by the Bellberry Human Research Ethics Committee ("HREC") in Australia to conduct a Phase 1 clinical study of inhaled KB407 in patients with CF. We previously received license to evaluate KB407 from Australia's Office of the Gene Technology Regulator ("OGTR"). We plan to initiate the Phase 1 clinical trial in Australia in the first half of 2022. We plan to file an IND with the FDA and initiate a Phase 1 clinical trial in the U.S. in the second half of 2022.

KB408 for Alpha-1 antitrypsin deficiency (“AATD”)

Disease Background

AATD is a genetic condition caused by mutations that lead to decreased levels and/or decreased functionality of the alpha-1- antitrypsin ("AAT") protein. AATD lung disease is a consequence of diminished or absent functional protein in the lungs due to impaired transport into, and low concentrations in, patient plasma. Low AAT serum levels can result in life threatening, progressive pulmonary impairment and severe respiratory insufficiency, manifesting as chronic obstructive pulmonary disease ("COPD") and panacinar emphysema. The lung degeneration observed in AATD patients derives from an unopposed, and therefore enhanced, neutrophil elastase ("NE") activity, leading to an excessive degradation of elastin, collagen, and fibronectin. The absence of proper NE inactivation by functional AAT ultimately results in lung tissue destruction, airway obstruction, and an increased inflammation state that compromises the integrity of the organ and contributes to an inadequate response to insults, including inefficient pulmonary bacterial clearance.

There are an estimated 90,000 to 100,000 people in the U.S. with severe AAT deficiency. Currently, many AATD patients undergo “augmentation therapy” consisting of weekly intravenous ("IV") infusions of either plasma-purified AAT or recombinant AAT. This therapy requires burdensome weekly IV infusions and often includes the risk of exposure to bloodborne pathogens connected with the use of blood-derived products.

KB408

KB408 is an inhaled (nebulized) formulation of our propeieatry vector, designed to deliver two copies of the *SERPINA1*

gene that encodes functional, full-length human protein, for the treatment of AATD. Preclinical studies to date have shown that KB408 successfully transduces patient-derived lung epithelial cells in vitro, leading to production and secretion of full-length human AAT protein capable of irreversibly binding its cognate target NE. In small animal models, analysis of lung tissue biopsies, serum, and bronchoalveolar lavage fluid harvested 24 and 48 hours after inhalation of KB408 shows secretion of full-length AAT protein, with no evidence of significant or systemic toxicity.

Other Programs

While our focus is on the development of gene therapies to treat serious rare diseases, we are also evaluating the potential of our platform to address more prevalent and/or non-genetic conditions. To that end, on April 24, 2019, we incorporated Jeune, Inc. (now Jeune Aesthetics, Inc.), a wholly-owned subsidiary, for the purposes of undertaking preclinical and clinical studies for aesthetic skin conditions.

KB301 for aesthetic skin conditions

Disease Background

The skin is largely composed of collagen-rich connective tissue, with dermal collagen, composed primarily of types 1 and 3 collagen fibrils, representing >90% (dry weight) of human skin. The characteristics of skin aging are largely due to aberrant collagen homeostasis, including reduced collagen biosynthesis, increased collagen fibril fragmentation, and progressive loss of dermal collagen culminating in a net collagen deficiency, resulting from both intrinsic (*e.g.*, passage of time, genetics) and extrinsic (*e.g.*, chronic light exposure, pollution) pressures.

Facial injectables, including hyaluronic acid, botulinum toxin type A, collagen, polymer fillers, and calcium hydroxyapatite microparticles, are intended to correct perceived facial defects (*e.g.*, fine lines, shallow wrinkles, and deeper furrows), and are administered for both cosmetic and therapeutic indications. In 2017, the global facial injectables market generated more than $7.2 billion in revenue from approximately 8.5 million procedures performed, with a majority (~70%) of revenue being generated in the aesthetic setting. While the United States and Europe represent the largest markets for facial injectables to-date, significant expansion in market share is projected for Asia and Latin America in the coming years. Due to the rising awareness of cosmetic procedures, the growing geriatric population, and a shift from invasive to minimally/non-invasive treatment options, the aesthetics facial injectables market is projected to grow to more than a $12 billion industry by 2025.

KB301

KB301 leverages our clinical experience in delivering genes of interest to the skin, and is designed to stimulate biorejuvenation of the skin via delivery of the gene that encodes for type III collagen ("COL3") when administered via intradermal injection. We believe that our approach of directed expression of full-length human type III collagen via intradermal application of KB301 provides a unique and straightforward approach to restoring collagen homeostasis, and by extension, reconstructing an optimal physiologic environment in the skin to treat wrinkles or other presentations of aged or damaged skin.

Clinical development of KB301

We initiated a Phase 1 clinical trial, the PEARL-1 trial, for the treatment of aesthetic skin conditions on August 25, 2020. The first Cohort enrolled 7 subjects and evaluated the safety and tolerability of intradermal injections of KB301 in healthy buttock tissue, as compared to uninjected or saline injected control sites. Data from this cohort was announced in March 2021.

In August 2021, we announced the initiation of dosing in the efficacy cohort of the PEARL-1 trial. Cohort 2 is a randomized, double-blind, saline-controlled trial to evaluate the safety and efficacy of KB301 for the improvement of skin quality attributes such as fine lines, texture, and skin thickness. This cohort enrolled 27 subjects across two trial sites. Bilateral treatment areas on the neck behind the ear, on the cheek below and above the zygomatic arch, and around the knee were chosen on Day 0 and randomized 2:1 to receive low dose KB301, high dose KB301, or saline. KB301 or saline was injected in multiple micro depot injections over the selected treatment area. We anticipate announcing top line data from the efficacy cohort in 1Q 2022.

Future Opportunities

We believe the ability to redose as well as the large payload capacity of our proprietary vectors will allow us to deliver multiple genes and other effectors, which could enable development of therapies to treat non-monogenic skin diseases like psoriasis and atopic dermatitis, as well as conditions that are not necessarily the result of an inherited genetic defect, such as chronic wounds. For example, as proof-of concept we have generated a library of vectors designed to deliver anti-inflammatory antibodies. Further, we evaluated one of these vectors in an animal model of atopic dermatitis where expression of the vector-encoded-antibody was confirmed and efficacy was observed.

If we are able to successfully generate product candidates to treat non-orphan diseases, we intend to seek collaborative alliances towards the development and potential commercialization of these therapies.

Manufacturing

In-House Current Good Manufacturing Practice ("cGMP") Facilities

We have built in-house cGMP facilities to enable better quality control, shorten lead times, lower costs and strengthen command over our intellectual property. Our first facility, ANCORIS, a commercial scale cGMP-compliant manufacturing facility, is producing the long-term extension study material for Vyjuvek at commercial scale and we expect to produce initial commercial launch material of Vyjuvek at the facility.

Our second commercial scale cGMP facility, ASTRA, is expected to be completed and validated in 2022. It is a state-of-the-art cGMP manufacturing facility that, in addition to adding significant capacity to support the growing pipeline, will also allow the in-house incorporation of raw material preparation, excipient manufacturing, testing, packaging, labeling and distribution, thereby fully integrating all components of the supply chain from starting materials to patient experience. We announced the ground breaking of ASTRA on January 24, 2020.

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

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

- Production of a master virus seed stock ("MVSS");
- Production of complementing master cell bank ("MCB"); and
- Optimized transduction parameters.

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

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

included to optimize gene expression. We also have optimized the transduction conditions to reproducibly obtain high yields of the virus.

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

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

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

- A proprietary vector manufacturing technique and a series of high-efficiency purification processes that produce highly purified therapeutic vectors and can be adapted for each product candidate; and
- A critical list of cGMP assays to accurately characterize our process and the HSV-1 vectors we produce.

Competition

The biotechnology and pharmaceutical industries are highly competitive. In particular, the field of gene therapy is characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. Some of our competitors have substantially greater financial resources and larger research and development organizations. In addition, our experience in clinical trials, obtaining FDA and other regulatory approvals, and manufacturing and commercialization of products may be more limited.

Epidermolysis Bullosa

A number of companies are developing drug candidates for EB. There is no approved treatment for dystrophic EB at this time. We believe our competitors fall into two broad categories:

- **Corrective approaches:** We are aware of two companies, Abeona and Castle Creek Pharmaceuticals, which are developing autologous or grafting gene therapy approaches to treating dystrophic EB. We are also aware of a recombinant-protein based approach being developed by Phoenix Tissue Repair.
- **Palliative Treatments:** We are aware of companies such, as Amryt Pharmaceuticals and Castle Creek Pharmaceuticals, who are developing product candidates taking a palliative approach to treating the disease.

Autosomal Recessive Congenital Ichthyosis ("ARCI")

We are aware of companies like Novartis Inc. and Patagonia Pharmaceuticals, LLC who have conducted clinical trials for ARCI in the past. We are unaware of any companies conducting active clinical trials in ARCI presently.

Netherton Syndrome

We are aware that Novartis Inc. has conducted clinical trials for Netherton Syndrome. We are unaware of any companies currently conducting active clinical trials in Netherton Syndrome presently.

Cystic Fibrosis

We are aware of several preclinical or early clinical stage nucleic-acid-based programs for the treatment of CF including TranslateBio, ReCode Therapeutics, Spirovant, and 4D Molecular Therapeutics.

Intellectual Property

Our success depends in part on our ability to maintain proprietary protection surrounding our product candidates, platform technology, and know-how, to operate without infringing the proprietary rights of others, and to prevent others from infringing

our proprietary rights. We have a portfolio of patents, patent applications and other intellectual property owned entirely by the Company - that protect our core platform technology and products based thereupon, and affords us freedom to use this platform for the development of novel therapeutics for multiple applications. We continue to advance our IP portfolio actively through the filing of new patent applications, divisionals, and continuations relating to our technologies as we deem appropriate.

In addition to our patents, we rely on trade secrets and know-how to develop and maintain our competitive position. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, and obtain and maintain ownership of certain technologies, in part, through confidentiality agreements and intellectual property assignment agreements with our employees, consultants and commercial partners. We also seek to preserve the integrity and confidentiality of our data, trade secrets, and know-how, including by implementing measures intended to maintain the physical and electronic security of our research and manufacturing facilities, as well as our information technology systems.

Platform

Patent Number	Country / Region*	Patent Type	Expiration Date**	Owner / Licensor
U.S. 10,441,614	United States	**Composition of Matter & Methods of Use** – The Skin TARgeted Delivery platform, or STAR-D, for skin-targeted therapeutics, as well as methods of its use for delivering any effector of interest to the skin	12/28/2036	Krystal
U.S. 11,185,564	United States	**Composition of Matter & Methods of Use** Composition of Matter & Methods of Use – Engineered HSV-1 vectors for skin-targeted therapeutics, as well as methods of their use for delivering any effector of interest to the skin	10/10/2039	Krystal

Vyjuvek (beremagene geperpavec)

Patent Number	Country / Region*	Patent Type	Expiration Date**	Owner / Licensor
U.S. 9,877,990	United States	**Composition of Matter & Methods of Use** – Compositions comprising HSV vectors encoding certain effectors, including the gene encoded in Vyjuvek, and methods of using the same for providing prophylactic, palliative or therapeutic relief of a wound, disorder or disease of the skin	12/28/2036	Krystal
U.S. 10,155,016	United States	**Composition of Matter & Methods of Use** – Covers compositions containing Vyjuvek, formulated for alternate routes of administration	12/28/2036	Krystal
EP 3 377 637 B1	Europe	**Composition of Matter & Methods of Use** – Pharmaceutical compositions comprising Vyjuvek, as well as uses thereof.	12/28/2036	Krystal

KB105

Patent Number	Country / Region*	Patent Type	Expiration Date**	Owner / Licensor
U.S. 10,525,090	United States	**Composition of Matter & Methods of Use** – KB105, as well as medical applications of this product for treating TGM1-deficient ARC	4/11/2039	Krystal

KB301

Patent Number	Country / Region*	Patent Type	Expiration Date**	Owner / Licensor
U.S. 10,786,438	United States	**Composition of Matter & Methods of Use** – Pharmaceutical compositions comprising HSV vectors encoding one or more cosmetic proteins, as well as methods of their use for improving skin condition, quality, and/or appearance.	4/26/2039	Krystal

KB407

Patent Number	Country / Region*	Patent Type	Expiration Date**	Owner / Licensor
U.S. 10,829,529	United States	**Methods of Use –** Methods of using KB407 for the treatment of Cystic fibrosis and other diseases causing progressive lung destruction	2/07/2040	Krystal

* Granted patents in the U.S. and Europe ("EP") are shown. Additional patent protection in the U.S. and Europe or other countries or regions through pending or granted counterparts may be available.
** Stated expiration dates do not account for any patent term extension, supplemental protection certificate, or pediatric extensions that may be available.

Government Regulation and Product Approval

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

Within the FDA, the Center for Biologics Evaluation and Research ("CBER") regulates gene therapy products. Within CBER, the review of gene therapy and related products is in the Office of Cellular, Tissue and Gene Therapies ("OCTGT") and the FDA has established the Cellular, Tissue and Gene Therapies Advisory Committee ("CTGTAC") to advise CBER on its reviews. CBER works closely with the NIH and the RAC, which makes recommendations to the NIH on gene therapy issues and engages in a public discussion of scientific, safety, ethical and societal issues related to proposed and ongoing gene therapy protocols. The FDA has provided guidance for the development of gene therapy products generally, including a growing body of guidance documents on CMC clinical investigations and other areas of gene therapy development, all of which are intended to facilitate the industry's development of gene therapy products.

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

U.S. Biologic Products Development Process

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

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

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

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

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

Human Clinical Trials Under an IND

Clinical trials involve the administration of the biologic product candidate to healthy volunteers or patients under the supervision of qualified investigators who generally are physicians not employed by or under the control of the trial sponsor. Clinical trials are conducted under written study protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters to be used to monitor subject safety, including stopping rules that assure a clinical trial will be stopped if certain adverse events should occur. Each protocol and any

amendments to the protocol must be submitted to the FDA as part of the IND. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to a proposed clinical trial and places the trial on clinical hold, including concerns that human research subjects will be exposed to unreasonable health risks. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Accordingly, submission of an IND may or may not result in the FDA allowing clinical trials to commence. Clinical trials must be conducted and monitored in accordance with the FDA's regulations comprising GCP requirements, including the requirement that all research subjects provide informed consent. Further, each clinical trial must be reviewed and approved by an IRB and IBC at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers items such as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the form and content of the informed consent that must be signed by each clinical trial subject, or their legal representative, reviews and approves the study protocol, and must monitor the clinical trial until completed. Clinical trials involving recombinant DNA also must be reviewed by an IBC, a local institutional committee that reviews and oversees basic and clinical research that utilizes recombinant DNA at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment.

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

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

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

Additional Regulation for Gene Therapy Clinical Trials

In addition to the regulations discussed above, there are a number of additional standards that apply to clinical trials involving the use of gene therapy. The FDA has issued various guidance documents regarding gene therapies, which outline additional factors the FDA will consider at each of the above stages of development and relate to, among other things: the proper preclinical assessment of gene therapies; the CMC information that should be included in an IND application; the proper design of tests to measure product potency in support of an IND or BLA application; and measures to observe delayed adverse effects in subjects who have been exposed to investigational gene therapies when the risk of such effects is high. Further, the FDA usually recommends that sponsors observe subjects for potential gene therapy-related delayed adverse events for a 15-year period, including a minimum of five years of annual examinations followed by 10 years of annual queries, either in person or by questionnaire. The NIH and the FDA have a publicly accessible database, the Genetic Modification Clinical Research Information System, which includes information on gene therapy trials and serves as an electronic tool to facilitate the reporting and analysis of adverse events on these trials.

U.S. Review and Approval Processes

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

The FDA reviews a BLA within 60 days of submission to determine if it is substantially complete before it accepts it for filing. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In that event, the BLA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth, substantive review of the BLA. The FDA reviews the BLA to determine, among other things, whether the proposed product candidate is safe and potent, or effective, for its intended use, has an acceptable purity profile and whether the product candidate is being manufactured in accordance with cGMP to assure and preserve the product candidate's identity, safety, strength, quality, potency and purity. The FDA may refer applications for novel biologic products or biologic products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. During the product approval process, the FDA also will determine whether a Risk Evaluation and Mitigation Strategies ("REMS") is necessary to assure the safe use of the product candidate.

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

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

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

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

The FDA has agreed to specified performance goals in the review of BLAs under the PDUFA. One such goal is to review standard BLAs in 10 months after the FDA accepts the BLA for filing, and priority BLAs in six months, whereupon a review decision is to be made. The FDA does not always meet its PDUFA goal dates for standard and priority BLAs and its review goals are subject to change from time to time. The review process and the PDUFA goal date may be extended by three months

if the FDA requests or the BLA sponsor otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

Fast Track Designation

Fast Track designation is granted to drugs being developed for the treatment of serious or life-threatening diseases or conditions where there is an unmet medical need. The purpose of the Fast Track designation provision is to help facilitate development and expedite the review and potential approval of drugs to treat serious and life-threatening conditions. Sponsors of drugs that receive Fast Track designation have the opportunity for more frequent interactions with the FDA review team throughout the development program. These can include meetings to discuss study design, data required to support approval, or other aspects of the clinical program. Additionally, products that have been granted Fast Track designation may be eligible for priority review of a BLA application and the FDA may consider reviewing portions of a New Drug Application ("NDA") before the sponsor submits the complete application, also known as a rolling review.

Orphan Drug Designation

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

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

Orphan medicinal product status in the European Union ("EU") has similar, but not identical benefits.

Regenerative Medicine Advanced Therapy (“RMAT”) Designation

Established under the 21st Century Cures Act, RMAT designation is a program designed to expedite the development and approval of regenerative medicine products, including gene therapy products. An investigational therapy is eligible for the RMAT designation if it is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition, and preliminary clinical evidence indicates a potential to address unmet medical needs for that disease or condition. The designation includes all the benefits of the FDA's Fast Track and Breakthrough Therapy designations and enables the ability to work more closely and frequently with the FDA to discuss surrogate or intermediate endpoints to support the potential acceleration of approval and satisfy post-approval requirements.

Prime Designation

The PRIME designation is awarded by the EMA to promising medicines that target an unmet medical need. These medicines are considered priority medicines by the EMA. To be eligible and accepted for PRIME, a medicine has to show its potential to benefit patients with unmet medical needs based on early clinical data coupled with non-clinical data. Through PRIME, the EMA offers enhanced support to medicine developers including early interaction and dialogue, and a pathway for accelerated evaluation by the agency. The program is intended to optimize development plans and expedite the review and approval process so that these medicines may reach patients as early as possible.

Rare Pediatric Disease Priority Review Voucher

The FDA also offers a rare pediatric disease drug designation. If a drug receives the designation of a “rare pediatric disease” drug, it is eligible during the FDA marketing process to apply for a Rare Pediatric Disease Priority Review Voucher. According to the FDA website, under the Rare Pediatric Priority Review Voucher Program, a sponsor who receives an approval for a drug or biologic for a “rare pediatric disease” may qualify for a voucher that can be redeemed to receive a priority review of a subsequent marketing application for a different product.

U.S. patent Term Restoration and Marketing Exclusivity

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

Post-Approval Requirements

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

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

Government Regulation Outside of the United States

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

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

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

Other Healthcare Laws and Regulations

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

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in cash or kind, in exchange for, or to induce, either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers, on the one hand, and prescribers, purchasers and formulary managers on the other. The Patient Protection and Affordable Care Act ("PPACA") amended the intent requirement of the federal Anti-Kickback Statute. A person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to commit a violation;
- the federal false claims and civil monetary penalties laws, including the civil False Claims Act ("FCA"), which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid or other third-party payors that are false or fraudulent, or making a false statement to avoid, decrease, or conceal an obligation to pay money to the federal government. Certain marketing practices, including off-label promotion, also may implicate the FCA. In addition, the PPACA codified case law that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the FCA;
- the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services ("CMS") information related to payments and other transfers of value to physicians, certain other healthcare providers and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members;
- the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA") imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and its implementing regulations, which imposes obligations, including mandatory contractual terms, with respect to safeguarding the transmission, security and privacy of protected health information;
- the federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services; and
- state and foreign law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

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

Coverage and Reimbursement

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

In the EU, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies. EU member states may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other member states allow companies to fix their own prices for products, but monitor and control company profits. The downward pressure on health care costs has become intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert competitive pressure that may reduce pricing within a country. Any country that has price controls or reimbursement limitations may not allow favorable reimbursement and pricing arrangements.

Health Reform

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

Additional Regulation

In addition to the foregoing, state and federal laws regarding environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservation and Recovery Act and the Toxic Substances Control Act, affect our business. These and other laws govern the use, handling and disposal of various biologic, chemical and radioactive substances used in, and wastes generated by, operations. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines. Equivalent laws have been adopted in other countries that impose similar obligations.

U.S. Foreign Corrupt Practices Act

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

Human Capital

As of February 18, 2022, we had 119 full-time employees, primarily engaged in research and development, manufacturing and administrative activities. None of our employees are represented by a labor union and we consider our employee relations to be good.

We believe our employees are among the most important assets to our company and are key to achieving our goals and expectations. Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, and incentivizing our existing and new employees. We offer robust compensation packages, including competitive base pay, incentive compensation and stock compensation programs, and provide a broad range of benefits. The principal purpose of our stock compensation program is to attract, retain and reward personnel through the granting of stock-based awards, in order to increase stockholder value and the success of our company by motivating such individuals to perform to the best of their abilities and achieve our objectives. In addition, we are committed to the professional advancement of our employees and offer various training programs and career development opportunities.

Corporate Information

We commenced operations on April 15, 2016. On March 31, 2017, we converted from a California limited liability company to a Delaware C-corporation, and changed our name from Krystal Biotech, LLC to Krystal Biotech, Inc. Our principal offices are located at 2100 Wharton Street, Suite 701, Pittsburgh, PA 15203, and our telephone number is 412-586-5830. On June 19, 2018, the Company incorporated Krystal Australia Pty Ltd., an Australian proprietary limited company, for the purpose of undertaking preclinical and clinical studies in Australia. On April 24, 2019, the Company incorporated Jeune, Inc. (now Jeune Aesthetics, Inc.) in Delaware, a wholly-owned subsidiary, for the purpose of undertaking preclinical studies for aesthetic skin conditions. Our website address is www.krystalbio.com. Our website and the information contained on, or that can be accessed through, the website will not be deemed to be incorporated by reference in, and are not considered part of, this Annual Report on Form 10-K. You should not rely on any such information in making your decision whether to purchase our common stock. Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, are available free of charge on the investor relations section of our website as soon as reasonably practicable after we electronically file such material with, or furnish it to the Securities and Exchange Commission, or the SEC. The SEC also maintains a website that contains reports, proxy and information statements, and other information regarding the Company that we file electronically with the SEC. The address of the website is http://www.sec.gov.

Item 1A. Risk Factors.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred net losses since inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.

Since inception, we have incurred recurring losses and negative cash flows from operations and, at December 31, 2021, we had an accumulated deficit of $140.8 million. Our ability to achieve profitability depends on our ability to successfully complete the development of, and obtain the regulatory approvals necessary to commercialize our product candidates. We do not anticipate generating revenues from product sales for the next year, if ever. We have devoted substantially all our efforts to date to research and development of our gene therapy product candidates as well as to building out our infrastructure. We expect that it could be a year, 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 Vyjuvek, KB105, and KB301, including our current clinical trials and planned future trials;
- initiate clinical trials for KB104 and KB407 and preclinical studies for any additional product candidates that we may pursue in the future;
- prepare our BLA, MAA and approvals in certain other countries for Vyjuvek;
- continue to operate our in-house commercial-scale cGMP manufacturing facility, ANCORIS, and complete build out of our second cGMP manufacturing facility, ASTRA;
- manufacture 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 Vyjuvek 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 the clinical trials for our product candidates, 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. If we were required to discontinue development of any of our product candidates, if any of our product candidates do not receive regulatory approval, if we do not obtain our targeted indications for our product candidates or if any of our product candidates 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 Vyjuvek, KB105, KB301, KB104 or KB407, KB408 product candidates 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 three product candidates, Vyjuvek, KB105, and KB301 in clinical trials and we may never develop, acquire or in-license additional product candidates. We may never succeed in any or all 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 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 Vyjuvek, KB105, and KB301 our expenses could increase and revenue could be further delayed.

We may need to raise additional funding in order to receive approval for our other product candidates. 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.

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

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

- the length of our open label study for Vyjuvek;
- the progress, timing results and costs of our Phase 1/2 clinical trials for KB105;
- the progress, timing, results and costs of our Phase 1 clinical trials for KB301;
- the continued development and the filing of investigational new drug ("IND"), applications for KB104 and KB407 and other product candidates;
- the initiation, scope, progress, timing, costs and results of drug discovery, laboratory testing, manufacturing, preclinical studies and clinical trials for any other product candidates that we may pursue in the future, if any;
- the costs of building and maintaining our own commercial-scale cGMP manufacturing facilities;
- the outcome, timing and costs of seeking regulatory approvals;
- the costs associated with the manufacturing process development and evaluation of third-party manufacturers, if necessary;
- the costs of future activities, including product sales, medical affairs, marketing, manufacturing and distribution, in the event we receive marketing approval for any of our current and future product candidates;
- 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;
- the costs of commercialization activities for our current and future product candidates if we receive marketing approval for such product candidates, including the costs and timing of establishing product sales, medical affairs, marketing, distribution and manufacturing capabilities;
- subject to receipt of marketing approval, if any, revenue received from commercial sale of our current and future product candidates;
- the terms and timing of any future collaborations, licensing, consulting or other arrangements that we may establish;
- the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, maintenance, defense and enforcement of any patents or other intellectual property rights, including milestone and royalty payments and patent prosecution fees that we are obligated to pay pursuant to our license agreements, if any;
- our current license agreements, if any, 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. 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 a year, 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 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. The terms of additional financing may be impacted by, among other things, general market conditions, the market's perception of our product candidates and growth potential and the market price per share of our common stock.

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 our product candidates have been limited to organizing and staffing our company, business planning, raising capital, developing our vector platform and related technologies, identifying potential gene therapy product candidates, and undertaking preclinical studies and clinical trials of Vyjuvek, KB105, KB301, KB104, KB407 and KB408. While we have conducted clinical trials of Vyjuvek, KB105, and KB301 we have not yet demonstrated the ability to complete clinical trials of KB105 and KB301, obtain marketing approvals for any of our products, manufacture a commercial-scale product or conduct sales and marketing activities necessary for successful commercialization. Consequently, any predictions you make about our future success, performance or viability may not be as accurate as they could be if we had more experience developing gene therapy products.

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 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

Business interruptions resulting from the COVID-19 pandemic or similar public health crises could cause a disruption of the development efforts for our product candidates and adversely impact our business.

The COVID-19 pandemic has previously adversely affected our business and could have a material adverse effect on our financial condition and results of operations. Authorities have imposed, and businesses and individuals have implemented, numerous measures to try to contain the virus or treat its impact, such as travel bans and restrictions, quarantines, shelter-in-place/stay-at-home and social distancing orders, shutdowns, and vaccine requirements. These measures have impacted and may further impact our workforce and operations, the operations of our customers, and those of our third-party partners.

The extent to which COVID-19 impacts our operations or those of our third-party partners will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the duration of the pandemic, additional or modified government actions, new information that will emerge concerning the severity and impact of COVID-19, including new strains, and the actions to contain COVID-19 or address its impact in the short and long term, among others.

Timely initiation and completion of planned clinical trials is dependent upon the availability of, for example, clinical trial sites, researchers and investigators, regulatory agency personnel, and materials, which may be adversely affected by global health matters, such as pandemics. We plan to conduct clinical trials in geographies that are currently being affected by COVID-19.

In the event that governmental authorities were to further modify current restrictions, our employees conducting research and development or manufacturing activities may not be able to access our laboratory or manufacturing spaces, and our core activities may be significantly limited or curtailed, possibly for an extended period of time.

Some factors from the COVID-19 pandemic that could delay or otherwise adversely affect the completion of our preclinical activities and the planned initiation of our clinical trials for our investigational drug product candidates, as well as our business operations generally, include:

- the potential diversion of healthcare resources away from the conduct of preclinical activities and clinical trials to focus on pandemic concerns, including the availability of necessary materials and the attention of physicians serving as our clinical trial investigators, hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our prospective clinical trials;

- limitations on travel that could interrupt key preclinical and clinical trial activities, such as clinical trial site initiations and monitoring, domestic and international travel by employees, contractors or patients to clinical trial sites, including any government-imposed travel restrictions or quarantines that will impact the ability or willingness of patients, employees or contractors to travel to our research, manufacturing and clinical trial sites or secure visas or entry permissions, any of which could delay or adversely impact the conduct or progress of our prospective clinical trials;

- interruption or delays in the operations of the FDA and comparable foreign regulatory agencies, which may impact our ability to conduct preclinical and clinical activities as well as product approval timelines;

- limitations on our business operations by local, state, or the federal government that could impact our ability to conduct our preclinical or clinical activities, including completing our IND-enabling studies or our ability to select future development candidates; and interruption in global shipping affecting the transport of clinical trial materials and other supplies used in our prospective clinical trials;

- interruption of, or delays in receiving, key materials from our suppliers and vendors due to staffing shortages, travel limitations, production slowdowns or stoppages and disruptions in delivery systems;

- interruption of, or delays in manufacturing our product candidates at our manufacturing facility in Pittsburgh or receiving supplies of our product candidates from our contract manufacturing organizations due to staffing shortages, travel limitations, production slowdowns or stoppages and disruptions in delivery systems; and

- business disruptions caused by potential office, manufacturing and laboratory closures and an increased reliance on employees working from home, disruptions to or delays in ongoing laboratory experiments and operations, staffing shortages, travel limitations, cyber security and data accessibility, or communication or mass transit disruptions, any of which could adversely impact our business operations or delay necessary interactions with local regulators, ethics committees, manufacturing sites, research sites and other important agencies and contractors.

These and other factors arising from COVID-19 could worsen, each of which could further adversely impact our ability to conduct clinical trials and our business generally, and could have a material adverse impact on our operations and financial condition and results.

In addition, the trading prices for our common stock and other biopharmaceutical companies have been highly volatile as a result of the COVID-19 pandemic. As a result, we may face difficulties raising capital through sales of our common stock or such sales may be on unfavorable terms. Further, conditions in the capital and credit markets may continue to deteriorate as a result of the pandemic such that our access to capital and other sources of funding may be constrained.

The COVID-19 outbreak continues to evolve. The extent to which the outbreak may impact our business, preclinical studies and planned clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the duration of the outbreak, travel restrictions and other actions to contain the outbreak or address its impact, such as social distancing and quarantines or lock-downs in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and address the disease.

We are a development-stage company. If we are unable to advance our product candidates through clinical trials, obtain regulatory approval and ultimately commercialize our product candidates, or if we experience significant delays in doing so, our business will be materially harmed.

We are a development stage company, and Vyjuvek entered its first clinical trial in May 2018, KB105 entered its first clinical trial in September 2019, and KB301 entered its first trial in August 2020. The development and commercialization of our product candidates are 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;

- successful development of our internal manufacturing processes on an ongoing basis and maintenance of our existing arrangements with third-party manufacturers for clinical supply;
- commercial launch of our product candidates, if and when approved, whether alone or in collaboration with others;
- acceptance of our product candidates, if and when approved, by patients, the medical community and third-party payors;

If we fail in one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business. If we do not receive regulatory approvals for our product candidates, our business, financial condition, results of operations and prospects could be materially and adversely affected.

Our lead candidate, Vyjuvek, has not been submitted to or reviewed by regulatory agencies, and we cannot predict when, or if, we will obtain regulatory approval to commercialize Vyjuvek and the approval may be for a narrower indication than we seek.

We cannot commercialize a product candidate until the appropriate regulatory authorities have reviewed and approved the product candidate. Even though Vyjuvek met 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 or 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 post-approval safety monitoring program. 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 Vyjuvek. Any of the foregoing scenarios could materially harm the commercial prospects for Vyjuvek and materially and adversely affect our business, financial condition, results of operations and prospects.

Vyjuvek 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. It is difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in either the United States or the European Union or how long it will take to commercialize our product candidates. Approvals by the European Commission may not be indicative of what FDA may require for approval and approval by the FDA may not be indicative of what the European Commission would require for approval.

Regulatory requirements and policy 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 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. If we were to engage a National Institutes of Health funded institution to conduct a clinical trial, that institution’s Institutional Biosafety Committee ("IBC") as well as its Institutional Review Board ("IRB"), would need to review the proposed clinical trial to assess the safety of the trial. 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 Vyjuvek or future product candidates or lead to significant post-approval limitations or restrictions. As we advance Vyjuvek, we may be required to consult with these regulatory and advisory groups and will need to comply with applicable requirements and guidelines. If we fail to do so, we may be required to delay or discontinue development of Vyjuvek. 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.

Vyjuvek 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.

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, our products for any or all targeted indications. Even if we can 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 our products, the commercial prospects of such product candidate may be harmed and our ability to generate product revenues from the product candidate may be delayed or eliminated. Any of these occurrences may harm our ability to develop product candidates, and may harm our business, financial condition and prospects significantly.

Additionally, if Vyjuvek receives marketing approval, the FDA could require us to adopt a post-approval safety monitoring program 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 Vyjuvek, 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 Vyjuvek 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 our products, 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 our products 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 our products 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, or be required to conduct additional confirmatory safety and/or efficacy studies;
- 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 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.

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 personnel and expect to experience significant expansion of our facilities, infrastructure and overhead as we develop our own manufacturing facilities 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. We will continue to incur costs related to regulatory compliance and are subject to risks related to non-compliance with or changes to applicable law and regulations, which would cause our product candidates to lose approval.

Even if we obtain any regulatory approval for Vyjuvek, 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 Vyjuvek may also be subject to a post-approval safety monitoring program, 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. 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 Vyjuvek 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, if any;
- 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 Vyjuvek or any future product candidates and adversely affect our business, financial condition, results of operations and prospects.

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 Vyjuvek or any future product candidates. 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 Vyjuvek, KB105, and KB407, 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, Vyjuvek, for the treatment of dystrophic EB 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 ("OMPD"), for Vyjuvek. On August 7, 2018, the FDA granted orphan drug designation to our second product candidate, KB105, currently in clinical development for treatment of patients with TGM1-ARCI, and on October 10, 2019, the European Commission granted the OMPD for KB105. On August 17, 2020, the FDA granted orphan drug designation to our most recent product candidate, KB407, currently in preclinical development, for the treatment of cystic fibrosis. 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 EMA 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 Vyjuvek, KB105 and KB407, 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 like 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 enough 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.

The FDA granted Fast Track designation in the United States for Vyjuvek on May 23, 2018 and for KB105 on October 24, 2019. In addition, Vyjuvek was granted RMAT by the FDA on June 21, 2019 and PRIME by the EMA in March 2019. 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 and EMA procedures and does not assure ultimate approval by either the FDA or EMA.

A RMAT/PRIME 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. Drugs designated as RMAT 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 Vyjuvek in December 2016, for KB105 in August 2018, for KB104 in April 2019, and for KB407 in September 2020, which could qualify us to receive a Rare Pediatric Priority Review Voucher.

There is no assurance we will receive RMAT, PRIME or 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 Vyjuvek, KB105, KB104, and KB407 we may not experience a faster review or approval for a subsequent marketing application.

We may expend our limited resources to pursue a product candidate or indication to the exclusion of other 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 Vyjuvek, KB105, KB301, KB104 and KB407 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 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 our lead product candidate, Vyjuvek or any future product candidate.

We are aware of several companies and institutions that are currently developing alternative autologous or palliative gene therapy approaches for dystrophic EB and cystic fibrosis. 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 Vyjuvek or any future product candidate uneconomical or obsolete, and we may not be successful in marketing Vyjuvek or any future product candidate against competitors.

In the future, even if we commercialize a product candidate faster than our competitors, we could also face competition from lower cost biosimilars in the United States or in Europe.

In addition, as a result of the expiration or successful challenge of our patent rights, we could face 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.

Risks Related to Manufacturing

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

Before we can begin to commercially manufacture our product candidates, whether in a third-party facility or in our own facilities, once established, we must pass a pre-approval inspection of our manufacturing facilities by the FDA before our product candidates 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. To obtain approval, we will need to ensure that all 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 our product candidates is complex, novel and has not been validated for commercial use. In order to produce enough quantities of our product candidates for future clinical trials and initial U.S. commercial demand, we will need to increase the scale of our manufacturing process. The production of our product candidates 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 our product candidates are 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 have established our own manufacturing facility for our product candidates, we may need 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.

Even if we obtain the validation from the FDA of our cGMP manufacturing facility, we intend to maintain third-party manufacturing capabilities in order to provide multiple sources of supply. In the event that these third-party manufacturers do

not successfully carry out their contractual duties, meet expected deadlines or manufacture our product candidates 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 of product candidates or the clinical trials required for approval of our product candidates. 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 our product candidates and would thereby have a material adverse effect on our business, financial condition, results of operations and prospects.

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 our product candidates 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 our product candidates 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.

Risks Related to Commercialization of Our Product Candidates

If we are unable to expand our market development capabilities or enter into agreements with third parties to market and sell our product candidates, we may be unable to generate any product revenue.

We currently have a small market development organization. To successfully commercialize our product candidates, if approved, we plan to expand our capabilities to promote market access and build awareness. To successfully commercialize any products that may result from our development programs, we will need to further expand our market development organization, either on our own or with a third party. The development of our own market development team will be expensive and time-consuming and could delay any product launch. Moreover, we cannot be certain that we will be able to successfully develop this capability. We may enter into collaboration agreements regarding any of our product candidates with third parties to utilize their established marketing and distribution capabilities, but we may be unable to enter into such agreements on favorable terms, if at all. If any future collaborators do not commit sufficient resources to commercialize our products, or we are unable to develop the necessary capabilities on our own, we will be unable to generate sufficient product revenue to sustain our business. We compete with many companies that currently have extensive, experienced and well-funded medical affairs, marketing and sales operations to recruit, hire, train and retain marketing and sales personnel. We also face competition in our search for third parties to assist us with the sales and marketing efforts of our product candidates. Without an internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.

Our efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may never be successful. Such efforts may require more resources than are typically required due to the complexity and uniqueness of our products. If any of our product candidates is approved but fails to achieve market acceptance among physicians, patients or third-party payors, we will not be able to generate significant revenues from such product, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

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. 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.

Our success also will depend upon physicians who specialize in the treatment of prescribing treatments that involve the use of our product candidates, 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 any product candidate we may develop.

If the market opportunities for our product candidates are smaller than we believe they are, our product revenues may be adversely impacted, and our business may suffer.

We have mainly focused our research and product development efforts to date on Vyjuvek for dystrophic EB. 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 Vyjuvek, 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 Vyjuvek 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 Vyjuvek 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 our product candidates will depend upon its degree of market acceptance by physicians, patients, third-party payors and others in the medical community.

Ethical, social and legal concerns about gene therapy could result in additional regulations restricting or prohibiting our product candidates. 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 our product candidates will depend, in part, on the acceptance of physicians, patients and health care payors of gene therapy products in general, and our product candidates, in particular, as medically necessary, cost-effective and safe. Any product that we commercialize may not gain acceptance by physicians, patients, health care payors and others in the medical community. 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 our product candidates, if approved for commercial sale, will depend on several factors, including:

- the efficacy and safety of our product candidates as demonstrated in clinical trials;
- the efficacy, potential and perceived advantages of our product candidates over alternative treatments, if available;
- the cost of our product candidates relative to alternative treatments, if any are available;
- the clinical indications for which our product candidates are approved by the FDA or the EMA;
- 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.

Government price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates, if approved, which would adversely affect our revenue and results of operations.

We expect that coverage and reimbursement of pharmaceuticals may be increasingly restricted both in the U.S. and internationally. The escalating cost of health care has led to increased pressure on the health care industry to reduce costs. Drug pricing by pharmaceutical companies recently has come under increased scrutiny and continues to be subject to intense political and public debate in the U.S. and abroad. Government and private third-party payors have proposed health care reforms and cost reductions. A number of federal and state proposals to control the cost of health care, including the cost of drug treatments, have been made in the U.S. Specifically, there have been several recent U.S. Congressional inquiries and proposed bills designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for drugs. In some international markets, the government controls the pricing, which can affect the profitability of drugs. Current government regulations and possible future legislation regarding health care may affect coverage and reimbursement for medical treatment by third-party payors, which may render our product candidates, if approved, not commercially viable or may adversely affect our anticipated future revenues and gross margins.

We cannot predict the extent to which our business may be affected by these or other potential future legislative or regulatory developments. However, future price controls or other changes in pricing regulation or negative publicity related to the pricing of pharmaceutical drugs generally could restrict the amount that we are able to charge for our future products, which would adversely affect our anticipated revenue and results of operations.

The insurance coverage and reimbursement status of newly approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for our products, if approved, could limit our ability to market those products and decrease our ability to generate product revenue.

We expect that coverage and reimbursement by government and private payors will be essential for most patients to be able to afford our products. Accordingly, sales of our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or will be reimbursed by government authorities, private health coverage insurers and other third-party payors. Coverage and reimbursement by a third-party payor may depend upon several factors, including the third-party payor’s determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Obtaining coverage and reimbursement for a product from third-party payors is a time-consuming and costly process that could require us to provide to the payor supporting scientific, clinical and cost-effectiveness data. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. If coverage and reimbursement are not available, or are available only at limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be adequate to realize a sufficient return on our investment.

There is significant uncertainty related to third-party coverage and reimbursement of newly approved products. In the United States, third-party payors, including government payors such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs and biologics will be covered and reimbursed. The Medicare and Medicaid programs increasingly are used as models for how private payors and government payors develop their coverage and reimbursement policies. Currently, no gene therapy product has been approved for coverage and reimbursement by the Centers for Medicare & Medicaid Services ("CMS"), the agency responsible for administering the Medicare program. It is difficult to predict what CMS will decide with respect to coverage and reimbursement for fundamentally novel products such as ours, as there is no body of established practices and precedents for these types of products. Moreover, reimbursement agencies in the European Union may be more conservative than CMS. For example, several cancer drugs have been approved for reimbursement in the United States and have not been approved for reimbursement in certain European Union Member States. It is difficult to predict what third-party payors will decide with respect to the coverage and reimbursement for our product candidates.

Outside the United States, international operations generally are subject to extensive government price controls and other market regulations and increasing emphasis on cost-containment initiatives in the European Union, Canada and other countries may put pricing pressure on us. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. It also can take a significant amount of time after approval of a product to secure pricing and reimbursement for such product in many counties outside the United States. In general, the prices of medicines under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for medical products but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable product revenues.

Moreover, increasing efforts by government and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for new products approved and, as a result, they may not cover or provide adequate payment for our product candidates. Payors increasingly are considering new metrics as the basis for reimbursement rates, such as Average Sales Price, Average Manufacturer Price, and Actual Acquisition Cost. The existing data for reimbursement based on some of these metrics is relatively limited, although certain states have begun to survey acquisition cost data for the purpose of setting Medicaid reimbursement rates, and CMS has begun making pharmacy National Average Drug Acquisition Cost and National Average Retail Price data publicly available on at least a monthly basis. Therefore, it may be difficult to project the impact of these evolving reimbursement metrics on the willingness of payors to cover candidate products that we are able to commercialize. We expect to experience pricing pressures in connection with the sale of any of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional potential legislative and administrative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become intense. As a result, increasingly high barriers are being erected to the entry of new products such as ours.

Ethical, legal and social issues related to genetic testing may reduce demand for our product candidates, if approved.

We anticipate that prior to receiving certain gene therapies, patients may be required to undergo genetic testing. Genetic testing has raised concerns regarding the appropriate utilization and the confidentiality of information provided by genetic testing. Genetic tests for assessing a person’s likelihood of developing a chronic disease have focused public attention on the need to protect the privacy of genetic information. For example, concerns have been expressed that insurance carriers and employers may use these tests to discriminate based on genetic information, resulting in barriers to the acceptance of genetic tests by consumers. Concerns have also been raised about the accuracy of genetic testing. This could lead to governmental authorities restricting genetic testing or calling for additional regulation of genetic testing, particularly for diseases for which there is no known cure. Any of these scenarios could decrease demand for our product candidates, if approved.

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 Vyjuvek 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 Vyjuvek 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 our product candidates will be harmed and our business, financial condition, results of operations and prospects will be adversely affected.

Risks Related to Our Business Operations

We may not be successful in our efforts to identify or discover additional product candidates and may fail to capitalize on programs or product candidates that may be a greater commercial opportunity or for which there is a greater likelihood of success.

The success of our business depends upon our ability to identify, develop and commercialize product candidates based on our gene therapy platform. Research programs to identify new product candidates require substantial technical, financial and human resources. Although certain of our product candidates are currently in clinical or preclinical development, we may fail to identify other potential product candidates for clinical development for several reasons. For example, our research may be unsuccessful in identifying potential product candidates or our potential product candidates may be shown to have harmful side effects, may be commercially impracticable to manufacture or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval.

Additionally, because we have limited resources, we may forego or delay pursuit of opportunities with certain programs or product candidates or for indications that later prove to have greater commercial potential. Our spending on current and future research and development programs may not yield any commercially viable products. If we do not accurately evaluate the commercial potential for a particular product candidate, we may relinquish valuable rights to that product candidate through strategic collaboration, licensing or other arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. Alternatively, we may allocate internal resources to a product candidate in a therapeutic area in which it would have been more advantageous to enter into a partnering arrangement.

If any of these events occur, we may be forced to abandon our development efforts with respect to a particular product candidate or fail to develop a potentially successful product candidate, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

If we are unable to manage expected growth in the scale and complexity of our operations, our performance may suffer.

If we are successful in executing our business strategy, we will need to expand our managerial, operational, financial and other systems and resources to manage our operations, continue our research and development activities and build a commercial infrastructure to support commercialization of any of our product candidates that are approved for sale. Future growth would impose significant added responsibilities on members of management. It is likely that our management, finance, development personnel, systems and facilities currently in place may not be adequate to support this future growth. Our need to effectively manage our operations, growth and product candidates requires that we continue to develop more robust business processes and improve our systems and procedures in each of these areas and to attract and retain enough numbers of talented employees. We may be unable to successfully implement these tasks on a larger scale and, accordingly, may not achieve our research, development and growth goals.

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 management 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. 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.

In the U.S., there have been and continue to be a number of legislative efforts to contain healthcare costs. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act ("PPACA"), was passed, which substantially changed 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 numerous judicial, administrative, executive, and legislative challenges to certain aspects of the PPACA, and we expect there will be additional challenges in the future. As a result, there have been delays in the implementation of, and action taken to repeal or replace, certain aspects of the PPACA. Most recently, under President Biden, the Department of Justice dropped support of two Supreme Court cases challenging the ACA in addition to a case before the U.S. Court of Appeals for the Fifth Circuit, and in June 2021, the Supreme Court upheld the ACA in a 7-2 opinion that the states and individuals that challenged the individual mandate did not have standing to challenge the law. Further, on January 28, 2021, President Biden signed an executive orders to expand access to ACA coverage, stating that it is the "policy" of the Biden administration to protect and strengthen the ACA and directing agencies to consider suspending, revising, or rescinding actions related to President Trump's executive orders that are inconsistent with this policy position. However, other legislators continue efforts to repeal and replace other elements of the ACA. While the ultimate outcome of ACA result of these efforts is not yet known, any changes that result in price controls reduce access to and reimbursement for care or add additional regulations may have an adverse effect on our financial condition and results of operations.

We cannot predict the impact that such actions against the ACA or other health care reform under the Biden administration will have on our business, and there is uncertainty as to what healthcare programs and regulations may be implemented or changed at the federal and/or state level in the United States, or the effect of any future legislation or regulation. However, it is possible that such initiatives could have an adverse effect on our ability to obtain approval and/or successfully commercialize products in the United States in the future. For example, any changes that reduce, or impede the ability to obtain, reimbursement for the type of products we intend to commercialize in the United States (or our products more specifically, if approved) could adversely affect our business plan to introduce our products in the United States.

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 ("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.

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.

Further, there has been heightened governmental scrutiny in recent years over the manner in which manufacturers set prices for their marketed products and the cost of prescription drugs to consumers and government healthcare programs, which have resulted in several recent Congressional inquiries and proposed and enacted bills designed to, among other things, reduce the cost of prescription drugs, 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 may affect our business, including 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.

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 our product candidates 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 our product candidates and begin commercializing them 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 claims 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;
- 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 ("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 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.

Often, to avoid the threat of treble damages and penalties under the False Claims Act, health care providers will resolve allegations in a settlement without admitting liability to avoid the potential treble damages. Any such settlement could materially affect our business, financial operations, and reputation.

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.

We also may incur substantial costs 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.

Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets, including conditions that are outside of our control, such as the current COVID-19 pandemic. Inflation and potential for rising interest rates have recent caused volatility in the capital and credit markets, and it is unclear how long such volatility will continue. A severe or prolonged economic downturn could result in a variety of risks to our business, including weakened demand for our product candidates and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could strain our suppliers, possibly resulting in supply disruption. Any of the foregoing could harm our business and we cannot anticipate all the ways in which the current economic climate and financial market conditions could adversely impact our business.

Our internal computer systems, or those of our collaborators or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

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

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, including the participants in our clinial trials. 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 confidential information of the patients who participate in our clinical trials. 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 third parties or government authorities.

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 that we have in place currently are limited and may not prove adequate in the event of a serious disaster or similar event. Substantially all our current supply of our product candidates is located at our manufacturing facility in Pittsburgh, Pennsylvania. We are constructing an additional manufacturing facility for the commercial supply of our products. 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 adequate U.S. and foreign patent protection for our product candidates, including Vyjuvek, KB105, KB301, KB104, KB407, and any future product candidates we may develop, and/or our vector platform, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technologies similar or identical to ours, and our ability to successfully commercialize our current product candidates, any future product candidates we may develop, and our platform technologies 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 Vyjuvek, KB105, KB301, KB104, KB407, and additional product candidates in our pipeline, current and future innovations related to our vector platform, and our institutional knowledge. The patent prosecution process is expensive, time-consuming and complex; we may not be able to file, prosecute, maintain, and/or enforce all necessary or desirable patent applications and issued patents at a reasonable cost or in a timely manner. We currently have seven issued patents in the United States: (1) U.S. Patent No. 9,877,990, covering, in part, pharmaceutical formulations comprising our lead clinical product Vyjuvek, as well as methods of its use for treating wounds, disorders, and diseases of the skin, which we refer to as the ’990 patent; (2) U.S. Patent No. 10,155,016 covering pharmaceutical compositions containing Vyjuvek formulated for myriad routes of administration; (3) U.S. Patent No. 10,441,614 covering aspects of our vector platform technology, and its uses in delivering any gene of interest to the skin; (4) U.S. Patent No. 10,525,090, covering pharmaceutical compositions comprising our second clinical product candidate, KB105, and methods of its use for treating TGM1-deficient autosomal recessive congenital ichthyosis; (5) U.S. Patent No. 10,786,438 covering pharmaceutical compositions comprising vectors encoding cosmetic proteins, including our third product candidate, KB301, and methods for their use for improving skin condition, quality, and/or appearance; (6) U.S. Patent No. 10,829,529 covering methods of using KB407 for the treatment of cystic fibrosis and other diseases causing progressive lung destruction; and (7) U.S. Patent No. 11,185,564 covering aspects of our vector platform technology, and its uses in delivering any gene of interest to the skin. Furthermore, we have nine international patent applications filed in accordance with the Paris Cooperation treaty directed to multiple discovery, preclinical, and clinical programs, including Vyjuvek, KB105, KB301, KB104, and KB407, as well as multiple patent applications filed in foreign jurisdictions stemming from these international applications. Vyjuvek is also the subject of patents granted in Australia, Europe, Japan, and New Zealand, including European Patent No. 3 377 637 B1, covering pharmaceutical compositions containing Vyjuvek as well as uses thereof.

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 does not preclude third parties from having intellectual property rights that could interfere with our freedom to use our platform, including for dermatological or pulmonary 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.

We also 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 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 each and every one of our product candidates, current and future innovations related to our vector platform, and our institutional knowledge 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 may 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 current and 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 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 freely use our proprietary technologies (e.g., 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. 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. On May 1, 2020, a complaint was filed against us in the United States District Court for the Western District of Pennsylvania by PeriphaGen Inc., which also named our Chief Executive Officer and Chief Operating Officer, Krish Krishnan and Suma Krishnan, respectively. The complaint alleges breach of contract and misappropriation of trade secrets, which secrets the plaintiff asserts were used to develop our product candidates, including the vector backbones, and our STAR-D platform. For more information, see "Item 3 – *Legal Proceedings*." We may in the future become party to, or be threatened with, other adversarial proceedings or litigation regarding intellectual property rights with respect to our product candidates 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 patent portfolio may therefore have no deterrent effect.

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 our products, including Vyjuvek. 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 our 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 Vyjuvek. We also 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 our technologies, including VYJUVEK, or force us to cease some or all 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 current or future 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 are subject to claims asserting that we, our employees or our advisors have wrongfully used or disclosed alleged trade secrets of other parties or claims asserting ownership of what we regard as our own intellectual property and we may face other such claims in the future.

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, as described below under “Item 3—Legal Proceedings,” on May 1, 2020, a complaint was filed against us by PeriphaGen, Inc., which also named our Chief Executive Officer and our Chief Operating Officer, Krish Krishnan and Suma Krishnan, respectively. The complaint alleges breach of contract and misappropriation of trade secrets, which secrets the plaintiff asserts we used to develop our vector platform and product candidates. 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.

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 current and former employees, 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 submissions 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. We cannot assure you that our efforts to seek patent protection for our technology and product candidates will not be negatively impacted by the future court decisions or changes in guidance or procedures issued by the USPTO. These decisions, and any guidance issued by the USPTO (or changes thereto), 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 in the process of registering our trademarks and trade names. Once trademarks or trade names have been registered, they 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 are important for building 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. There also could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trade names 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 patents, 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 current and 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 our current patents, or of 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 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 current or future issued claims, thus not infringing our intellectual property rights;
- it is possible that our filed or future patent applications will not lead to issued patents;
- issued patents to which we currently hold rights or to which we may hold rights in the future may be held invalid or unenforceable, including as a result of legal challenges by third parties or 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 application covering certain of our trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

Should any of these events occur, they could significantly harm our business, financial condition, results of operations and prospects.

Risks Related to Ownership of Our Common Stock

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

As of December 31, 2021, 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 15% 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 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 specifically has experienced extreme volatility that has often been unrelated to the operating performance of such 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 will continue to incur costs as a result of being a public company, and such costs may increase as a result of no longer being an "emerging growth company."

As a public company, we expect to continue to incur significant legal, accounting, insurance and other expenses, including costs associated with public company reporting requirements. The expenses incurred by public companies generally for reporting and corporate governance purposes have been increasing. We expect compliance with these public reporting requirements and associated rules and regulations to increase expenses, particularly because we are no longer an emerging growth company, although we are currently unable to estimate these costs with any degree of certainty. As of December 31, 2021, we are no longer an emerging growth company. We will incur additional costs applicable to public companies that are not emerging growth companies.

If we fail to maintain effective internal control over financial reporting, we may not be able to accurately report our financial results, which may adversely affect investor confidence in our company and, as a result, the value of our common stock.

Our management is responsible for establishing and maintaining adequate internal control over financial reporting and is required to have an independent auditor assess the effectiveness of our internal control over financial reporting, pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, as amended (the "Sarbanes-Oxley Act"). We cannot give any assurances that material weaknesses will not be identified in the future in connection with our compliance with the provisions of Section 404 of the Sarbanes-Oxley Act. The existence of any material weakness would preclude a conclusion by management and our independent auditors that we maintained effective internal control over financial reporting. Our management may be required to devote significant time and expense to remediate any material weaknesses that may be discovered and may not be able to remediate any material weakness in a timely manner. The existence of any material weakness in our internal control over financial reporting could also result in errors in our financial statements that could require us to restate our financial statements, cause us to fail to meet our reporting obligations and cause investors to lose confidence in our reported financial information, all of which could lead to a decline in the per-share trading price of our common stock.

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.

We have broad discretion in the use of our cash, cash equivalents and marketable securities and may not use them effectively.

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

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 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.

Third-party expectations relating to environmental, social and governance factors may impose additional costs and expose us to new risks.

There is an increasing focus from certain investors and other stakeholders concerning corporate responsibility, specifically related to environmental, social and governance factors. Some investors may use these factors to guide their investment strategies and, in some cases, may choose not to invest in us if they believe our policies relating to corporate responsibility are inadequate. Third-party providers of corporate responsibility ratings and reports on companies have increased in number, resulting in varied and in some cases inconsistent standards. In addition, the criteria by which companies' corporate responsibility practices are assessed are evolving, which could result in greater expectations of us and cause us to undertake costly initiatives to satisfy such new criteria. Alternatively, if we elect not to or are unable to satisfy such new criteria or do not meet the criteria of a specific third-party provider, some investors may conclude that our policies with respect to corporate responsibility are inadequate. We may face reputational damage in the event that our corporate responsibility procedures or standards do not meet the standards set by various constituencies. Furthermore, if our competitors' corporate responsibility performance is perceived to be greater than ours, potential or current investors may elect to invest with our competitors instead. In addition, in the event that we communicate certain initiatives and goals regarding environmental, social and governance matters, we could fail, or be perceived to fail, in our achievement of such initiatives or goals, or we could be criticized for the scope of such initiatives or goals. If we fail to satisfy the expectations of investors and other stakeholders or our initiatives are not executed as planned, our reputation and financial results could be adversely affected

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

Issuances of additional shares of our common stock could cause the price of our common stock to decline.

As of December 31, 2021, we had 25,207,985 million shares of common stock issued and outstanding. As of December 31, 2021, we also had outstanding options to purchase 2,043,179 million shares of common stock with a weighted-average exercise price of $57.00 per share. Outstanding vested options are likely to be exercised if the market price of our common stock exceeds the applicable exercise price, and, in the future, we expect to issue additional equity awards to directors and employees. As of December 31, 2021, we had 98,800 non-vest restricted stock awards ("RSAs") at a weighted-average price of $78.89. In addition, we may issue additional common stock or restricted securities in the future as part of financing activities or business development activities and any such issuances may have a dilutive effect on our then-existing shareholders. Sales of substantial amounts of our common stock in the open market, or the availability of such shares for sale, could adversely affect the price of our common stock. The issuance of restricted common stock or common stock upon exercise of any outstanding options would be dilutive, and may cause the market price for a share of our common stock to decline.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

As of December 31, 2021, we lease approximately 44,000 square feet of combined laboratory and office space in Pittsburgh, Pennsylvania that we use for our research, development and manufacturing efforts. This lease expires in October 2031.

On December 26, 2019, we entered into a lease agreement for our second commercial gene therapy facility ("ASTRA") in the Pittsburgh, Pennsylvania area, which contained an option to purchase the building. On January 29, 2021, we entered into a Purchase and Sale Agreement with Northfield I, LLC, an Ohio limited liability company to acquire ASTRA, and the related purchase closed on March 5, 2021. On June 30, 2021, we entered into a Standard Form of Contract for Construction and the corresponding General Conditions of the Contract for Construction with The Whiting-Turner Contracting Company (“Whiting-Turner”), pursuant to which Whiting-Turner is constructing and managing the construction of ASTRA. The facility is under construction and expected to be completed and validated in 2022. Refer to Note 6 of the Notes to the Consolidated Financial Statements included in Part II of Item 8 of this Annual Report on Form 10-K for more information regarding this transaction.

Item 3. Legal Proceedings.

The information set forth in Note 6 of the Notes to the Consolidated Financial Statements included in Part II Item 8 of this Annual Report on Form 10-K is incorporated by reference into this Item 3.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Market Information

Our common stock has been listed on the Nasdaq Capital Market under the symbol "KRYS" since September 20, 2017. Prior to that, there was no public market for our common stock.

On February 18, 2022, there were four stockholders of record of our common stock. We are unable to estimate the total number of stockholders represented by these record holders, as many of our shares are held by brokers and other institutions on behalf of our stockholders. The closing price of our common stock was $60.86 per share as of February 18, 2022 as reported on the Nasdaq Capital Market.

Dividend Policy

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

Purchases of Equity Securities by the Issuer or Affiliated Purchasers

There were no repurchases of shares of common stock made during the year ended December 31, 2021.

Sales of Unregistered Securities

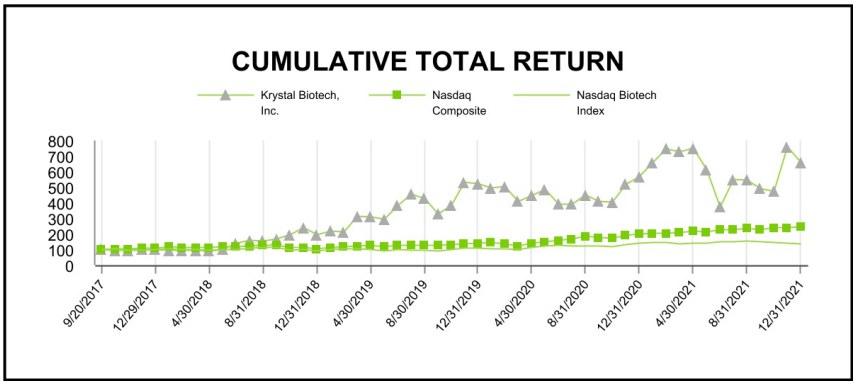
There were no sales of unregistered securities by us during the fourth quarter of 2021. In addition, we did not repurchase any of our equity securities during 2021.

Stock Performance Graph

Set forth below is a graph comparing the cumulative total return on an indexed basis of a $100 investment in the Company's common stock, the Nasdaq Composite Index and the Nasdaq Biotechnology Index commencing on September 20, 2017 (the date our common stock began trading on The Nasdaq Stock Market) and continuing through December 31, 2021. The graph assumes our closing sale price on September 20, 2017 of $10.64 per share as the initial value of our common stock for indexing purposes. Points on the graph represent the performance as of the last business day of each of the months indicated.

The comparisons shown in the graph below are based upon historical data. We caution that the stock price performance shown in the graph below is not necessarily indicative of, nor is it intended to forecast, the potential future performance of our common stock.

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



Item 6. [Reserved]

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

The following information should be read in conjunction with the consolidated financial statements and related notes thereto included in this Annual Report on Form 10-K. In addition to historical information, this report contains forward-looking statements that involve risks and uncertainties which may cause our actual results to differ materially from plans and results discussed in forward-looking statements. We encourage you to review the risks and uncertainties discussed in the sections entitled Item 1A. "Risk Factors" and "Forward-Looking Statements" included at the beginning of this Annual Report on Form 10-K. The risks and uncertainties can cause actual results to differ significantly from those forecast in forward-looking statements or implied in historical results and trends. We caution readers not to place undue reliance on any forward-looking statements made by us, which speak only as of the date they are made. We disclaim any obligation, except as specifically required by law and the rules of the SEC, to publicly update or revise any such statements to reflect any change in our expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements.

This section of this Form 10-K generally discusses 2021 and 2020 items and year-to-year comparisons between 2021 and 2020 of the Company. Discussions of 2019 items and year-to-year comparisons between 2020 and 2019 that are not included in this Form 10-K can be found in "Management's Discussion and Analysis of Financial Condition and Results of Operations" in Part II, Item 7 of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2020.

Overview

We are a clinical stage biotechnology company leading the field of redosable gene delivery. Using our patented platform that is based on engineered HSV-1, we create vectors that efficiently deliver therapeutic transgenes to cells of interest in multiple organ systems. The cell's own machinery then transcribes and translates the encoded effector to treat or prevent disease. We formulate our vectors for non-invasive or minimally invasive routes of administration at a doctor's office or potentially in the patient's home by a healthcare professional. Our goal is to develop easy-to-use medicines to dramatically improve the lives of patients living with rare diseases and chronic conditions. Our innovative technology platform is supported by in-house, commercial scale cGMP manufacturing capabilities. Refer to *Part I, Item 1 - Business* for more information about our clinical development pipeline and research programs and the status of our product candidates.

Pipeline Highlights:

- Vyjuvek is a topical gel containing our novel vector designed to deliver two copies of the *COL7A1* transgene for the treatment of dystrophic epidermolysis bullosa ("dystrophic EB"), a serious rare skin disease caused by missing or mutated type VII collagen protein ("COL7"). Our randomized, double-blind, placebo-controlled GEM-3 pivotal study was designed to evaluate topical Vyjuvek as compared to placebo in dystrophic EB patients. On November 29, 2021, we announced positive topline results from the GEM-3 study. Details of the pivotal study can be found at www.clinicaltrials.gov under NCT identifier NCT04491604. We expect to file a BLA with the FDA in 1H22, and an MAA with the EMA in 2H22. During 2Q21, we began enrolling patients into an open label extension ("OLE") study, including patients who participated in the Phase 3 study, as well as new participants who meet all enrollment criteria. Details of the OLE study can be found at www.clinicaltrials.gov under NCT identifier NCT04917874. Nothing included on this website shall be deemed incorporated by reference into this Annual Report on Form 10-K.
- KB105 is a topical gel containing our novel vector designed to deliver two copies of the *TGM1* transgene for the treatment of TGM1-deficient autosomal recessive congenital ichthyosis ("TGM1-ARCI"), a serious rare skin disorder caused by missing or mutated TGM1 protein. A randomized, placebo-controlled Phase 1/2 study is ongoing. On July 1, 2021, we announced data from the fourth patient dosed in the trial, showing repeat topical KB105 dosing continued to be well tolerated with no adverse events or evidence of immune response. Details of the Phase 1/2 study can be found at www.clinicaltrials.gov under NCT identifier NCT04047732. Nothing included on this website shall be deemed incorporated by reference into this Annual Report on Form 10-K.
- KB407 is an inhaled (nebulized) formulation of our novel vector designed to deliver two copies of the full-length *CFTR* transgene for the treatment of cystic fibrosis, a serious rare lung disease caused by missing or mutated cystic fibrosis transmembrane conductance regulator ("CFTR") protein. On September 29, 2021, we announced that the Bellberry Human Research Ethics Committee in Australia granted approval to conduct a Phase 1 clinical study of inhaled KB407 in patients with cystic fibrosis, and trial initiation is anticipated in 1H22. More detailed data from the Good Laboratory Practice "GLP" toxicology and biodistribution study was presented at the virtual 2021 North American Cystic Fibrosis Conference that took place November 2-5, 2021. We plan to submit an IND and initiate a Phase 1 trial in the U.S. in 2H22.

- KB104 is a topical gel formulation of our novel vector designed to deliver two copies of the *SPINK5* transgene for the treatment of Netherton Syndrome, a debilitating autosomal recessive skin disorder caused by missing or mutated SPINK5 protein. We expect to initiate a Phase 1 clinical study in 2022.
- KB408 is an inhaled (nebulized) formulation of our novel vector designed to deliver two copies of the *SERPINA1* transgene, that encodes for normal human alpha-1 antitrypsin protein, for the treatment of alpha-1 antitrypsin deficiency. We presented preclinical pharmacology data for KB408 at the European Society of Gene & Cell Therapy Virtual Congress that was held October 19-22, 2021.

We have several other product candidates in various stages of preclinical development.

We are also leveraging the ability of our platform to deliver proteins of interest to cells in the skin in the context of aesthetic medicine via our wholly-owned subsidiary Jeune Aesthetics, Inc ("Jeune"). A Summary description of Jeune's key product candidate and its status is as follows:

- KB301 is a solution formulation of our novel vector for intradermal injection designed to deliver two copies of the *COL3A1* transgene to address signs of aging or damaged skin caused by declining levels of, or damaged proteins within the extracellular matrix, including type III collagen. A Phase 1 study is currently ongoing. We anticipate announcing top line data from the efficacy cohort in 1Q 2022. Details of the Phase 1 study can be found at www.clinicaltrials.gov under NCT identifier NCT04540900. Nothing included on this website shall be deemed incorporated by reference into this Annual Report on Form 10-K.

Jeune has several other aesthetic medicine product candidates in various stages of preclinical development.

Business Highlights:

- On January 29, 2021, the Company entered into a Purchase and Sale Agreement for ASTRA with Northfield related to the purchase option exercised by the Company on October 15, 2020 for a purchase price of $9.4 million. The transaction closed on March 5, 2021.
- On February 1, 2021, the Company completed a public offering of 2,211,538 shares of its common stock, at $65.00 per share. Net proceeds to the Company from the offering were $134.9 million after deducting underwriting discounts.
- On March 24, 2021, the Company announced the appointment of Dr. Bhushan Hardas, M.D., MBA as President of Jeune.
- On May 3, 2021, the Company announced the appointment of Andy Orth to the position of Chief Commercial Officer of Krystal Biotech.
- On June 30, 2021, the Company entered into a Standard Form of Contract for Construction and the corresponding General Conditions of the Contract for Construction with Whiting-Turner, pursuant to which Whiting-Turner is constructing and managing the construction of ASTRA located in the Pittsburgh, Pennsylvania area. The ASTRA facility is under construction and expected to be completed and validated in 2022.
- On September 15, 2021, we announced the appointment of Laurent Goux as the General Manager of Europe.
- On October 12, 2021, we announced a collaboration with GeneDx, Inc., a wholly-owned subsidiary of BioReference Laboratories, Inc., an OPKO Health company, to offer no-charge genetic testing for all types of Epidermolysis Bullosa (EB). The goal of the program, called Krystal Decode DEB™, is to help patients with the dystrophic form of this genetic condition, also known as dystrophic EB, get a definitive diagnosis sooner, with highly accurate results obtained with a blood or cheek swab sample.
- On December 3, 2021, the Company completed a public offering of 2,866,667 shares of its common stock, which includes 200,000 shares purchased by the underwriters, at $75.00 per share. Net proceeds to the Company from the offering were $201.9 million after deducting underwriting discounts and commissions and other offering expenses payable by the Company.
- On January 18, 2022, we announced that Jing Marantz, MD, PhD, MBA had resigned from the Board of Directors to accept the position as Chief Business Officer with the Company and E. Rand Sutherland was appointed as a member of the Board of Directors to fill the vacancy.

COVID-19

The COVID-19 pandemic has prompted governments and businesses to take unprecedented measures, such as restrictions on travel and business operations, temporary closures of businesses, and quarantines. In an effort to slow the spread of the virus, The Commonwealth of Pennsylvania where the Company's primary offices, laboratory and manufacturing spaces are located, enacted stay-at-home orders, and sweeping restrictions to travel were initiated by corporations and governments. Although these restrictions have been lifted, it is not known at this time whether they will be reestablished or the extent to which the Company will be impacted. The degree of the pandemic's effect on the Company's clinical, operational and financial performance will depend on future developments, including additional protective measures that may be implemented by governmental authorities or the Company to protect its employees, or by investigators, caregivers or patients to minimize exposure, all of which are uncertain and difficult to predict. To date the impact of the pandemic on our business and clinical trials in the U.S. has been minimal and the increased vaccination rates in the U.S. are encouraging. We will continue to assess the potential impact of the pandemic on our business and operations, including our supply chain and preclinical and clinical trial activities. Outside of the U.S., we have experienced pandemic-related delays in clinical trial initiation in Australia, and we will continue to closely monitor this rapidly evolving situation. For additional information regarding the impact of the coronavirus pandemic, please see "Risk Factor - Business interruptions resulting from the pandemic or similar public health crises could cause a disruption of the development efforts of our product candidates and adversely impact our business."

Financial Overview

Revenue

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

Research and Development Expenses

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

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

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

We expect our research and development expenses will increase as we continue the manufacturing of preclinical and clinical materials and manage the clinical trials of, and seek regulatory approval for, our product candidates and expand our product portfolio. In the near term, we expect that our research and development expenses will increase as we continue our OLE study for Vyjuvek, our Phase 1/2 clinical trial for KB105, our Phase 1 safety and efficacy study for KB301, and incur preclinical expenses for our other product candidates. Due to the numerous risks and uncertainties associated with product development, we cannot determine with certainty the duration, costs and timing of clinical trials, and, as a result, the actual costs to complete clinical trials may exceed the expected costs.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in our executive, commercial, business development and other administrative functions. General and administrative expenses also include legal fees relating to intellectual property and corporate matters, professional fees for accounting, auditing, tax and consulting services, insurance costs, travel, facility related expenses and other operating costs.

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

ASTRA Capital Expenditures

On March 5, 2021, we closed on the purchase of the building that was constructed to house our second cGMP facility, ASTRA. We are currently in the process of constructing the interior build-out of this facility and we have entered into a contract with Whiting-Turner who will manage the construction of ASTRA. Further, we have entered into various non-cancellable purchase agreements for long-lead materials to help avoid potential schedule disruptions or material shortages. These contracts typically call for the payment of fees for services or materials upon the achievement of certain milestones. We expect to continue to incur significant capital expenditures related to ASTRA as we construct and validate this facility, which is expected to be completed in 2022.

Interest Income

Interest income consists primarily of income earned from our cash, cash equivalents and investments.

Interest Expense

Interest expense consists primarily of non-cash interest expense recognized to accrete the build to suit financial obligation to a balance that equaled the cash consideration that was paid upon the close of the purchase of ASTRA.

Critical Accounting Policies and Significant Judgments and Estimates

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

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

Accrued Research and Development Expenses

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

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

Stock-Based Compensation

We have applied the fair value recognition provisions of Financial Accounting Standards Board Accounting Standards Codification, or ASC, Topic 718, *Compensation—Stock Compensation* ("ASC 718"), to account for stock-based compensation. We recognize compensation costs related to stock options granted based on the estimated fair value of the awards on the date of grant. Described below is the methodology we have utilized in measuring stock-based compensation expense.

ASC 718 requires all stock-based payments, including grants of stock options and restricted stock, to be recognized in the statements of operations based on their grant-date fair values. Compensation expense is recognized on a straight-line basis based on the grant-date fair value over the associated service period of the award, which is generally the vesting term.

Determining the amount of stock-based compensation to be recorded requires us to develop estimates of the fair value of stock-based awards as of their measurement date. We recognize stock-based compensation expense over the requisite service period, which is the vesting period of the award. Calculating the fair value of stock-based awards requires that we make highly subjective assumptions. We use the Black-Scholes option pricing model to value our stock option awards. Use of this valuation methodology requires that we make assumptions as to the volatility of our common stock, the risk-free interest rate for a period that approximates the expected term of our stock options and our expected dividend yield. Once the Company's own sufficient historical volatility data was obtained, the Company eliminated the use of a representative peer group and as of Q4 2021 the Company uses only its own historical volatility data in its estimate of expected volatility given that there is now sufficient amount of historical information regarding the volatility of its own stock price. We use the simplified method to calculate the expected term as prescribed by the SEC Staff Accounting Bulletin No. 107, *Share-Based Payment* as we do not have sufficient historical stock option activity data to provide a reasonable basis upon which to estimate the expected term of stock options granted to employees. We utilize a dividend yield of zero based on the fact that we have never paid cash dividends and have no current intention of paying cash dividends. The risk-free interest rate used for each grant is based on the U.S. Treasury yield curve in effect at the time of grant for instruments with a similar expected life.

Leases

We account for our lease agreements in accordance with FASB ASC Topic 842, *Leases* ("ASC 842"). As the Company's lease agreements do not provide an implicit rate and as the Company does not have external borrowings, we use an estimated incremental borrowing rate based on the information available at lease commencement in determining the present value of lease payments. The incremental borrowing rate is the rate of interest that the Company would expect to borrow on a collateralized and fully amortizing basis over a similar term an amount equal to the lease payments in a similar economic environment.

For lease arrangements where it has been determined that the Company has control over an asset that is under construction and is thus considered the accounting owner of the asset during the construction period, the Company records a construction-in-progress asset ("CIP") and corresponding financial obligation on the consolidated balance sheet. Once the construction is complete, an assessment will be performed to determine whether the lease meets certain "sale-leaseback" criteria. If the sale-leaseback criteria are determined to be met, the Company will remove the asset and related financial obligation from the balance sheet and treat the building lease as either an operating or finance lease based on our assessment of the guidance. If, upon completion of construction, the project does not meet the "sale-leaseback" criteria, the lease will be treated as a financing obligation and the Company will depreciate the asset over its estimated useful life for financial reporting purposes.

Results of Operations

Years Ended December 31, 2021, 2020 and 2019

(in thousands)	Years Ended December 31, 2021	2020	2019	Change 2021 vs. 2020	2020 vs. 2019
Expenses					
Research and development	$ 27,884	$ 17,936	$ 15,616	$ 9,948	$ 2,320
General and administrative	40,391	15,063	6,465	25,328	8,598
Total operating expenses	68,275	32,999	22,081	35,276	10,918
Loss from operations	(68,275)	(32,999)	(22,081)	(35,276)	(10,918)
Other Expense					
Interest and other income, net	197	832	2,993	(635)	(2,161)
Interest expense	(1,492)	—	—	(1,492)	—
Total interest and other income, net	(1,295)	832	2,993	(2,127)	(2,161)
Net loss	$ (69,570)	$ (32,167)	$ (19,088)	$ (37,403)	$ (13,079)

Research and Development Expenses

Research and development expenses increased $9.9 million for the year ended December 31, 2021 compared to the year ended December 31, 2020. Higher research and development expenses were due to increases in preclinical, clinical and pre-commercial manufacturing activities of $3.3 million, payroll related expenses of approximately $3.1 million which is primarily driven by an increase in personnel to support overall growth and includes a $2.4 million increase in stock-based compensation, an increase in outsourced research and development activities of $2.0 million, travel related expenses associated with our clinical trial sites of $187 thousand, and other research and development expenses of $1.3 million, primarily due to depreciation and rent.

Research and development expenses increased $2.3 million for the year ended December 31, 2020 compared to the year ended December 31, 2019. Higher research and development expenses were due to increases in lab supplies of $142 thousand, payroll related expenses of approximately $2.0 million which is primarily driven by an increase in personnel to support overall growth and includes a $417 thousand increase in stock-based compensation, and other research and development expenses of $757 thousand, with a decrease in outsourcing research and development activities of $560 thousand.

General and Administrative Expenses

General and administrative expenses increased $25.3 million for the year ended December 31, 2021 compared to the year ended December 31, 2020. Higher general and administrative spending was due largely to increased payroll related expenses of approximately $14.7 million which is primarily driven by an increase in personnel to support overall growth and includes an approximate $9.6 million increase in stock-based compensation, commercial preparedness expenses of approximately $3.8 million, legal and professional fees of approximately $3.7 million which is net of $2.1 million of insurance proceeds, software related costs of $1.0 million, medical affairs costs of $508 thousand, insurance costs of $427 thousand and other administrative expenses of 1.2 million.

General and administrative expenses increased $8.6 million for the year ended December 31, 2020 compared to the year ended December 31, 2019. Higher general and administrative spending was due largely to increased payroll related expenses of approximately $4.0 million which is primarily driven by an increase in headcount to support overall growth and includes an approximate $1.6 million increase in stock-based compensation, market research related expenses of approximately $2.0 million, legal and professional fees of approximately $1.6 million, insurance expense of $693 thousand and other administrative expenses of $295 thousand.

Other Income (Expense)

Interest and other income for the year ended December 31, 2021 and 2020 was $197 thousand and $832 thousand, respectively, and consisted of interest and dividend income earned from our cash, cash equivalents and investments. This decrease was driven by a decline in market interest rates.

Interest expense for the year ended December 31, 2021 and 2020 was $1.5 million and zero, respectively, and related to accretion of the financial obligation for the build to suit lease liability during the year ended December 31, 2021 to a balance that equaled the purchase consideration for ASTRA.

Interest and other income for the year ended December 31, 2020 and 2019 was $832 thousand and $3.0 million, respectively, and consisted of interest and dividend income earned from our cash, cash equivalents and investments. This decrease was driven by a decline in market rates.

Liquidity and Capital Resources

Overview

At December 31, 2021, our cash, cash equivalents and short-term investments balance was approximately $438.1 million. Since operations began, we have incurred operating losses. Our net losses were $69.6 million and $32.2 million for the years ended December 31, 2021 and 2020, respectively. At December 31, 2021, we had an accumulated deficit of $140.8 million. With the net proceeds raised from its public and private securities offerings, including the public offerings of its common stock completed in February and December of 2021, the Company believes that its cash, cash equivalents and short-term investments will be sufficient to allow us to fund our operations for at least 12 months from the filing date of this Form 10-K.

As the Company continues to incur losses, a transition to profitability is dependent upon the successful development, approval and commercialization of our product candidates and the achievement of a level of revenues adequate to support the Company's cost structure. The Company may never achieve profitability, and unless and until it does, the Company will continue to need to raise additional capital.

Costs related to clinical trials can be unpredictable and therefore there can be no guarantee that we will have sufficient capital to fund our continued clinical studies of Vyjuvek, KB105, KB301 or our planned preclinical studies for our other product candidates, or our operations. Further, we do not expect to generate any product revenues until 2022, at the earliest, assuming we receive marketing approval for Vyjuvek on the schedule we currently contemplate. While we are in the process of building out our internal vector manufacturing capacity, some of our manufacturing activities will be contracted out to third parties. Additionally, we currently utilize third-party contract research organizations to carry out our clinical development activities. As we seek to obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses as we prepare for product sales, marketing, manufacturing, and distribution. Our funds may not be sufficient to enable us to conduct pivotal clinical trials for, seek marketing approval for or commercially launch Vyjuvek, KB105, KB301 or any other product candidate. Accordingly, to obtain marketing approval for and to commercialize this or any other product candidates, we may be required to obtain further funding through public or private equity offerings, debt financings, collaboration and licensing arrangements or other sources. Adequate additional financing may not be available to us on acceptable terms, if at all. Our failure to raise capital when needed could have a negative effect on our financial condition and our ability to pursue our business strategy.

Operating Capital Requirements

Our primary uses of capital are, and we expect will continue to be for the near future, compensation and related expenses, manufacturing costs for preclinical and clinical materials, third party clinical trial research and development services, laboratory and related supplies, clinical costs, legal and other regulatory expenses and general overhead costs. In order to complete the process of obtaining regulatory approval for any of our product candidates and to build the sales, manufacturing, marketing and distribution infrastructure that we believe will be necessary to commercialize our product candidates, if approved, we may require substantial additional funding.

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

- the timeline and costs of our OLE study for Vyjuvek;
- the progress, timing and costs of our ongoing Phase 1/2 clinical trials for KB105;
- the progress, results and costs of our Phase 1 clinical trials for KB301;
- the progress, timing, and costs of manufacturing of Vyjuvek;
- the continued development and the filing on an IND application for future product candidates;
- the initiation, scope, progress, timing, costs and results of drug discovery, laboratory testing, manufacturing, preclinical studies and clinical trials for any other product candidates that we may pursue in the future, if any;
- the costs of maintaining our own commercial-scale cGMP manufacturing facilities;

- the outcome, timing and costs of seeking regulatory approvals;
- 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 our current and future product candidates;
- 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;
- the costs of commercialization activities for our current and future product candidates if we receive marketing approval for such product candidates we may develop, including the costs and timing of establishing product sales, medical affairs, marketing, distribution and manufacturing capabilities;
- subject to receipt of marketing approval, if any, revenue received from commercial sale of our current and future product candidates;
- the terms and timing of any future collaborations, licensing, consulting or other arrangements that we may establish;
- the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, maintenance, defense and enforcement of any patents or other intellectual property rights, including milestone and royalty payments and patent prosecution fees that we are obligated to pay pursuant to our license agreements;
- 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.

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

Contractual Obligations

Operating Leases

Operating lease payments represent the Company's commitments for future minimum rent made under non-cancelable leases for our corporate headquarters in Pittsburgh, PA, office location in Boston, Massachusetts, and for the ground lease associated with our second cGMP manufacturing facility, ASTRA. The total future payments for our operating lease obligations at December 31, 2021 are $18.2 million, of which $1.4 million is due in the next twelve months and the remaining payments are due over the terms of the respective leases. For additional details regarding our leases, see Note 6 to our consolidated financial statements included in this Annual Report on Form 10-K.

Clinical Supply and Product Manufacturing Agreements

The Company enters into various agreements in the normal course of business with Contract Research Organizations ("CROs"), Contract Manufacturing Organizations ("CMOs") and other third parties for preclinical research studies, clinical trials and testing and manufacturing services. The Company is obligated to make milestone payments under certain of these agreements. The estimated remaining commitment as of December 31, 2021 under these agreements is approximately $3.0 million, all of which is expected to be due in the next twelve months.

Commercial Preparedness Agreements

The Company has contracted with various third parties to facilitate, coordinate and perform agreed upon commercial preparedness and market research activities relating to our lead product candidate, Vyjuvek. These contracts typically call for the payment of fees for services upon the achievement of certain milestones. The estimated remaining commitment as of December 31, 2021 is $2.4 million, all of which is expected to be due in the next twelve months.

ASTRA Contractual Obligations

The Company has contracted with various third parties to construct our second cGMP facility, ASTRA. Additionally, we have entered into various non-cancellable purchase agreements for long-lead materials to help avoid potential schedule disruptions or material shortages. These contracts typically call for the payment of fees for services or materials upon the achievement of certain milestones. The estimated remaining commitment as of December 31, 2021 is $24.7 million, all of which is expected to be due in the next twelve months.

Cash Flows

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

	Years Ended December 31,	
	2021	2020
Net cash used in operating activities	$ (47,938)	$ (26,083)
Net cash used in investing activities	(226,770)	(11,181)
Net cash provided by financing activities	347,685	118,019
Net increase in cash	$ 72,977	$ 80,755

Operating Activities

Net cash used in operating activities for the year December 31, 2021 was $47.9 million and consisted primarily of a net loss of $69.6 million adjusted for non-cash items of $18.1 million made up of depreciation and amortization of $2.8 million and stock-based compensation expense of $15.3 million, build to suit interest expense of $1.5 million, and cash used by decreases in net operating liabilities of approximately $2.1 million.

Net cash used in operating activities for the year ended December 31, 2020 was $26.1 million and consisted primarily of a net loss of $32.2 million adjusted for non-cash items of $5.2 million primarily made up of depreciation and amortization of $1.9 million and stock-based compensation expense of $3.3 million, and cash used by decreases in net operating liabilities of approximately $928 thousand.

Investing Activities

Net cash used in investing activities for the year ended December 31, 2021 was approximately $226.8 million and consisted primarily of purchases of $190.5 million of available-for-sale investment securities, and expenditures of $68.3 million on the build-out of our ASTRA facility, leasehold improvement of new office space, and purchases of computer and laboratory equipment, partially offset by proceeds of $32.0 million from maturities of investments.

Net cash used in investing activities for the year ended December 31, 2020 was $11.2 million and consisted primarily of purchases of $3.2 million of short-term available-for-sale investment securities, and expenditures of $14.8 million on the build-out of our ASTRA facility, leasehold improvement of new office space, and purchases of computer and laboratory equipment, partially offset by proceeds of $6.9 million from maturities of short-term investments.

Financing Activities

Net cash provided by financing activities for the year ended December 31, 2021 was $347.7 million and was primarily from proceeds from follow-on public offerings of 2,211,538 shares of its common stock, including 288,461 shares purchased by the underwriters, at $65.00 per share and 2,866,667 shares of its common stock, including 200,000 shares purchased by the underwriters, at $75.00 per share. Net proceeds to the Company from the offerings were $336.8 million after deducting underwriting discounts and commissions of approximately $21.5 million, and other offering expenses payable by the Company of $425 thousand.

Net cash provided by financing activities for the year ended December 31, 2020 was $118.0 million and was primarily from proceeds from our public offering on May 21, 2020 of 2,275,000 shares of our common stock to the public at $55 per

share. Net proceeds to the Company from the offering were $117.2 million after deducting underwriting and commissions of approximately $7.5 million and other offering expenses of approximately $463 thousand.

Off-Balance Sheet Arrangements

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

Recent Accounting Pronouncements

In October 2020, the FASB issued ASU 2020-08, *Codification Improvements to Subtopic 310-20, Receivables - Nonrefundable Fees and Other Costs* ("ASU 2020-08") to provide further clarification and update the previously issued guidance in ASU 2017-08, *Receivables - Nonrefundable Fees and Other Costs (Subtopic 310-20: Premium Amortization on Purchased Callable Debt Securities)* ("ASU 2017-08"). ASU 2017-08 shortened the amortization period for certain callable debt securities purchased at a premium by requiring that the premium be amortized to the earliest call date. ASU 2020-08 requires that at each reporting period, to the extent that the amortized cost of an individual callable debt security exceeds the amount repayable by the issuer at the next call date, the excess premium shall be amortized to the next call date. The new standard was effective beginning January 1, 2021 and should be applied on a prospective basis as of the beginning of the period of adoption for existing or newly purchased callable debt securities. The adoption of ASU 2020-08 did not have a material impact on the Company's financial position or results of operations upon adoption.

Item 7A. Qualitative and Quantitative Disclosures About Market Risk

We had cash, cash equivalents and short-term investments of approximately $438.1 million as of December 31, 2021, which consist primarily of money market funds, certificates of deposit, commercial paper, corporate bonds, and government agency securities. The investments in these financial instruments are made in accordance with an investment policy which specifies the categories, allocations and ratings of securities we may consider for investment. The primary objective of our investment activities is to preserve principal while at the same time maximizing the income we receive without significantly increasing risk. Some of the financial instruments in which we invest could be subject to market risk. This means that a change in prevailing interest rates may cause the value of the instruments to fluctuate. For example, if we purchase a security that was issued with a fixed interest rate and the prevailing interest rate later rises, the value of that security will probably decline. To minimize this risk, we intend to maintain a portfolio which may include cash, cash equivalents and short-term investment securities available-for-sale in a variety of securities which may include money market funds, government and non-government debt securities and commercial paper, all with various maturity dates. Based on our current investment portfolio, we do not believe that our results of operations or our financial position would be materially affected by an immediate change of 10% in interest rates.

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

Item 8. Financial Statements and Supplementary Data.

INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

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

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Krystal Biotech, Inc. (the "Company") as of December 31, 2021 and 2020, and the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the years in the two-year period ended December 31, 2021, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2021 and 2020, and the results of their operations and their cash flows for each of the two years in the period ended December 31, 2021, in conformity with accounting principles generally accepted in the United States of America.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the Company's internal control over financial reporting as of December 31, 2021, based on criteria established in the 2013 Internal Control - Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) and our report dated February 28, 2022 expressed an unqualified opinion on the Company's internal control over financial reporting.

Basis for Opinion

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

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matters

Critical audit matters are matters arising from the current period audit of the financial statements that were communicated or required to be communicated to the audit committee and that (1) relate to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. We determined that there were no critical audit matters.

/s/ Mayer Hoffman McCann P.C.

We have served as the Company's auditor since 2017.
San Diego, California
February 28, 2022

Krystal Biotech, Inc.
Consolidated Balance Sheets

(In thousands, except shares and per share data)	December 31, 2021	December 31, 2020
Assets		
Current assets		
Cash and cash equivalents	$ 341,246	$ 268,269
Short-term investments	96,850	2,993
Prepaid expenses and other current assets	4,171	3,796
Total current assets	442,267	275,058
Property and equipment, net	112,355	30,876
Long-term investments	64,371	—
Right-of-use assets	7,228	3,298
Other non-current assets	74	1,612
Total assets	$ 626,295	$ 310,844
Liabilities and Stockholders' Equity		
Current liabilities		
Accounts payable	$ 8,398	$ 2,105
Current portion of lease liability	1,041	638
Accrued expenses and other current liabilities	16,297	5,109
Build-to-suit lease liability	—	7,600
Total current liabilities	25,736	15,452
Lease liability	6,983	3,308
Total liabilities	32,719	18,760
Commitments and contingencies (Note 6)		
Stockholders' equity		
Preferred stock; $0.00001 par value; 20,000,000 shares authorized at December 31, 2021 and 2020; 2,061,773 shares issued, and no shares outstanding at December 31, 2021 and 2020	—	—
Common stock; $0.00001 par value; 80,000,000 shares authorized at December 31, 2021 and 2020; 25,207,985 and 19,714,220 shares issued and outstanding at December 31, 2021 and 2020, respectively	—	—
Additional paid-in capital	734,523	363,292
Accumulated other comprehensive income	(163)	6
Accumulated deficit	(140,784)	(71,214)
Total stockholders' equity	593,576	292,084
Total liabilities and stockholders' equity	$ 626,295	$ 310,844

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

Krystal Biotech, Inc.
Consolidated Statements of Operations and Comprehensive Loss

(In thousands, except share and per share data)	Year Ended December 31, 2021	2020
Expenses		
Research and development	$ 27,884	$ 17,936
General and administrative	40,391	15,063
Total operating expenses	68,275	32,999
Loss from operations	(68,275)	(32,999)
Other Income (Expense)		
Interest and other income, net	197	832
Interest expense	(1,492)	—
Net loss	(69,570)	(32,167)
Unrealized loss on available-for-sale securities and other	(169)	(4)
Comprehensive loss	$ (69,739)	$ (32,171)
Net loss per common share: Basic and diluted	$ (3.13)	$ (1.71)
Weighted-average common shares outstanding: Basic and diluted	22,196,846	18,787,161

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

Krystal Biotech, Inc.
Consolidated Statements of Stockholders' Equity

(In thousands, except shares)	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balances at January 1, 2019	17,354,310	$ —	$ 241,951	$ 10	$ (39,047)	$ 202,914
Issuance of common stock, net	2,359,910	—	118,035	—	—	118,035
Stock-based compensation expense	—	—	3,306	—	—	3,306
Unrealized loss on investments and other	—	—	—	(4)	—	(4)
Net loss	—	—	—	—	(32,167)	(32,167)
Balances at December 31, 2020	19,714,220	$ —	$ 363,292	$ 6	$ (71,214)	$ 292,084
Issuance of common stock, net	5,493,765	—	355,628	—	—	355,628
Stock-based compensation expense	—	—	15,603	—	—	15,603
Unrealized loss on investments and other	—	—	—	(169)	—	(169)
Net loss	—	—	—	—	(69,570)	(69,570)
Balances at December 31, 2021	25,207,985	$ —	$ 734,523	$ (163)	$ (140,784)	$ 593,576

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

Krystal Biotech, Inc.
Consolidated Statements of Cash Flows

(In thousands)	Year Ended December 31, 2021	2020
Operating Activities		
Net loss	$ (69,570)	$ (32,167)
Adjustments to reconcile net loss to net cash used in operating activities		
Depreciation and amortization	2,769	1,851
Stock-based compensation expense	15,319	3,272
Loss on disposal of fixed assets	—	33
Non-cash interest expense	1,492	—
Changes in operating assets and liabilities		
Prepaid expenses and other current assets	(1,145)	(1,911)
Other non-current assets	65	(934)
Lease liability	(285)	685
Accounts payable	712	783
Accrued expenses and other current liabilities	2,705	2,305
Net cash used in operating activities	(47,938)	(26,083)
Investing Activities		
Purchases of property and equipment	(68,336)	(14,843)
Purchases of investments	(190,462)	(3,205)
Proceeds from maturities of investments	32,028	6,867
Net cash used in investing activities	(226,770)	(11,181)
Financing Activities		
Proceeds from issuance of common stock, net	355,645	118,019
Repayment of ASTRA build to suit liability	(7,960)	—
Net cash provided by financing activities	347,685	118,019
Net increase in cash and cash equivalents	72,977	80,755
Cash and cash equivalents at beginning of year	268,269	187,514
Cash and cash equivalents at end of year	$ 341,246	$ 268,269
Supplemental Disclosures of Non-Cash Investing and Financing Activities		
Unpaid purchases of property and equipment	$ 15,363	$ 9,697
Initial recognition of right-of-use assets	$ 4,396	$ 911
Unpaid offering costs	$ —	$ 131

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

1. Organization

Krystal Biotech, Inc. (the “Company,” or “we” or other similar pronouns) commenced operations on April 15, 2016. On March 31, 2017, the Company converted from a California limited liability company to a Delaware C-corporation, and changed its name from Krystal Biotech LLC to Krystal Biotech, Inc. On June 19, 2018, the Company incorporated Krystal Australia Pty Ltd., an Australian proprietary limited company, for the purpose of undertaking preclinical and clinical studies in Australia. On April 24, 2019, the Company incorporated Jeune Aesthetics, Inc, formerly known as Jeune, Inc., in Delaware, a wholly-owned subsidiary, for the purpose of undertaking preclinical and clinical studies for aesthetic skin conditions.

We are a clinical stage biotechnology company leading the field of redosable gene delivery. Using our patented platform that is based on engineered herpes simplex virus type 1 ("HSV-1"), we create vectors that efficiently deliver therapeutic transgenes to cells of interest in multiple organ systems. The cell’s own machinery then transcribes and translates the encoded effector to treat or prevent disease. We formulate our vectors for non-invasive or minimally invasive routes of administration at a doctor’s office or potentially in the patient’s home. Our goal is to develop easy to use medicines to dramatically improve the lives of patients living with rare diseases and chronic conditions. Our innovative technology platform is supported by in-house, commercial scale current good manufacturing practices ("cGMP") manufacturing capabilities.

Liquidity

As of December 31, 2021, the Company had an accumulated deficit of $140.8 million. With the net proceeds raised from its public, including the public offerings of its common stock completed in February and December of 2021, the Company believes that its cash, cash equivalents and short-term investments of approximately $438.1 million as of December 31, 2021 will be sufficient to allow the Company to fund its planned operations for at least the next 12 months from the date of this Annual Report on Form 10-K. As the Company continues to incur losses, a transition to profitability is dependent upon the successful development, approval and commercialization of its product candidates and the achievement of a level of revenues adequate to support the Company’s cost structure. The Company may never achieve profitability, and unless and until it does the Company will continue to need to raise additional capital or obtain financing from other sources. Management intends to fund future operations through the sale of equity and debt financings and may also seek additional capital through arrangements with strategic partners or other sources. There can be no assurance that additional funding will be available on terms acceptable to the Company, if at all.

The Company is subject to risks common to companies in the biotechnology industry, including but not limited to the failure of product candidates in clinical and preclinical studies, the development of competing product candidates or other technological innovations by competitors, dependence on key personnel, protection of proprietary technology, compliance with government regulations and the ability to commercialize product candidates.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America (“GAAP”) as found in the Accounting Standards Codification (“ASC”), the Accounting Standards Update (“ASU”) of the Financial Accounting Standards Board (“FASB”) and the rules and regulations of the U.S. Securities and Exchange Commission (“SEC”). All intercompany balances and transactions have been eliminated in consolidation. Certain prior period amounts have been reclassified to conform to the current period presentation. The reclassified amounts have no impact on the Company’s previously reported financial position or results of operation.

Risks and Uncertainties

The novel coronavirus ("COVID-19") pandemic has resulted, and is likely to continue to result, in significant national and global economic uncertainty and may adversely affect our business. The Company is continuing to actively monitor the impact of the COVID-19 pandemic and the related effects on its financial condition, liquidity, operations, suppliers, industry, and workforce. However, the full extent, consequences, and duration of the COVID-19 pandemic and the resulting impact on the Company cannot currently be predicted. To date the impact of the pandemic on our business and clinical trials in the U.S. has been minimal and the increased vaccination rates in the U.S. are encouraging. Outside of the U.S., the Company has experienced pandemic-related delays in clinical trial initiation in Australia. The Company will continue to evaluate the impact that these events could have on the operations, including our supply chain and preclinical and clinical trial activities, financial position, and the results of operations and cash flows during fiscal year 2022.

Use of Estimates

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

Segment and Geographical Information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company and the Company’s chief operating decision maker view the Company’s operations and manage its business in one operating segment, which is the business of developing and commercializing pharmaceuticals.

Concentrations of Credit Risk and Off-Balance Sheet Risk

Financial instruments that potentially subject the Company to credit risk consist of cash, cash equivalents and investments. The Company’s policy is to invest its cash, cash equivalents and investments in money market funds, certificates of deposit, corporate bonds, commercial paper, government agency securities and various other bank deposit accounts. The counterparties to the agreements relating to the Company’s investments consist of financial institutions of high credit standing. The Company is exposed to credit risk in the event of default by the financial institutions to the extent amounts recorded on the balance sheets are in excess of insured limits. The Company has not experienced any credit losses in such accounts and does not believe it is exposed to any significant credit risk on these funds. The Company has no financial instruments with off-balance sheet risk of loss.

Cash, Cash Equivalents and Investments

Cash and cash equivalents consist of money market funds and bank deposits. Cash equivalents are defined as short-term, highly liquid investments with original maturities of 90 days or less at the date of purchase.

Investments with maturities of greater than 90 days but less than one year are classified as short-term investments on the consolidated balance sheets and consist of certificates of deposit, commercial paper, corporate bonds, and government agency securities. Investments with maturities of greater than one year are classified as long-term investments on the consolidated balance sheets and consist of corporate bonds and government agency securities. Accrued interest on investments is also classified as short-term investments.

As our entire investment portfolio is considered available for use in current operations, we classify all investments as available-for-sale securities. Available-for-sale securities are carried at fair value, with unrealized gains and losses reported in accumulated other comprehensive loss, which is a separate component of stockholders’ equity in the consolidated balance sheets. Any premium arising at purchase is amortized to the earliest call date and any discount arising at purchase is accreted to maturity. Amortization and accretion of premiums and discounts are recorded in interest and other income, net in the consolidated statement of operations.

Fair Value of Financial Instruments

Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. There is a three-level hierarchy that prioritizes the inputs used in determining fair value by their reliability and preferred use, as follows:

- *Level 1*—Valuations based on quoted prices in active markets for identical assets or liabilities.
- *Level 2*—Valuations based on quoted prices in active markets for similar assets and liabilities, quoted prices for identical or similar assets and liabilities in inactive markets, or other inputs that are observable, or can be corroborated by observable market data.
- *Level 3*—Valuations based on inputs that are both significant to the fair value measurement and unobservable.

To the extent that a valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized within Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

There have been no significant changes to the valuation methods utilized by the Company during the periods presented. There have been no transfers between Level 1, Level 2, and Level 3 in any periods presented.

The carrying amounts of financial instruments consisting of cash and cash equivalents, investments, prepaid expenses and other current assets, accounts payable, accrued expenses and other current liabilities included in the Company's financial statements, are reasonable estimates of fair value, primarily due to their short maturities. Marketable securities are classified as long-term investments if the Company has the ability and intent to hold them and such holding period is longer than one year. The Company classifies all of its investments as available-for-sale.

Our available-for-sale, short-term investments, which consist of certificates of deposit, commercial paper, corporate bonds, and government agency securities are considered to be Level 2 valuations. The fair value of Level 2 financial assets is determined using inputs that are observable in the market or can be derived principally from or corroborated by observable market data such as pricing for similar securities, recently executed transactions, cash flow models with yield curves, and benchmark securities. In addition, Level 2 financial instruments are valued using comparisons to like-kind financial instruments and models that use readily observable market data as their basis.

Property and Equipment, net

Property and equipment, net, is stated at cost, less accumulated depreciation. Maintenance and repairs that do not improve or extend the lives of the respective assets are expensed to operations as incurred, while costs of major additions and betterments are capitalized. Upon disposal, the related cost and accumulated depreciation is removed from the accounts and any resulting gain or loss is included in the results of operations. Depreciation is recorded using the straight-line method over the estimated useful lives of the respective assets, which are as follows:

Computer equipment and software	3 - 5 years
Laboratory and manufacturing equipment	3 - 7 years
Furniture and fixtures	3 - 7 years
Leasehold improvement	lesser of remaining useful life or remaining life of lease

Construction-in-progress ("CIP") is not depreciated until the asset is placed in service.

Impairment of Long-Lived Assets

The Company evaluates long-lived assets for potential impairment when events or changes in circumstances indicate the carrying value of the assets may not be recoverable. An impairment loss would be recognized when estimated future cash flows expected to result from the use of the asset and its eventual disposition are less than the carrying amount of the asset. The Company has not recognized any impairment losses for the years ended December 31, 2021 and 2020.

Leases

The Company accounts for its lease agreements in accordance with FASB ASC Topic 842, Leases. Right-of-use lease assets represent our right to use an underlying asset during the lease term and the lease obligations represent our commitment to make lease payments arising from the lease. Right-of-use lease assets and obligations are recognized based on the present value of remaining lease payments over the lease term. As the Company's lease agreements do not provide an implicit rate and as the Company does not have any external borrowings, we have used an estimated incremental borrowing rate based on the information available at lease commencement in determining the present value of lease payments. Operating lease expense is recognized on a straight-line basis over the lease term. Variable lease expense is recognized in the period in which the obligation for the payment is incurred. In addition, the Company also has made an accounting policy election to exclude leases with an initial term of twelve months or less from its balance sheet and to account for lease and non-lease components of its operating leases as a single component.

For lease arrangements where it has been determined that the Company has control over an asset that is under construction and is thus considered the accounting owner of the asset during the construction period, the Company records a construction in progress asset and corresponding financial obligation on the consolidated balance sheet. Once the construction is complete, an assessment is performed to determine whether the lease meets certain "sale-leaseback" criteria. If the sale-leaseback criteria are determined to be met, the Company will remove the asset and related financial obligation from the condensed consolidated balance sheet and treat the lease as either an operating or finance lease based on our assessment of the guidance. If, upon completion of construction, the project does not meet the "sale-leaseback" criteria, the lease will be treated as a financing obligation and the Company will depreciate the asset over its estimated useful life for financial reporting purposes once the asset has been placed into service.

Research and Development Expenses

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

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

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

Stock-Based Compensation Expense

The Company applies the fair value recognition provisions of Financial Accounting Standards Board Accounting Standards Codification, or ASC, Topic 718, *Compensation—Stock Compensation* ("ASC 718"), to account for stock-based compensation. Compensation costs related to stock options granted is based on the estimated fair value of the awards on the date of grant.

ASC 718 requires all stock-based payments, including grants of stock options and restricted stock, to be recognized in the statements of operations based on their grant-date fair values. Compensation expense is recognized on a straight-line basis based on the grant-date fair value over the associated service period of the award, which is generally the vesting term.

The Company estimates the fair value of its stock options using the Black-Scholes option pricing model, which requires the input of subjective assumptions, including: (i) the expected stock price volatility; (ii) the expected term of the award; (iii) the risk-free interest rate; and (iv) expected dividends. Once the Company's own sufficient historical volatility data was obtained, the Company eliminated the use of a representative peer group and uses only its own historical volatility data in its estimate of expected volatility given that there is now a sufficient amount of historical information regarding the volatility of its own stock price.

The Company estimates the expected term of its stock options using the "simplified" method, whereby the expected term equals the arithmetic mean of the vesting term and the original contractual term of the option. The risk-free interest rates are based on US Treasury securities with a maturity date commensurate with the expected term of the associated award. The

Company has never paid and does not expect to pay dividends in the foreseeable future. The Company accounts for forfeitures as they occur. Stock-based compensation expense recognized in the financial statements is based on awards for which service conditions are expected to be satisfied.

Income Taxes

For the year ended December 31, 2021 and 2020, income taxes were recorded in accordance with FASB ASC Topic 740, Income Taxes ("ASC 740"), which provides for deferred taxes using an asset and liability approach. Under this method, we record deferred tax assets and liabilities for the expected future tax consequences of temporary differences between the financial statement carrying amounts and the tax basis of assets and liabilities using enacted tax rates expected to be in effect when the differences are expected to reverse. Valuation allowances are provided when necessary to reduce net deferred tax assets to the amount that is more likely than not to be realized. Based on the available evidence, we are unable, at this time, to support the determination that it is more likely than not that our deferred tax assets will be utilized in the future. Accordingly, we recorded a full valuation allowance as of December 31, 2021 and 2020. We intend to maintain a valuation allowance until sufficient evidence exists to support its reversal.

The Company accounts for uncertain tax positions in accordance with the provisions of ASC 740. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances. As of December 31, 2021 and 2020, the Company did not have any significant uncertain tax positions.

The Company may recognize interest and penalties related to uncertain tax positions in income tax expense. As of December 31, 2021 and 2020, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in the Company's statements of operations and comprehensive loss.

Comprehensive Loss

Comprehensive loss is defined as the change in equity during a period from transactions from non-owner sources. Unrealized gains or losses on available-for-sale securities is a component of other comprehensive gains or losses and is presented net of taxes. We have not recorded any reclassifications from other comprehensive gains or losses to net loss during any period presented.

Recent Accounting Pronouncements

ASU No. 2020-08, Codification Improvements to Subtopic 310-20, Receivables - Nonrefundable Fees and Other Costs

In October 2020, the FASB issued ASU 2020-08, *Codification Improvements to Subtopic 310-20, Receivables - Nonrefundable Fees and Other Costs* ("ASU 2020-08") to provide further clarification and update the previously issued guidance in ASU 2017-08, *Receivables - Nonrefundable Fees and Other Costs (Subtopic 310-20: Premium Amortization on Purchased Callable Debt Securities)* ("ASU 2017-08"). ASU 2017-08 shortened the amortization period for certain callable debt securities purchased at a premium by requiring that the premium be amortized to the earliest call date. ASU 2020-08 requires that at each reporting period, to the extent that the amortized cost of an individual callable debt security exceeds the amount repayable by the issuer at the next call date, the excess premium shall be amortized to the next call date. The new standard was effective beginning January 1, 2021 and should be applied on a prospective basis as of the beginning of the period of adoption for existing or newly purchased callable debt securities. The adoption of ASU 2020-08 did not have a material impact on the Company's financial position or results of operations upon adoption.

3. Net Loss Per Share Attributable to Common Stockholders

Basic net loss per share attributable to common stockholders is calculated by dividing net loss attributable to common stockholders by the weighted average shares outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share attributable to common stockholders is computed by dividing the net loss by the weighted-average number of shares of common stock and common share equivalents outstanding for the period. Stock options are common share equivalents. There were 2,043,179 and 853,614 common share equivalents outstanding in the form of stock options and 98,800 and zero common share equivalents outstanding in the form of restricted stock awards as of December 31, 2021 and 2020, respectively, that have been excluded from the calculation of diluted net loss per common share as their effect would be anti-dilutive for all periods presented.

(In thousands, except share and per share data)	Year Ended December 31,	
	2021	2020
Numerator:		
Net loss per common share	$ (69,570)	$ (32,167)
Denominator:		
Weighted-average basic and diluted common shares	22,196,846	18,787,161
Basic and diluted net loss per common share	$ (3.13)	$ (1.71)

4. Fair Value Instruments

The following tables show the Company's cash, cash equivalents and available-for-sale securities by significant investment category as of December 31, 2021 and 2020, respectively (in thousands):

	December 31, 2021						
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Aggregate Fair Value	Cash and Cash Equivalents	Short-term Marketable Securities (1)	Long-term Marketable Securities (2)
Level 1:							
Cash and cash equivalents	$ 341,246	$ —	$ —	$ 341,246	$ 341,246	$ —	$ —
Subtotal	341,246	—	—	341,246	341,246	—	—
Level 2:							
Commercial paper	40,469	1	(4)	40,466	—	40,466	—
Corporate bonds	83,300	10	(114)	83,196	—	35,768	47,428
U.S government agency securities	37,621	—	(62)	37,559	—	20,616	16,943
Subtotal	161,390	11	(180)	161,221	—	96,850	64,371
Total	$ 502,636	$ 11	$ (180)	$ 502,467	$ 341,246	$ 96,850	$ 64,371

	December 31, 2020						
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Aggregate Fair Value	Cash and Cash Equivalents	Short-term Marketable Securities (1)	Long-term Marketable Securities (2)
Level 1:							
Cash and cash equivalents	$ 268,269	$ —	$ —	$ 268,269	$ 268,269	$ —	$ —
Subtotal	268,269	—	—	268,269	268,269	—	—
Level 2:							
Certificates of deposit	2,986	7	—	2,993	—	2,993	—
Subtotal	2,986	7	—	2,993	—	2,993	—
Total	$ 271,255	$ 7	$ —	$ 271,262	$ 268,269	$ 2,993	$ —

(1) The Company's short-term marketable securities mature in one year or less.
(2) The Company's long-term marketable securities mature between one year and two years.

See Note 2 to these consolidated financial statements for additional discussion regarding the Company's fair value measurements.

5. Balance Sheet Components

Property and Equipment, Net

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

	December 31, 2021	December 31, 2020
Construction-in-progress	$ 104,340	$ 23,031
Leasehold improvements	5,723	4,631
Furniture and fixtures	891	870
Computer equipment and software	85	82
Laboratory and manufacturing equipment	5,530	4,630
Total property and equipment	116,569	33,244
Accumulated depreciation and amortization	(4,214)	(2,368)
Property and equipment, net	$ 112,355	$ 30,876

Depreciation expense was $1.8 million and $1.5 million for the years ended December 31, 2021 and 2020, respectively.

Refer to Note 6 for further discussion over construction-in-progress.

Accrued Expenses and Other Current Liabilities

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

	December 31, 2021	December 31, 2020
Accrued preclinical and clinical expenses	$ 1,602	$ 1,179
Accrued professional fees	2,011	1,198
Accrued payroll and benefits	2,882	1,486
Accrued taxes	83	40
Accrued construction in progress	9,606	1,049
Accrued financing fees	26	131
Other current liabilities	87	26
Total	$ 16,297	$ 5,109

6. Commitments and Contingencies

Significant Contracts and Agreements

Lease Agreements

On May 26, 2016, the Company signed an operating lease for laboratory and office space that commenced in June 2016 and expired on October 31, 2017 (the “2016 Lease”). The 2016 Lease has been amended several times to increase the area leased, which currently consists of approximately 44,000 square feet and includes the commercial scale cGMP-compliant manufacturing facility, ANCORIS. As a result of the lease amendments, the lease expiration date was extended to October 31, 2031.

On December 26, 2019, we entered into a lease agreement for our second commercial gene therapy facility, ASTRA, in the Pittsburgh, Pennsylvania area ("ASTRA lease") with Northfield I, LLC (the "Landlord" or "Northfield") with an initial lease term that expired on October 31, 2035. The ASTRA lease contained an option ("Purchase Option") to purchase the building, related improvements and take corresponding assignment of the Landlord's rights under its existing Ground Lease (the "Ground Lease"). A cash contribution in the amount of $2.4 million was paid to escrow on January 21, 2020. The contribution was intended to reduce the amount of the building construction costs and had the effect of reducing the base rental rate of the lease and as such, was recorded as prepaid rent in the consolidated balance sheet at time of payment.

On October 5, 2020, the Company was provided with notice that the initial delivery conditions of the building had been met, including completion of the building shell, interior slab, and exterior doors, and on October 15, 2020, the Company gave the Landlord notice of its intent to purchase ASTRA for approximately $9.4 million, subject to the parties entering into a commercially reasonable purchase and sale agreement. As a result of the Company's ability to exercise its option to purchase ASTRA, the Company obtained control over the construction in progress of ASTRA as of October 5, 2020. The Company recorded a $10 million CIP asset and a corresponding build-to-suit lease liability related to the costs incurred by the Landlord, offset by the previous cash contribution of $2.4 million.

On January 29, 2021, the Company entered into a Purchase and Sale Agreement ("PSA") for ASTRA with Northfield related to the purchase option exercised by the Company on October 15, 2020, for a purchase price of $9.4 million. The Company held approximately $1.5 million on deposit with Northfield under the existing lease agreement and applied this deposit as a credit against the purchase price at closing. On February 1, 2021, Northfield delivered the space as substantially complete and made the space available for access by the Company, thus triggering lease commencement. As a result, the Company concluded that this transaction did not qualify for sale-leaseback accounting because it did not meet the definition of a sale. As control did not transfer to the Lessor at lease commencement, the transaction continued to be accounted for as construction in progress and a financing obligation. On March 5, 2021, the purchase closed and the Company determined that reclassification of the construction in progress to buildings and leasehold improvements was not appropriate as the interior of the building was not yet ready for its intended use. The building continues to be held under construction in progress as of December 31, 2021. The interior of the building is currently under construction and is expected to be completed and validated in 2022. From construction completion to the closing of the purchase, the Company recognized interest expense to accrete the financial obligation to a balance that equaled the cash consideration that was paid upon the close of purchase. For more information about the expected construction costs associated with ASTRA, see "ASTRA Contractual Obligations" below.

As part of the transaction, the Company also became the accounting owner of the Ground Lease, due to obtaining control over ASTRA, and recorded the applicable operating right-of-use asset and corresponding lease liability as of October 5, 2020. When the PSA was finalized, the Company took assignment of the Lessor's Ground Lease, in accordance with the Purchase Option, of which lease payments are based on annual payments of $82 thousand, and are subject to a cumulative 10% escalation clause every 5 years through 2071.

As of December 31, 2021, future minimum commitments under the Company’s operating leases were as follows (in thousands):

	Operating Leases
2022	$ 1,094
2023	1,114
2024	1,135
2025	1,162
2026	1,186
Thereafter	11,600
Future minimum operating lease payments	$ 17,291
Less: Interest	9,267
Present value of lease liability	$ 8,024

On December 15, 2021, the Company entered into a 3 year lease agreement for our Boston, Massachusetts office (the "Boston Lease") location that commences in January 2022 and expires in January 2025. As of December 31, 2021, the Company has not recorded a right-of-use asset or corresponding lease liability as the Company has not yet gained control over the Boston Lease. Future minimum operating lease payments under this lease are $280 thousand, $311 thousand, $316 thousand, and $26 thousand for the years ending 2022, 2023, 2024, and 2025, respectively.

Supplemental balance sheet information related to leases is as follows:

	December 31, 2021		December 31, 2020	
Operating leases:				
Right-of-use assets	$ 7,228		$ 3,298	
Current portion of lease liability	1,041		638	
Lease liability	6,983		3,308	
Total lease liability	$ 8,024		$ 3,946	
Weighted average remaining lease term, in years		14.4		16.4
Weighted average discount rate	9.5	%	9.4	%

The Company recorded operating lease costs of $1.3 million and $767 thousand for the years ended December 31, 2021 and 2020, respectively, and variable lease costs of $160 thousand and $57 thousand for the years ended December 31, 2021 and 2020, respectively.

Agreements with Contract Manufacturing Organizations and Contract Research Organizations

The Company enters into various agreements in the normal course of business with Contract Research Organizations ("CROs"), Contract Manufacturing Organizations ("CMOs") and other third parties for preclinical research studies, clinical trials and testing and manufacturing services. The agreements with CMOs relate to the manufacturing of sterile gel that is mixed with in-house produced vectors as part of the final drug product applied in certain of our clinical trials. These agreements may also include research and development activities, storage, packaging, labeling, and/or testing of our preclinical and clinical-stage products. The Company is obligated to make milestone payments under certain of these agreements. The estimated remaining commitment as of December 31, 2021 under these agreements is approximately $3.0 million. The Company has incurred expenses under these agreements of $5.0 million and $4.6 million for the years ended December 31, 2021 and 2020, respectively.

Commercial Preparedness Activities

The Company has contracted with various third parties to facilitate, coordinate and perform agreed upon commercial preparedness and market research activities relating to our lead product candidate, Vyjuvek. These contracts typically call for the payment of fees for services upon the achievement of certain milestones. The estimated remaining commitment as of

December 31, 2021 is $2.4 million. The Company has incurred expenses under these activities of $6.1 million and $1.9 million for the years ended December 31, 2021 and 2020, respectively.

ASTRA Contractual Obligations

The Company has contracted with various third parties to construct our second cGMP facility, ASTRA. Additionally, we have entered into various non-cancellable purchase agreements for long-lead materials to help avoid potential schedule disruptions or material shortages. These contracts typically call for the payment of fees for services or materials upon the achievement of certain milestones. The estimated remaining commitment as of December 31, 2021 is $24.7 million. The Company has included costs incurred to-date associated with ASTRA within construction in progress as of December 31, 2021.

On June 30, 2021, the Company entered into a Standard Form of Contract for Construction and the corresponding General Conditions of the Contract for Construction (collectively, the “Agreement”) with Whiting-Turner, pursuant to which Whiting-Turner is constructing and managing the construction of ASTRA. Subject to certain conditions in the Agreement, the Company will pay Whiting-Turner a contract price consisting of the cost of work plus a fee equal to 1.75% of the cost of work, subject to a guaranteed maximum price to be agreed upon in an amendment to the Agreement at a later date.

Effective September 13, 2021, the Company entered into a guaranteed maximum price amendment (the "Amendment") to the Agreement to set forth the guaranteed maximum price, as well as the date by which Whiting-Turner is to achieve Substantial Completion (as defined in the Agreement). Under the Amendment, the guaranteed maximum price to be paid by the Company is $80.8 million, subject to certain additions and deductions by change orders as provided by the Agreement. Whiting-Turner’s work under the Agreement represents a portion of the work necessary to complete construction of the ASTRA facility and, therefore the date of Substantial Completion of Whiting-Turner’s work under the Agreement does not equate to the date of completion of ASTRA. The guaranteed maximum price under the Agreement constitutes only a portion of the total estimated cost of building and equipping ASTRA.

Legal Proceedings

On May 1, 2020, a complaint was filed against us in the United States District Court for the Western District of Pennsylvania by PeriphaGen, Inc. ("PeriphaGen"), which also named our Chief Executive Officer and Chief Operating Officer, Krish Krishnan and Suma Krishnan, respectively. The complaint alleges breach of contract and misappropriation of trade secrets, which secrets the plaintiff asserts were used to develop our product candidates, including the vector backbones, and our STAR-D platform. We answered the complaint on June 26, 2020 by denying the allegations and brought a counterclaim asking the court to declare that we did not misappropriate PeriphaGen’s trade secrets or confidential information, and to further declare that we are the rightful and sole owner of our product candidates and STAR-D platform. In addition, we filed a third-party complaint against two principals of PeriphaGen, James Wechuck and David Krisky, alleging breach of contract and seeking contribution and indemnification from them in the event PeriphaGen is awarded damages. On July 29, 2020, PeriphaGen filed its response to our answer and counterclaim, denying the allegations in the counterclaim. On the same day, Messrs. Wechuck and Krisky filed a motion to dismiss the third-party complaint on various grounds, and we opposed the motion. On December 1, 2020, the court ruled on Messrs. Wechuck and Krisky's motion to dismiss. The court determined our claims for contribution and indemnification based on PeriphaGen's state law claims for unfair competition and misappropriation of trade secrets can proceed. Our breach of contract claim will also go forward in full. Fact discovery is ongoing.

PeriphaGen is seeking monetary damages, injunctive relief, attorneys' fees and costs. While we are unable to provide any assurances as to the ultimate outcome of the case, we believe the allegations in the complaint are without merit, and we intend to vigorously defend against them. We are currently unable to estimate the costs and timing of any litigation, including any potential damages if PeriphaGen were to prevail on its claims.

The Company has received insurance proceeds during fiscal year 2021 relating to legal defense costs and expenses associated with the PeriphaGen litigation. During the year ended December 31, 2021, the Company has received $1.6 million of insurance proceeds and we have recorded an additional $560 thousand as a receivable within Prepaid Expenses and Other Current Assets on the Consolidated Balance Sheet as management determined that the amount was probable of collection. Of the amount recorded as a receivable, $403 thousand was received in January 2022 and $157 thousand is estimated to be received in the second quarter. The reimbursements have been recorded as an offset to our legal fees included in General and Administrative expenses on the Consolidated Statements of Operations and within Operating Activities on the Condensed Consolidated Statements of Cash Flows.

7. Capitalization

Sale of Common Stock

On December 3, 2021, the Company completed a public offering of 2,866,667 shares of its common stock, including 200,000 shares purchased by the underwriters, at $75.00 per share. Net proceeds to the Company from the offering were $201.9 million after deducting underwriting discounts and commissions of approximately $12.9 million, and other offering expenses payable by the Company of $227 thousand.

On February 1, 2021, the Company completed a public offering of 2,211,538 shares of its common stock, including 288,461 shares purchased by the underwriters, at $65.00 per share. Net proceeds to the Company from the offering were $134.9 million after deducting underwriting discounts and commissions of approximately $8.6 million, and other offering expenses payable by the Company of $198 thousand.

On December 31, 2020, the Company entered into a sales agreement (the "Sales Agreement") with Cowen and Company, LLC ("Cowen") with respect to an at-the-market equity offering program ("ATM Program"), under which Cowen will act as the Company's agent and/or principal and may issue and sell from time to time, during the term of the Sales Agreement, shares of our common stock, having an aggregate offering price up to $150.0 million ("Placement Shares"). Related offering expenses payable by the Company were $172 thousand. The issuance and sale of the Placement Shares by the Company under the Sales Agreement will be made pursuant to the Company's effective "shelf" registration statement on Form S-3. During the year ended December 31, 2021, 262,500 shares of common stock were issued pursuant to the ATM Program at a weighted average price of $66.50 per share for net proceeds of $16.9 million after deducting underwriting discounts and commissions of approximately $524 thousand, resulting in a remaining $132.5 million available for issuance under the ATM Program.

On May 21, 2020, the Company completed a public offering of 2,275,000 shares of its common stock to the public at $55.00 per share. Net proceeds to the Company from the offering were $117.2 million after deducting underwriting discounts and commissions of approximately $7.5 million, and other offering expenses payable by the Company of approximately $463 thousand.

8. Stock-Based Compensation

Stock Options

Options granted to employees and non-employees vest ratably over a four-year period and options granted to directors of the company vest ratably over one year to four-year periods. Stock options have a life of ten years.

The Company granted 1,422,450 and 891,250 stock options to employees, non-employees, and directors during the year ended December 31, 2021 and 2020, respectively.

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

	Stock Options Outstanding	Weighted-average Exercise Price	Weighted-average Remaining Contractual Life (Years)	Aggregate Intrinsic Value (In thousands) (1)
Balance at January 1, 2020	420,766	$ 17.71	8.4	$ 15,859
Granted	891,250	47.29		
Exercised	(84,285)	10.45		
Cancelled or forfeited	(374,117)	38.24		
Expired	—	—		
Balance at December 31, 2020	853,614	$ 40.31	9.0	$ 16,804
Granted	1,422,450	66.88		
Exercised	(54,260)	38.12		
Cancelled or forfeited	(175,750)	61.35		
Expired	(2,875)	75.82		
Balance at December 31, 2021	2,043,179	$ 57.00	9.0	$ 31,331
Exercisable at December 31, 2021	307,250	$ 33.00	7.5	$ 11,354

(1) Aggregate intrinsic value represents the difference between the closing stock price of our common stock on December 31, 2021 and the exercise price of outstanding in-the-money options.

The total intrinsic value (the amount by which the fair market value exceeded the exercise price) of stock options exercised during the year ended December 31, 2021 and 2020 was $1.3 million and $3.1 million, respectively.

The weighted-average grant-date fair value per share of options granted to employees, non-employees, and directors during the years ended December 31, 2021 and 2020 was $43.05 and $30.99, respectively.

There was $59.1 million of unrecognized stock-based compensation expense related to employees', non-employees', and directors' awards that is expected to be recognized over a weighted-average period of 3.2 years as of December 31, 2021.

The Company has recorded aggregate stock-based compensation expense related to the issuance of stock option awards in the Consolidated Statements of Operations for the years ended December 31, 2021 and 2020 as follows (in thousands):

	Year Ended December 31,	
	2021	2020
Research and development	$ 3,434	$ 994
General and administrative	10,235	2,278
Total stock-based compensation	$ 13,669	$ 3,272

We capitalize the portion of stock-based compensation that relates to work performed on the construction of new buildings. There was $284 thousand and $34 thousand of stock-based compensation that was capitalized in the years ended December 31, 2021 and 2020, respectively.

The Company recorded stock-based compensation expense of $13.7 million and $3.3 million for the years ended December 31, 2021 and 2020, respectively. The fair value of options granted was estimated at the date of grant using the Black-Scholes valuation model with the following weighted-average assumptions for the years ended December 31, 2021 and 2020:

	Year Ended December 31,	
	2021	2020
Expected stock price volatility	72 %	75 %
Expected term of the award (years)	6.2	6.2
Risk-free interest rate	1.10 %	0.64 %
Weighted average exercise price	$ 66.88	$ 47.29
Forfeiture Rate	— %	14.74 %

Restricted Stock Awards

Restricted stock awards ("RSAs") granted to employees vest ratably over a four-year period. The Company granted 98,800 and zero RSAs to employees of the Company during the year ended December 31, 2021and 2020 respectively.

The following table summarizes the Company's RSA activity:

	Number of Shares	Weighted Average Grant Date Fair Value
Non-vested RSAs as of December 31, 2020	—	$ —
Granted	98,800	$ 78.89
Vested	—	$ —
Forfeited	—	$ —
Non-vested RSAs as of December 31, 2021	98,800	$ 78.89

There was $6.1 million of unrecognized stock-based compensation expense related to employees' awards that is expected to be recognized over a weighted-average period of 3.2 years as of December 31, 2021.

The Company recorded stock-based compensation expense related to RSAs of $1.7 million and zero for the year ended December 31, 2021 and 2020, respectively, within General and Administrative expenses in the accompanying Consolidated Statements of Operations (in thousands):

	Year Ended December 31, 2021
General and administrative	$ 1,650
Total stock-based compensation	$ 1,650

Shares remaining available for grant under the Company's stock incentive plan were 1,135,606, with a sublimit for incentive stock options of 315,383, at December 31, 2021.

9. Income Taxes

We did not record a current or deferred income tax expense or benefit for the years ended December 31, 2021 and 2020 due to the Valuation Allowance position. A reconciliation of income tax expense (benefit) computed at the statutory federal and state income tax rate for the year to income tax expense (benefit) as reflected in our financial statements for years ended December 31, 2021 and 2020 are as follows (in thousands):

	December 31, 2021	December 31, 2020
Federal income tax expense (benefit) at statutory rate	$ (14,578)	$ (6,752)
Change in valuation allowance	20,689	11,112
State income tax expense net of federal benefit	(5,436)	(2,632)
Credits	(1,295)	(887)
Other non-deductible expenses	675	(216)
Other	(55)	(625)
Total tax expense (benefit)	$ —	$ —

The significant components of the Company's deferred tax assets as of December 31, 2021 and 2020 are as follows (in thousands):

	December 31, 2021	December 31, 2020
Deferred tax assets:		
Net operating loss carryforwards	$ 33,170	$ 19,189
Stock compensation	3,906	664
Build-to-suit lease liability	—	2,893
Lease liability	2,344	1,142
Depreciation	679	123
Accrued expenses	817	46
Capitalized costs	884	—
Credits	3,607	2,311
Total deferred tax assets	45,407	26,368
Valuation allowance	(42,732)	(22,043)
Deferred tax assets	2,675	4,325
Deferred tax liabilities:		
ASTRA capitalized construction costs	—	(2,893)
Right-of-use assets	(2,111)	(954)
Prepaid expenses	(613)	(476)
Unrealized loss on marketable securities	49	(2)
Total deferred tax liabilities	(2,675)	(4,325)
Net deferred tax assets	$ —	$ —

The Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets. Based on the Company's history of operating losses, the Company has concluded that it is more likely than not that the benefit of its deferred tax assets will not be realized. Accordingly, the Company has provided a full valuation allowance for deferred tax assets as of December 31, 2021.

As of December 31, 2021 and 2020, the Company had federal research and development credit carryforwards of approximately $2.4 million and $1.4 million, respectively. The federal tax credit carryforwards will begin to expire in 2039 if not utilized. As of December 31, 2021 and 2020, the Company also had orphan drug tax credit carryforwards of approximately $910 thousand and $724 thousand, respectively. The orphan drug tax credit carryforwards will begin to expire in 2038 if not utilized. The Company has not completed a formal research and development credit analysis, and as such, when an analysis is finalized, the Company plans to update its research and development credit carryforward and orphan drug tax credit carryforwards.

As of December 31, 2021 and 2020, the Company had state research and development credit carryforwards of approximately $321 thousand and $226 thousand, respectively. The state tax credit carryforwards will begin to expire in 2032 if not utilized.

As of December 31, 2021, the Company had cumulative U.S. federal NOL carryforwards of approximately $114.0 million. Of this amount, $5.0 million is available to offset future income tax liabilities and will expire in 2037, the remaining $109.0 million is available indefinitely to offset future income tax liabilities with no expiration period.

As of December 31, 2021, the Company had cumulative U.S. state NOL carryforwards of approximately $117.1 million. The state NOLs are available to offset future state income tax liabilities and will begin to expire in 2037.

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

The Company files income tax returns in the United States at the federal level and in states in which the Company conducts business activities. The federal and state income tax returns are generally subject to tax examinations for the tax year ended December 31, 2018, 2019 and 2020. To the extent the Company has tax attribute carryforwards, the tax years in which the attribute was generated may still be adjusted upon examination by the Internal Revenue Service or state tax authorities to the extent utilized in a future period.

10. Related Party Transactions

In December 2019 the Company advanced $420 thousand to a member of our management team to cover the personal payroll and income taxes on their taxable income from NSO exercises. This employee repaid the Company in the full amount on January 6, 2020.

11. Subsequent Events

The Company evaluates events or transactions that occur after the balance sheet date, but prior to the issuance of the financial statements, to identify matters that require disclosure. On January 7, 2022, the Company incorporated Krystal Biotech Switzerland GmbH, for the purpose of establishing initial operations in Europe for the development and commercialization of Krystal's pipeline.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.

None

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Under the supervision of our Chief Executive Officer and Chief Accounting Officer, we evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) of the Exchange Act as of December 31, 2021. Based on that evaluation, our Chief Executive Officer and Chief Accounting Officer have concluded that our disclosure controls and procedures were effective as of December 31, 2021 to ensure that information required to be disclosed by us in the reports we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Accounting Officer, as appropriate to allow timely discussion regarding required disclosures. In designing and evaluating our disclosure controls and procedures, management recognizes that any disclosure controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply its judgment in evaluating the benefits of possible controls and procedures relative to their costs.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rules 13a-15(f) and 15d-15(f). Our management conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2021 based on the criteria established in *Internal Control - Integrated Framework* (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission.

Based on the results of its evaluation, management concluded that our internal control over financial reporting was effective as of December 31, 2021. The effectiveness of our internal control over financial reporting as of December 31, 2021 has been audited by Mayer Hoffman McCann P.C., an independent registered public accounting firm, as stated in their report which is included herein.

Inherent Limitations on Controls and Procedures

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

We intend to review and evaluate the design and effectiveness of our disclosure controls and procedures on an ongoing basis and to improve our controls and procedures over time and to correct any deficiencies that we may discover in the future. While our Chief Executive Officer and Chief Accounting Officer have concluded that, as of December 31, 2021, the design of our disclosure controls and procedures, as defined in Rule 13a-15(e) under the Exchange Act, was effective, future events affecting our business may cause us to significantly modify our disclosure controls and procedures.

Changes in Internal Control over Financial Reporting

We are in the process of implementing new enterprise resource planning software, Microsoft Dynamics D365 (“Dynamics”), as part of a plan to integrate and upgrade our systems and processes. The implementation of this software is scheduled to continue in phases over a number of years. During the second and third quarter of 2021, we completed the implementation of the financial reporting and consolidation modules and the procurement modules, respectively. As the phased implementation of this system occurs, we expect certain changes to our processes and procedures which, in turn, will result in changes to our internal control over financial reporting. We expect Dynamics to strengthen our internal financial controls by automating a number of accounting and reporting processes and activities, thereby decreasing the number of manual processes previously required. Management will continue to evaluate and monitor our internal controls as processes and procedures in each of the affected areas evolve.

Other than as discussed above, there was no change in our internal control over financial reporting identified in connection with the evaluation required by Rules 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the year ended December 31, 2021 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Report of Independent Registered Public Accounting Firm

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

Opinion on Internal Control over Financial Reporting

We have audited Krystal Biotech Inc.’s (“Company”) internal control over financial reporting as of December 31, 2021, based on criteria established in Internal Control—Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO criteria). In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2021, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (“PCAOB”), the consolidated balance sheet and related statement of operations and comprehensive loss, stockholders’ equity, cash flows and the related notes of the Company and our report dated February 28, 2022 expressed an unqualified opinion.

Basis for Opinion

The Company’s management is responsible for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management’s Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company’s internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audit also included performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control over Financial Reporting

A company’s internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with accounting principles generally accepted in the United States of America. A company’s internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and

directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Mayer Hoffman McCann P.C.

San Diego, California
February 28, 2022

Item 9B. Other Information.

None

Item 9C. Disclosure Regarding Foreign Jurisdictions That Prevent Inspections.

Not Applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

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

Item 11. Executive Compensation.

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

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

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

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

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

Item 14. Principal Accounting Fees and Services.

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

PART IV

Item 15. Exhibits, Financial Statement Schedules.

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

(1) Financial statements

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

(2) Financial statement schedule.

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

(3) Exhibits.

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

Exhibit Index

Exhibit Number	Description
3.1	Second Amended and Restated Certificate of Incorporation of Krystal Biotech, Inc. (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K, as filed with the SEC on September 25, 2017)
3.2	Amended and Restated Bylaws of Krystal Biotech, Inc. (incorporate by reference to Exhibit 3.2 to the Company's Current Report on Form 8-K, as filed with the SEC on September 25, 2017)
4.1	Form of Common Stock Certificate (incorporated by reference to Exhibit 4.1 to the Company's Amendment No. 2 to the Company's Registration Statement on Form S-1 (Reg. No. 333-220085), as filed with the SEC on September 14, 2017)
4.2	Form of Indenture (including form of Debt Securities) (incorporated by reference to Exhibit 4.5 to the Company's Registration Statement on Form S-3 (Reg. No. 333-227632), as filed with the SEC on October 1, 2018)
4.3*	Description of Common Stock (incorporated by reference to Exhibit 4.3 to the Company's Annual Report on Form 10-K, as filed with the SEC on March 1, 2021)
10.1#	Indemnification Agreement by and between Krystal Biotech, Inc. and each of its directors and executive officers (incorporated by reference to Exhibit 10.1 to the Company's Amendment No. 2 to the Company's Registration Statement on Form S-1 (Reg. No. 333-220085), as filed with the SEC on September 14, 2017)
10.2#	Executive Employment Agreement, effective July 1, 2017, by and between Krystal Biotech, Inc. and Krish S. Krishnan (incorporated by reference to Exhibit 10.2 to the Company's Amendment No. 1 to the Company's Registration Statement on Form S-1 (Reg. No. 333-220085), as filed with the SEC on September 7, 2017)
10.3#	Executive Employment Agreement, effective May 1, 2017, by and between Krystal Biotech, Inc. and Suma M. Krishnan (incorporated by reference to Exhibit 10.3 to the Company's Amendment No. 1 to the Company's Registration Statement on Form S-1 (Reg. No. 333-220085), as filed with the SEC on September 7, 2017)
10.4#	Executive Employment Agreement, effective January 20, 2020, by and between Krystal Biotech, Inc. and Kathryn A. Romano (incorporated by reference to Exhibit 10.4 to the Company's Annual Report on Form 10-K, as filed with the SEC on March 1, 2021)
10.5#	Executive Employment Agreement, effective May 3, 20201 by and between Krystal Biotech, Inc. and Andy Orth
10.6#	Executive Employment Agreement, effective January 18, 2022, by and between Krystal Biotech, Inc. and Jing Marantz
10.7#	Krystal Biotech, Inc. 2017 Stock Incentive Plan (incorporated by reference to Exhibit 10.6 to the Company's Amendment No. 2 to the Company's Registration Statement on Form S-1 (Reg. No. 333-220085), as filed with the SEC on September 14, 2017)

Exhibit Number	Description
10.8#	Krystal Biotech, Inc. 2017 IPO Stock Incentive Plan (incorporated by reference to Exhibit 10.7 to the Company's Amendment No. 2 to the Company's Registration Statement on Form S-1 (Reg. No. 333-220085), as filed with the SEC on September 14, 2017)
10.9#	Form of Krystal Biotech, Inc. 2017 Stock Incentive Plan Notice of Stock Option Award (incorporated by reference to Exhibit 10.8 to the Company's Amendment No. 2 to the Company's Registration Statement on Form S-1 (Reg. No. 333-220085), as filed with the SEC on September 14, 2017)
10.10#	Form of Krystal Biotech, Inc. 2017 IPO Stock Incentive Plan Notice of Stock Option Award (incorporated by reference to Exhibit 10.9 to the Company's Amendment No. 2 to the Company's Registration Statement on Form S-1 (Reg. No. 333-220085), as filed with the SEC on September 14, 2017)

10.11	Lease Agreement, dated as of May 26, 2016, by and between Wharton Lender Associates, L.P. and Krystal Biotech, LLC (incorporated by reference to Exhibit 10.10 to the Company's Amendment No. 1 to the Company's Registration Statement on Form S-1 (Reg. No. 333-220085), as filed with the SEC on September 7, 2017)
10.12	Second Amendment to Lease Agreement, dated as of February 27, 2017, by and between Wharton Lender Associates, L.P. and Krystal Biotech, LLC (incorporated by reference to Exhibit 10.11 to the Company's Amendment No. 1 to the Company's Registration Statement on Form S-1 (Reg. No. 333-220085), as filed with the SEC on September 7, 2017)
10.13	Investors' Rights Agreement, dated as of August 7, 2017, by and among Krystal Biotech, Inc. and the investors listed on Schedule A thereto (incorporated by reference to Exhibit 10.9 to Form S-1 (Reg. No. 333-220085), as filed with the SEC on August 21, 2017)
10.14	Third amendment to Lease Agreement, dated as of May 31, 2018, by and between Wharton Lender Associate, L.P. and Krystal Biotech, Inc. (incorporated by reference to Exhibit 10.13 to the Company's Annual Report on Form 10-K, as filed with the SEC on March 1, 2021)
10.15	Fourth amendment to Lease Agreement, dated as of October 22, 2018, by and between Wharton Lender Associate, L.P. and Krystal Biotech, Inc. (incorporated by reference to Exhibit 10.14 to the Company's Annual Report on Form 10-K, as filed with the SEC on March 1, 2021)
10.16	Fifth amendment to Lease Agreement, dated as of December 10, 2018, by and between Wharton Lender Associate, L.P. and Krystal Biotech, Inc. (incorporated by reference to Exhibit 10.15 to the Company's Annual Report on Form 10-K, as filed with the SEC on March 1, 2021)
10.17*	Sixth amendment to Lease Agreement and first amendment to storage space agreement, dated as of January 13, 2021, by and between Wharton Lender Associates, L.P. and Krystal Biotech, Inc.
10.18*	Seventh amendment to Lease Agreement, dated as of May 11, 2021, by and between Wharton Lender Associates, L.P. and Krystal Biotech, Inc.
10.19*	Eighth amendment to Lease Agreement, dated as of July 21, 2021, by and between Wharton Lender Associates, L.P. and Krystal Biotech, Inc.
10.20*	Ninth amendment to Lease Agreement, dated as of January 4, 2022, by and between Wharton Lender Associates, L.P. and Krystal Biotech, Inc.
10.21	Purchase and Sale Agreement, dated January 29, 2021, by and between Krystal Biotech, Inc. and Northfield I, LLC. (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K, as filed with the SEC on February 2, 2021)
10.22	Standard Form of Contract for Construction and the corresponding General Conditions of the Contract for Construction with The Whiting-Turner Contracting Company, dated June 30, 2021 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q, as filed with the SEC on August 9, 2021)
10.23	Guaranteed Maximum Price Amendment to Standard Form of Contract for Construction and the corresponding General Conditions of the Contract for Construction with The Whiting-Turner Contracting Company dated September 13, 2021 (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K, as filed with the SEC on September 16, 2021)
21.1*	Subsidiaries of Krystal Biotech, Inc.
23.1*	Consent of Mayer Hoffman McCann P.C.
31.1*	Certification of Periodic Report by Chief Executive Officer under Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Periodic Report by Chief Accounting Officer under Section 302 of the Sarbanes-Oxley Act of 2002.
32.1*	Certification of Chief Executive Officer Pursuant to 18 U.S.C. Section 1350 as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2*	Certification of Chief Accounting Officer Pursuant to 18 U.S.C. Section 1350 as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document

101.LAB	XBRL Taxonomy Extension Label Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

* Filed herewith.
\# Indicates a management contract or compensatory plan or arrangement.

Item 16. Form 10-K Summary.

The Company has elected to not include a summary.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Pittsburgh, State of Pennsylvania, on February 28, 2022.

KRYSTAL BIOTECH, INC.

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

By: /s/ Kathryn A. Romano
Kathryn A. Romano
Chief Accounting Officer

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

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

Signature	Title	Date
/s/ Krish S. Krishnan Krish S. Krishnan	President and Chief Executive Officer and Director (Principal Executive Officer)	February 28, 2022
/s/ Kathryn A. Romano Kathryn A. Romano	Chief Accounting Officer (Principal Financial Officer)	February 28, 2022
/s/ Suma M. Krishnan Suma M. Krishnan	Chief Operating Officer and Director	February 28, 2022
/s/ Daniel S. Janney Daniel S. Janney	Director	February 28, 2022
/s/ Dino A. Rossi Dino A. Rossi	Director	February 28, 2022
/s/ Kirti Ganorkar Kirti Ganorkar	Director	February 28, 2022
/s/ Julian Gangolli Julian Gangolli	Director	February 28, 2022
/s/ Chris Mason Chris Mason	Director	February 28, 2022
/s/ E. Rand Sutherland E. Rand Sutherland	Director	February 28, 2022

Krystal

EMPLOYMENT AGREEMENT

This Employment Agreement ("the Agreement"), dated April 2nd, 2021, is between Krystal Biotech, Inc., a Delaware corporation (the "Company") and Andy Orth ("Employee") and reflects the Company's and Employee's desire to establish a full employment relationship. We kindly request this document be signed and returned to us before April 9th, 2021.

1. POSITION AND RESPONSIBILITIES

a. Position. Employee is employed by the Company to render services to the Company in the position of Executive Vice President and Chief Commercial Officer commencing May 3rd, 2021 ("Start Date"). This position will report to the CEO, Krish Krishnan, and will be part of the senior leadership team of the Company, including designation as a Section 16 officer. The employee shall perform such duties and responsibilities as are normally related to similar positions in accordance with the standards of the industry and any additional duties now or hereafter assigned to Employee by the Company. Employee shall abide by the rules, regulations, and practices as adopted or modified from time to time in the Company's sole discretion. Employee's primary location shall be in Boston, MA, with travel to Company's Headquarters in Pittsburgh, PA, as required. This employment offer is subject to approval by the board of directors and is contingent upon the completion of a satisfactory reference check, background check and drug screen.

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

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

2. COMPENSATION AND BENEFITS

a. Base Salary and Bonus. In consideration of the services to be rendered under this Agreement, the Company shall pay Employee a base salary at the rate of FOUR HUNDRED AND TWENTY FIVE THOUSAND DOLLARS ($425,000) per year ("Base Salary") with a target bonus of up to 45% of the annual base salary, subject to meeting corporate and individual goals. The target bonus will be prorated during Employee's first year of employment. This position is considered Tier 2, which means 25% of the target bonus will be based upon individual performance, while 75% of the target bonus will be based upon corporate performance. The corporate performance portion of the bonus will be measured upon attainment of performance objectives during the calendar year as determined by the Krystal Biotech board of directors. The bonus payout shall occur upon Krystal Biotech board of directors approval of the attainment of goals, likely to be on or before March 15th following the calendar year in which the bonus is measured. Employee must be employed by the Company and be in good standing at the time of payout in order to be eligible to receive payment.

b. The Base Salary shall be paid in accordance with the Company's regularly established payroll practice.

c. Employee's Total Compensation will be reviewed by the Compensation Committee from time to time in accordance with the established procedures of the Company for adjusting salaries for similarly situated employees and may be adjusted in the sole discretion of the Company.

d. Equity Grants. The Employee will be awarded options to purchase 205,000 shares of the common stock of Krystal, as adjusted by any stock splits that may occur. The exercise price per share of any approved options will be the closing price of Krystal's common stock on May 31st, 2021. Any and all equity grants shall vest in four equal annual installments commencing on the Employee's first anniversary. Employee's entitlement to any equity grant is conditioned upon Employee's signing of an appropriate Equity Incentive Agreement and the terms of the relevant equity incentive plans under which the options are granted, including vesting requirements.

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

f. Expenses. The Company shall reimburse Employee for reasonable business expenses incurred in the performance of Employee's duties hereunder, in accordance with the Company's travel and expense policy.

3. AT-WILL EMPLOYMENT; TERMINATION BY COMPANY

a. At-Will Termination by Company. The employment of Employee shall be "at-will" at all times. The Company may terminate Employee's employment with the Company at any time, without any advance notice, for any reason or no reason at all, notwithstanding anything to the contrary contained in or arising from any statements, policies or practices of the Company relating to the employment, discipline or termination of its employees. Upon and after such termination, all obligations of the Company under this Agreement shall cease. In the event of any such termination by the Company for any reason other than Cause, the Company shall pay to Employee an amount equal to six months of his then-current Base Salary, which payment may, at the request of the Company, be conditioned upon Employee's execution of a usual and customary general release in favor of the Company. "Cause" shall be defined as any of the following: (i) an intentional act of fraud, embezzlement, theft or any other material violation of law that occurs during or in the course of Employee's employment with company; (ii) intentional damage to the Company's assets; (iii) intentional disclosure of Company's confidential information contrary to Company's policies; (iv) intentional breach of Employee's obligations under this agreement; (v) intentional engagement in any competitive activity which would constitute a breach of Employee's duty of loyalty or of Employee's obligations under this agreement; (vi) intentional breach of any of the Company's policies; (vii) the willful and/or continued failure to substantially perform Employee's duties for company (other than as a result of incapacity due to physical or mental illness); (viii) inability to make agreed upon improvements resulting from a clearly outlined and mutually agreed upon Performance Improvement Plan ("PIP") or (ix) willful conduct by Employee that is demonstratably and materially injurious to company, monetarily or otherwise.

4. AT-WILL EMPLOYMENT; TERMINATION BY EMPLOYEE

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

5. TERMINATION OBLIGATIONS

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

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

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

6. INVENTIONS AND PROPRIETARY INFORMATION; PROHIBITION ON THIRD PARTY INFORMATION

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

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

c. Noncompetition. In consideration of the Company's extension to Employee of full time employment with the Company, the Employee agrees that at no time during the Employee's employment with the Company, and for a period of one (1) year immediately following the termination of such employment (regardless of the

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

7. AMENDMENTS; WAIVERS; REMEDIES

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

8. ASSIGNMENT; BINDING EFFECT

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

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

9. NOTICES

All notices or other communications required or permitted hereunder shall be made in writing and shall be deemed to have been duly given if delivered: (a) by hand; (b) by a nationally recognized overnight courier service; or (c) by United States first class registered or certified mail, return receipt requested, to the principal address of the other party, as set forth below. The date of notice shall be deemed to be the earlier of (i) actual receipt of notice by any permitted means, or (ii) five business days following dispatch by overnight delivery service or the United States Mail. Employee shall be obligated to notify the Company in writing of any change in Employee's address. Notice of change of address shall be effective only when done in accordance with this paragraph.

Company's Notice Address:

Krystal Biotech, Inc.
2100 Wharton Street, Suite 310
Pittsburgh, PA 15203
Attention: Josh Suskin
Email: jsuskin@krystalbio.com

Employee's Contact Information:

Andy Orth
12 Great Rock Road
Hingham, MA 02043
andy.orth@gmail.com

10. SEVERABILITY

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

11. TAXES

All amounts paid under this Agreement shall be paid less all applicable state and federal tax withholdings and any other withholdings required by any applicable jurisdiction or authorized by Employee.

12. GOVERNING LAW

This Agreement shall be governed by and construed in accordance with the laws of the Commonwealth of Pennsylvania without regard to the conflict of law principles. Parties agree to first try to mediate any conflict arising under this Agreement or a matter related thereto. If such a conflict cannot be resolved through mediation then any suit or action shall be brought in an appropriate federal or state court located in Allegheny County, Pennsylvania.

13. INTERPRETATION

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

14. COUNTERPARTS

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

15. AUTHORITY

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

16. ENTIRE AGREEMENT

This Agreement is intended to be the final, complete, and exclusive statement of the terms of Employee's employment by the Company and may not be contradicted by evidence of any prior or contemporaneous statements or agreements, except for agreements specifically referenced herein (including the Employee Proprietary Information and Inventions Agreement attached as Exhibit A and the Company's Equity Incentive Plan and Equity Incentive Agreement). To the extent that the practices, policies or procedures of the Company, now or in the future, apply to

Employee and are inconsistent with the terms of this Agreement, the provisions of this Agreement shall control. Any subsequent change in Employee's duties, position, or compensation will not affect the validity or scope of this Agreement.

17. EMPLOYEE ACKNOWLEDGEMENT

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

IN WITNESS WHEREOF, the parties have duly executed this Agreement as of the date first written above.

KRYSTAL BIOTECH, INC.

DocuSigned by:
By: Kathryn A. Romano
0FB2276B0996400...

Kathryn Romano

Title: Chief Accounting Officer

Andy Orth

Name: Andy Orth

Employee

5Apr-21

EMPLOYMENT AGREEMENT

This Employment Agreement ("the Agreement"), dated December 6, 2021, is between Krystal Biotech, Inc., a Delaware corporation (the "Company") and Jing L. Marantz ("Employee") and reflects the Company's and Employee's desire to establish a full employment relationship. We kindly request this document be signed and returned to us before December 13, 2021.

1. POSITION AND RESPONSIBILITIES

a. Position. Employee is employed by the Company to render services to the Company in the position of Executive Vice President and Chief Business Officer commencing January 18, 2022 ("Start Date"). This position will report to the CEO, Krish Krishnan, and will be part of the senior leadership team of the Company, including designation as a Section 16 officer. Effective as of the Start Date, Employee will also step down from her position as a member of Krystal's board of directors. Employee shall perform such duties and responsibilities as are normally related to similar positions in accordance with the standards of the industry and any additional duties now or hereafter assigned to Employee by the Company. Employee shall abide by the rules, regulations, and practices as adopted or modified from time to time in the Company's sole discretion. Employee's primary location shall be in Boston, MA, with travel to Company's Headquarters in Pittsburgh, PA, as required. This employment offer is subject to approval by the board of directors and is contingent upon the completion of a satisfactory reference check, background check and drug screen.

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

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

2. COMPENSATION AND BENEFITS

a. Base Salary and Bonus. In consideration of the services to be rendered under this Agreement, the Company shall pay Employee a base salary at the rate of FOUR HUNDRED AND TWENTY-FIVE THOUSAND DOLLARS ($425,000) per year ("Base Salary") with a target bonus of up to 45% of the annual base salary, subject to meeting corporate and individual goals. The target bonus will be prorated during Employee's first year of employment. This position is considered Tier 2, which means 25% of the target bonus will be based upon individual performance, while 75% of the target bonus will be based upon corporate performance. The corporate performance portion of the bonus will be measured upon attainment of performance objectives during the calendar year as determined by the Krystal board of directors. The bonus payout shall occur upon Krystal board of directors' approval of the attainment of goals, likely to be on or before March 15th following the calendar year in which the bonus is measured. Employee must be employed by the Company and be in good standing at the time of payout in order to be eligible to receive payment.

b. The Base Salary shall be paid in accordance with the Company's regularly established payroll practice.

c. Employee's Total Compensation will be reviewed by the Compensation Committee from time to time in accordance with the established procedures of the Company for adjusting salaries for similarly situated employees and may be adjusted in the sole discretion of the Company.

d. Equity Grants. The Employee will be awarded options to purchase 205,000 shares of the common stock of Krystal, as adjusted by any stock splits that may occur. The exercise price per share of any approved options will be the closing price of Krystal's common stock on January 31, 2022. Any and all equity grants shall vest in four equal annual installments commencing on the Employee's first anniversary. Employee's entitlement to any equity grant is conditioned upon Employee's signing of an appropriate Equity Incentive Agreement and the terms of the relevant equity incentive plans under which the options are granted, including vesting requirements.

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

f. Expenses. The Company shall reimburse Employee for reasonable business expenses incurred in the performance of Employee's duties hereunder, in accordance with the Company's travel and expense policy.

3. AT-WILL EMPLOYMENT; TERMINATION BY COMPANY

a. At-Will Termination by Company. The employment of Employee shall be "at-will" at all times. The Company may terminate Employee's employment with the Company at any time, without any advance notice, for any reason or no reason at all, notwithstanding anything to the contrary contained in or arising from any statements, policies or practices of the Company relating to the employment, discipline or termination of its employees. Upon and after such termination, all obligations of the Company under this Agreement shall cease. In the event of any such termination by the Company for any reason other than Cause, the Company shall pay to Employee an amount equal to six months of her then-current Base Salary, which payment may, at the request of the Company, be conditioned upon Employee's execution of a usual and customary general release in favor of the Company. "Cause" shall be defined as any of the following: (i) an intentional act of fraud, embezzlement, theft or any other material violation of law that occurs during or in the course of Employee's employment with company; (ii) intentional damage to the Company's assets; (iii) intentional disclosure of Company's confidential information contrary to Company's policies; (iv) intentional breach of Employee's obligations under this agreement; (v) intentional engagement in any competitive activity which would constitute a breach of Employee's duty of loyalty or of Employee's obligations under this agreement; (vi) intentional breach of any of the Company's policies; (vii) the willful and/or continued failure to substantially perform Employee's duties for company (other than as a result of incapacity due to physical or mental illness); (viii) inability to make agreed upon improvements resulting from a clearly outlined and mutually agreed upon Performance Improvement Plan ("PIP") or (ix) willful conduct by Employee that is demonstrably and materially injurious to company, monetarily or otherwise.

4. AT-WILL EMPLOYMENT; TERMINATION BY EMPLOYEE

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

5. TERMINATION OBLIGATIONS

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

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

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

6. INVENTIONS AND PROPRIETARY INFORMATION; PROHIBITION ON THIRD PARTY INFORMATION

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

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

c. Noncompetition. In consideration of the Company's extension to Employee of full time employment with the Company, the Employee agrees that at no time during the Employee's employment with the Company, and for a period of one (1) year immediately following the termination of such employment (regardless of the

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

7. AMENDMENTS; WAIVERS; REMEDIES

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

8. ASSIGNMENT; BINDING EFFECT

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

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

9. NOTICES

All notices or other communications required or permitted hereunder shall be made in writing and shall be deemed to have been duly given if delivered: (a) by hand; (b) by a nationally recognized overnight courier service; or (c) by United States first class registered or certified mail, return receipt requested, to the principal address of the other party, as set forth below. The date of notice shall be deemed to be the earlier of (i) actual receipt of notice by any permitted means, or (ii) five business days following dispatch by overnight delivery service or the United States Mail. Employee shall be obligated to notify the Company in writing of any change in Employee's address. Notice of change of address shall be effective only when done in accordance with this paragraph.

Company's Notice Address:

Krystal Biotech, Inc.
2100 Wharton Street, Suite 310
Pittsburgh, PA 15203
Attention: Josh Suskin
Email: jsuskin@krystalbio.com

Employee's Contact Information:

Jing L. Marantz
157 Aspinwall Avenue
Brookline, MA 02446
Email: jnj.marantz@gmail.com

10. SEVERABILITY

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

11. TAXES

All amounts paid under this Agreement shall be paid less all applicable state and federal tax withholdings and any other withholdings required by any applicable jurisdiction or authorized by Employee.

12. GOVERNING LAW

This Agreement shall be governed by and construed in accordance with the laws of the Commonwealth of Pennsylvania without regard to the conflict of law principles. Parties agree to first try to mediate any conflict arising under this Agreement or a matter related thereto. If such a conflict cannot be resolved through mediation, then any suit or action shall be brought in an appropriate federal or state court located in Allegheny County, Pennsylvania.

13. INTERPRETATION

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

14. COUNTERPARTS

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

15. AUTHORITY

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

16. ENTIRE AGREEMENT

This Agreement is intended to be the final, complete, and exclusive statement of the terms of Employee's employment by the Company and may not be contradicted by evidence of any prior or contemporaneous statements or agreements, except for agreements specifically referenced herein (including the Employee Proprietary Information and Inventions Agreement attached as Exhibit A and the Company's Equity Incentive Plan and Equity Incentive Agreement). To the extent that the practices, policies or procedures of the Company, now or in the future, apply to

Employee and are inconsistent with the terms of this Agreement, the provisions of this Agreement shall control. Any subsequent change in Employee's duties, position, or compensation will not affect the validity or scope of this Agreement.

17. EMPLOYEE ACKNOWLEDGEMENT

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

IN WITNESS WHEREOF, the parties have duly executed this Agreement as of the date first written above.

KRYSTAL BIOTECH, INC.

By: DocuSigned by: Kathryn Romano 9FB22765999540D...

Kathryn Romano

Title: Chief Accounting Officer

Jing L. Marantz

DocuSigned by: Jing Marantz 2D1CBA3E27784D5...

Name:

Employee

SIXTH AMENDMENT TO LEASE AGREEMENT /
FIRST AMENDMENT TO STORAGE SPACE AGREEMENT

THIS SIXTH AMENDMENT TO LEASE AGREEMENT / FIRST AMENDMENT TO STORAGE SPACE AGREEMENT (this "***Amendment***") is made as of the 13th day of January 2021, by and between Wharton Lender Associates, LP, a Pennsylvania limited partnership ("***Landlord***"), and Krystal Biotech, Inc., a Delaware corporation, formerly known as Krystal Biotech, LLC, a California limited liability company ("***Tenant***").

WITNESSETH:

WHEREAS, by Lease dated May 26, 2016 (the "***Original Lease***"), as amended by First Amendment to Lease Agreement dated July 26, 2016, Second Amendment to Lease Agreement dated February 27, 2017, Third Amendment to Lease Agreement dated May 31, 2018, Fourth Amendment to Lease Agreement dated October 22, 2018, (the "***Fourth Amendment***"), and Fifth Amendment to Lease Agreement dated December 10, 2018 (the "***Fifth Amendment***") (the Original Lease as amended, collectively, the "***Lease***"), Landlord currently leases to Tenant and Tenant currently leases from Landlord certain premises consisting of a total of 25,376 rentable square feet (the "***Current Premises***") located in that certain building known as 2100 Wharton Street, Pittsburgh, Pennsylvania (the "***Building***"), being comprised of 10,978 rentable square feet on the 7th Floor of the Building and 14,398 rentable square feet on the 3rd floor of the Building; and

WHEREAS, by Storage Space Agreement dated April 27, 2020 (the "***Storage Space Agreement***"), Landlord currently leases to Tenant and Tenant currently leases from Landlord certain storage space consisting of 2,060 square feet on the 3rd Floor of the Building (the "***Storage Space***"); and

WHEREAS, Landlord and Tenant now desire to amend the Lease to: (i) lease to Tenant an additional 2,494 rentable square feet of office space located on the 3rd Floor of the Building, as outlined on Exhibit "A" attached hereto and made a part hereof (the "***Third Floor Additional Space***"), thereby increasing Tenant's rentable area of office space in the Building to a total of 27,870 rentable square feet of office space in the Building; and (ii) modify certain other terms of the Lease, all in accordance with the terms and provisions hereof

WHEREAS, Landlord and Tenant also desire to amend the Storage Space Agreement in accordance with the terms and provisions hereof.

NOW THEREFORE, the parties hereto, in consideration of the mutual premises contained herein, and intending to be legally bound hereby, do covenant and agree as follows:

1. Recitals. The foregoing preamble is incorporated by reference herein as if set forth at length. Capitalized terms not otherwise defined herein shall have the meaning given to such terms in the Lease. All references herein to the Lease shall include this Amendment.

2. Third Floor Additional Space; Third Floor Additional Space Commencement Date.

(a) Effective as of the Third Floor Additional Space Commencement Date (as defined below), the Premises shall be comprised of the Current Premises and the Third Floor Additional Space, for a total of 27,870 rentable square feet, consisting of 10,978 rentable square feet on the 7th Floor of the Building and 16,892 rentable square feet on the 3rd Floor of the Building.

(b) Third Floor Additional Space Commencement Date; Expiration Date. The Term of the Lease for the Third Floor Additional Space and Tenant's obligation to pay Fixed Rent and additional rent for the Third Floor Additional Space shall commence on the earlier to occur of the following (as applicable the earlier to occur, the "***Third Floor Additional Space Commencement Date***"): (i) the date that Tenant occupies and begins conducting business operations in all or part of the Third Floor Additional Space; (ii) the date upon which Landlord's Third Floor Additional Space Work (as defined in Section 6(a) below) has been Substantially Completed (as defined in Section 6(b) below); *provided, however*, that (x) in no event shall the Third Floor Additional Space Commencement Date occur prior to March 1, 2021 and (y) if a Tenant Delay (as defined in Section 2(e) below) occurs and Tenant has been notified thereof as required by Section 2(e) below, then the Third Floor Additional Space Commencement Date shall be deemed to be the date that the Landlord's Third Floor Additional Space Work would have been Substantially Completed but for the Tenant Delay, as determined by Landlord in good faith. Promptly after the occurrence of the Third Floor Additional Space Commencement Date, Landlord and Tenant shall execute a memorandum that memorializes the Third Floor Additional Space Commencement Date. The expiration date of the Third Floor Additional Space Term shall be the Expiration Date set forth in the Lease for the Current Premises.

(c) Landlord's Failure to Timely Deliver Third Floor Additional Space. Subject to any Force Majeure Delay (as defined in Section 2(d) below) and any Tenant Delay, and provided that this Amendment is executed by Tenant by January 15, 2021, time being of the essence, in the event Landlord's Third Floor Additional Space Work has not been Substantially Completed on or before May 31, 2021 (the "***Outside Delivery Date***"), Tenant shall be entitled to Fixed Rent abatement for the Third Floor Additional Space only equal to one (1) day of Fixed Rent for the Third Floor Additional Space only for each one (1) day of delay beyond the Outside Delivery Date on a day for day basis until the Landlord's Third Floor Additional Space Work has been Substantially Completed.

(d) Force Majeure Delay. As used herein, "***Force Majeure Delay***" means any actual delay (measured in days) that Landlord encounters in the performance of Landlord's Third Floor Additional Space Work, to the extent that such delay is directly caused by any "Force Majeure" event of a type contemplated in Section 24.J of the Original Lease. In order for Landlord to claim a Force Majeure Delay, Landlord must provide written notice to Tenant via email only to kromano@krystalbio.com within five (5) business days of the date upon which Landlord actually learns of the applicable act or event that will result in such a delay, which notice must specify Landlord's reasonable determination of the cause of the delay, Landlord's plans to restart work following such delay. For the sake of clarity, Landlord's failure to provide

the written notice contemplated in the previous sentence (x) shall in no event entitle Tenant to claim Landlord is in default of any obligation under the Lease, but (y) shall preclude Landlord from claiming a Force Majeure Delay for any period for which such written notice has not been provided.

(e) Tenant Delay. As used herein, "***Tenant Delay***" means any actual delay (measured in days) that Landlord encounters in the performance of Landlord's Third Floor Additional Space Work, to the extent that such delay is directly caused by (1) any act or omission by Tenant or its employees, agents or contractors which interferes with the performance of Landlord's Third Floor Additional Space Work, (2) changes to Landlord's Third Floor Additional Space Work requested by Tenant and agreed by Landlord following the date of this Amendment, or (3) Tenant's failure to respond to Landlord within five (5) days after Landlord seeks Tenant's feedback for any item of Landlord's Third Floor Additional Space Work, when Tenant's feedback is required to continue work in respect of such item. In order for Landlord to claim a Tenant Delay, Landlord must provide written notice to Tenant via email only to kromano@krystalbio.com within five (5) business days of the date upon which Landlord actually learns of the applicable act or omission that will result in such a delay, which notice must specify Landlord's reasonable determination of the cause of the delay. For the sake of clarity, Landlord's failure to provide the written notice contemplated in the previous sentence (x) shall in no event entitle Tenant to claim Landlord is in default of any obligation under the Lease, but (y) shall preclude Landlord from claiming a Tenant Delay for any period for which such written notice has not been provided.

3. Fixed Rent for the Third Floor Additional Space. Commencing on the Third Floor Additional Space Commencement Date and thereafter for the remainder of the Lease Term, Tenant shall pay Landlord Fixed Rent for the Third Floor Additional Space pursuant to the terms of the Lease and in accordance with the following table at the annual rates as follows:

LEASE PERIOD	PORTION OF PREMISES	$PER RENTABLE SQ FT	MONTHLY FIXED RENT INSTALLMENT	ANNUAL FIXED RENT AMOUNT
Additional Third Floor Space Commencement Date – 2/28/22	2,494 rsf Third Floor Additional Space	23.41	$4,865.38	$58,384.56
3/1/22 – 2/28/23	2,494 rsf Third Floor Additional Space	23.88	$4,963.06	$59,556.72
3/1/23 – 2/29/24	2,494 rsf Third Floor Additional Space	24.36	$5,062.82	$60,753.84
3/1/24 – 2/28/25	2,494 rsf Third Floor Additional Space	24.85	$5,164.66	$61,975.92
3/1/25 – 2/28/26	2,494 rsf Third Floor Additional Space	25.35	$5,268.58	$63,222.96

3/1/26 – 2/28/27	2,494 rsf Third Floor Additional Space	25.86	$5,374.57	$64,494.84

All Fixed Rent shall be payable in equal monthly installments in advance on the first day of each month during the Term without demand, notice, offset or deduction.

4. Tenant's Share; Tenant's Percentage. Commencing as of the Third Floor Additional Space Commencement Date, "Tenant's Percentage" as defined in Paragraph 1.L. of the Original Lease and "Tenant's Share", as defined in Paragraph 4.A.(ii) of the Original Lease shall mean "12.32%", and all references in the Lease to "Tenant's Share" and "Tenant's Percentage" shall mean "12.32%".

5. Condition of the Premises. Notwithstanding anything contained in the Lease to the contrary, except solely for Landlord's Third Floor Additional Space Work (as defined in Section 6 below): (i) Landlord shall deliver the Third Floor Additional Space to Tenant and Tenant accepts delivery and possession of the Third Floor Additional Space in its current "as-is" where is condition; and (ii) Tenant shall perform, at Tenant's sole cost and expense, all other work and modifications to the Premises that is required, necessary or desired; and (iii) Tenant's continued possession of the Current Premises for the shall be in its current "as-is" where is condition.

6. Landlord's Third Floor Additional Space Work.

(a) Notwithstanding anything to the contrary contained in the Lease, the Third Floor Additional Space shall be delivered in its current "as-is" condition, except that Landlord shall perform the work described in Exhibit "B" attached hereto and made a part hereof (the "***Landlord's Third Floor Additional Space Work***"). Landlord shall construct the Landlord's Third Floor Additional Space Work in a good and workmanlike manner and, upon Substantial Completion, the Landlord's Third Floor Additional Space Work shall be in compliance with all applicable laws, statutes, ordinances, codes, orders rules, regulations and other legal requirements applicable to such work. In no event and under no circumstances will Landlord's Third Floor Additional Space Work entail or will Landlord be obliged to perform any work or supply any materials in excess of the work and materials described with particularity in Exhibit "B". All work in the Third Floor Additional Space other than Landlord's Third Floor Additional Space Work, shall be performed by Tenant at Tenant's sole cost and expense. If, during the course of Landlord's performance of the Landlord's Third Floor Additional Space Work or any work performed by Tenant in the Third Floor Additional Space, hazardous materials (including, without limitation, asbestos-containing material) that exceed or are not in compliance with applicable laws are discovered in the Third Floor Additional Space, Landlord shall promptly remove or remediate all such hazardous materials (as and to the extent required by applicable law) at its sole cost and expense.

(b) The Third Floor Additional Space Work shall be deemed to be "***Substantially Completed***" when: (i) the Landlord's Third Floor Additional Space Work shown on Exhibit "B" has been completed (for the sake of clarity, Landlord's Third Floor Additional Space Work does not include any work or improvements to be performed by Tenant, including,

but not limited to Tenant's Data Work (as defined below); and (ii) the Third Floor Additional Space is free of hazardous materials that violate any applicable law or exceed any applicable legal limit, free of construction debris, in broom-clean condition, and with all HVAC and other Building systems serving the Third Floor Additional Space in good working order. Tenant hereby covenants to Landlord that neither Tenant nor any of its employees, agents or contractors shall interfere with Landlord's performance of the Third Floor Additional Space Work. Notwithstanding anything to the contrary contained herein, Tenant shall be responsible, at Tenant's sole cost and expense, for all furniture costs (including, but not limited to, moving and installation), data service and telecommunication wiring, cabling and systems (collectively, "***Tenant's Data Work***"). Tenant shall use fire rated telephone cable for Tenant's phone system.

7. Vehicle Parking. Section 10 of the Fifth Amendment and Section 7. of the Fourth Amendment are hereby deleted in their entirety and replaced with the following (to be effective as of the date of this Amendment):

> "Subject to the Parking Rules set forth in Exhibit B to the Original Lease, as modified by Landlord from time to time (the "***Rules***"), Tenant shall be entitled to use up to fifty-seven (57) unreserved parking spaces in the parking facility of the Property, subject to availability, at the rate of One Hundred Forty and 00/Dollars ($140.00) per month per parking space. Tenant shall pay Landlord, as additional rent, without demand, notice, offset or deduction, the foregoing rate per parking space per month for each month of the remainder of the Term hereof for each of the parking spaces utilized by Tenant. Notwithstanding the foregoing, so long as Tenant is not in material default under the terms of the Lease beyond the expiration of all applicable notice and cure periods, if any, nineteen (19) of the foregoing unreserved parking spaces shall be provided at no charge. Landlord shall use commercially reasonable efforts to accommodate Tenant's future parking spaces requirements, subject to availability of parking spaces (the "***Additional Spaces***") and pursuant to the Rules, at the then current prevailing rate per month per parking space. Tenant shall pay Landlord, as additional rent, without demand, notice, offset or deduction, the then current prevailing rate(s) per parking space per month for each month of the Term for each of the Additional Spaces used, utilized or requested by Tenant.

8. Renewal Option.

(a) So long as no "event of default" by Tenant then exists under the terms of the Lease, Tenant may, at Tenant's option, extend the Term of the Lease for one (1) renewal term of five (5) years commencing on the day immediately following the Expiration Date of the initial Term and terminating on the date that is five (5) years after the Expiration Date of the initial Term (the "***Renewal Term***"). The exercise of the option to renew the Lease must be made by Tenant, in writing ("***Renewal Notice***"), and delivered to Landlord not later than February 28, 2026 ("***Renewal Deadline***"), time being of the essence. Failure by Tenant to deliver to Landlord the Renewal Notice on or before the Renewal Deadline shall be deemed a conclusive waiver of Tenant's option to extend the Term of the Lease. The Renewal Term shall be upon the same terms and conditions set forth in the Lease, subject to the following:

(i) the Fixed Rent for the Renewal Term shall be at a rate per annum equal to the then current fair market rental rate for comparable office and wet lab space in the Pittsburgh, Pennsylvania Metropolitan Statistical Area ("***Fair Market Rent***"); *provided, however*, that in no event will the Fair Market Rent for the Renewal Term be less than the escalated Fixed Rent payable during the last year of the initial Term of this Lease, plus increases of 2% per annum in each year of the Renewal Term, commencing with the second (2nd) year of the Renewal Term; and

(ii) the Base Year for the Renewal Term shall be calendar year 2027.

(b) Landlord shall notify Tenant in writing of Landlord's determination of the Fair Market Rent for the Renewal Term within thirty (30) days following receipt of Tenant's Renewal Notice for its exercise of the Renewal Term ("***Landlord's FMR Notice***"). Tenant shall notify Landlord in writing thirty (30) days after its receipt of Landlord's FMR Notice whether or not it accepts Landlord's determination of Fair Market Rent. If Tenant accepts Landlord's determination, then the Fair Market Rent set forth in Landlord's FMR Notice shall be final and binding upon Tenant for the Renewal Term. Tenant's failure to respond to Landlord's FMR Notice within the aforementioned 30-day period shall be deemed an acceptance by Tenant of Landlord's determination of Fair Market Rent for the Renewal Term. If Tenant delivers written notice ("***Tenant's Rejection Notice***") to Landlord within the aforementioned 30-day period rejecting either Landlord's determination of Fair Market Rent, the parties agree to negotiate their differences in good faith within the following thirty (30) days following Landlord's receipt of Tenant's Rejection Notice (the "***FMR Negotiation Period***").

(c) Tenant may exercise the option to renew only for all of the Premises. Tenant may exercise this option to renew only by delivering its written Renewal Notice to Landlord not later than the Renewal Deadline. Failure by Tenant to deliver to Landlord the Renewal Notice on or before the Renewal Deadline shall be deemed a conclusive waiver of Tenant's option to extend the Term of the Lease.

(d) After a final determination has been made of the Fair Market Rent as of the commencement of the Renewal Term, Landlord and Tenant shall execute and deliver to each other a signed Lease amendment memorializing the Fixed Rent for the Renewal Term as hereinabove determined.

9. Expiration Date of Storage Space Agreement. The second sentence of Section 3 of the Storage Space Agreement shall be deleted in its entirety and replaced with the following:

"This Storage Space Agreement shall terminate on the date upon which the Office Lease expires or terminates (the "Expiration Date")."

10. Tenant's Generators; Insurance. During the Term of this Lease, Tenant shall have the right to maintain Tenant's three (3) generators (the "***Tenant's Generators***") in their existing locations under the terms and conditions in this Section 10. Tenant's Generators are currently (and shall remain) located on the area of the roof and outside of the first floor of the Building as set forth in Exhibit "C" attached hereto and made a part hereof. Landlord shall not charge any

fee for the Tenant's Generators, *provided, however*, that, notwithstanding anything to the contrary contained in the Lease, Tenant shall be solely responsible for all costs and expenses associated with the Tenant's Generators, including, but not limited to the costs of design, permits, approvals, installation, maintenance, utilities, cleaning, power, structural issues, roof warranty compliance, repair, removal, liability and operation of and relating to Tenant's Generators all generator devices and equipment. Tenant shall be solely liable for the Tenant Generators and any and all matters arising from and/or in connection with Tenant's Generators. Tenant's Generators and all equipment or any portion thereof shall be at Tenant's sole risk. Tenant releases, remises, discharges and acquits the Landlord along with its agents, representatives, assigns, predecessors, successors, insurers, sureties and mortgage lenders from any and all claims which the Tenant may have against any of them arising from, relating to, or in connection with the Tenant's Generators. In addition, Tenant agrees to indemnify, defend and hold harmless Landlord and its representatives from and against all claims, actions, losses, liabilities, damages, liabilities, costs and expenses of any nature whatsoever (including attorneys' and other legal fees and costs) arising from or relating to the Tenant's Generators and related equipment, including, but not limited installation, maintenance, replacement, use or removal of Tenant's Generators and all related facilities and equipment (including, without limitation, for any liabilities or damages related to any of Tenant's Generators failing to comply with any applicable laws, regulations or ordinances, or for any damage caused by the Tenant's Generators or as a result of servicing Tenant's Generators which damages the roof of the Building or otherwise voids the warranty for the roof of the Building). Except as otherwise expressly set forth herein, Landlord shall maintain responsibility for all maintenance obligations set forth in Paragraph 13 of the Original Lease. For the sake of clarification, Tenant shall be liable for all costs and expenses for all roof repairs and restoration arising from Tenant's Generators and/or related facilities and equipment. Upon Tenant's execution of this Amendment and at any time during the Term upon Landlord's request, Tenant shall deliver to Landlord a certificate of insurance naming Landlord as additional insured and satisfactory to Landlord covering the Tenant's Generators and Tenant's contractual obligations of indemnification with respect to the Tenant's Generators as set forth in this paragraph. To the maximum extent allowed by applicable law, Landlord and its property manager shall not be responsible or liable for, and Tenant hereby expressly waives all claims against Landlord for, injury to persons caused by the installation and operation of the Tenant's Generators (and the wiring and other equipment related thereto) or damage to the Tenant's Generators or any equipment related thereto (unless caused by the gross negligence or willful misconduct of Landlord or its affiliates, or any of their respective agents, representatives, employees or contractors. Tenant warrants and represents to Landlord that Tenant has not received any notice of violations with regards to Tenant's Generators and, to Tenant's knowledge, Tenant has received all required permits and approvals for all of Tenant's Generators and each of Tenant's Generators conforms with and shall at all times conform with all applicable laws, regulations and ordinances (including Landmarks Preservation Commission). Tenant shall pay all fees to any and all governmental and quasi-governmental authorities relating to or arising from the Tenant's Generators. Tenant shall, at its sole cost and expense, maintain and operate Tenant's Generators in good, clean and safe condition and repair. Tenant shall, during the Term, retain reasonable ingress and egress access to and from the Tenant's Generators in order to permit Tenant with the ability to so maintain and operate the Tenant's Generators under the terms and conditions of this Section 10. The Tenant's Generators shall be used only for periodic testing or in the event Tenant's primary electrical service is interrupted. The Tenant's

Generators shall be used only for backup power and may not be used as a primary power source, nor may any of the Tenant's Generators be used by any occupant of the Building besides Tenant. Tenant shall be solely responsible, at Tenant's sole cost, expense and liability, for Tenant's Generators, and Tenant shall at all times ensure that the Tenant's Generators do not (i) damage the roof or any area of or outside the Building or (ii) interfere with any other tenant's use of the Building or (iii) interfere with any of the Building's communications systems, roof warranty, or any other Building systems. Upon Landlord's request upon the expiration or earlier termination of this Lease, Tenant shall remove the Tenant's Generators and all related equipment. Tenant shall repair and restore the areas of the Building (including the roof of the Building and outdoor areas surrounding the Building) at Tenant's expense, in accordance with this Section 10 and the terms of Paragraphs 11 and 12 of the Original Lease, provided, that in the event of any inconsistency between this Section 10 and Paragraphs 11 and 12 of the Original Lease, this Section 10 shall control. For the sake of clarity, Tenant shall be responsible for all costs and expenses arising from Tenant's installation, maintenance and/or removal of Tenant's Generators including, but not limited to, all damage to the roof and the Building that is caused by or arising from Tenant's installation, maintenance or removal of Tenant's Generators.

11. Broker. Landlord and Tenant each hereby represents and warrants to the other that it has not dealt with any real estate broker, sales person, or finder in connection with this Amendment except for Landlord's Broker, CBRE, Inc. ("***Broker***"). Landlord shall be responsible for the payment of any commission owed to the Broker based upon Landlord's separate agreement with such Broker. Landlord and Tenant each agree to indemnify and hold harmless the other party and their respective agents and employees, from and against any and all liabilities and claims for commissions and fees arising out of a breach of the foregoing representation (including without limitation, any other broker claiming to have been engaged by such indemnifying party in connection with this Amendment).

12. Full Force and Effect. Except as specifically set forth herein, the terms, covenants and conditions of the Lease shall remain in full force and effect. The Lease and this Amendment shall not be further modified or amended, except in writing signed by both Landlord and Tenant. This Amendment sets forth the entire understanding of the parties with respect to the matters set forth herein and there are no other rights, including but not limited to, any renewals, extensions, expansions, purchases, rights of first refusal, allowances, etc., granted to Tenant other than those expressly set forth in the Lease that have not been deleted or otherwise nullified or this Amendment. Landlord and Tenant hereby ratify and affirm all of the remaining terms and conditions of the Lease not modified or supplemented by this Amendment. Tenant hereby acknowledges that, as of the date of this Amendment, Landlord is not in default of any of the terms and conditions of the Lease.

13. Provisions Binding. All rights and liabilities herein given to or imposed upon the parties to this Amendment shall extend to, and be binding upon and inure to the benefit of, the parties hereto and their respective successors and assigns.

14. Confidentiality. Tenant agrees that it shall maintain in confidence and shall not divulge to any third party (except to its employees, brokers, attorneys, accountants or other professional service providers as needed, or as may otherwise be required by the Securities and

Exchange Commission or applicable law) any of the items, covenants and conditions of the Lease and this Amendment, including without limitation, any information related to the rental rate, the length of the Term, and any other terms and conditions thereof. Tenant further agrees to take commercially reasonable precautions to prevent the unauthorized disclosure of any such information to any third parties. Tenant's obligations under this Section 14 shall survive the termination of the Lease.

15. Counterparts; Delivery. This Amendment may be executed in any number of counterparts, and by each of the parties on separate counterparts, each of which, when so executed, shall be deemed an original, but all of which shall constitute but one and the same instrument provided that all parties execute and deliver a counterpart to the other party. Delivery of an executed counterpart of this Amendment by electronic delivery shall be equally as effective as delivery of a manually executed counterpart of this Amendment. Any party delivering an executed counterpart of this Amendment by electronic delivery shall also endeavor to deliver a manually executed counterpart of this Amendment, but the failure to deliver a manually executed counterpart shall not affect the validity, enforceability or binding effect of this Amendment.

[SIGNATURE PAGE FOLLOWS]

IN WITNESS WHEREOF, the parties hereto have executed this Sixth Amendment to Lease Agreement / First Amendment to Storage Space Agreement on the day and year set forth below.

LANDLORD:

WHARTON LENDER ASSOCIATES, LP,
a Pennsylvania Limited Partnership

By: WHARTON LENDER PROPERTIES, LLC,
a Pennsylvania Limited Liability Company,
its General Partner

By: _____
Name: Larry Walsh
Title: COO
Date: January ___, 2021

TENANT:

KRYSTAL BIOTECH INC.,
a Delaware corporation

By: _____
Name: Kathryn A. Romano
Title: CAO
Date: January 12, 2021

LEGAL

EXHIBIT "A"

Third Floor Additional Space

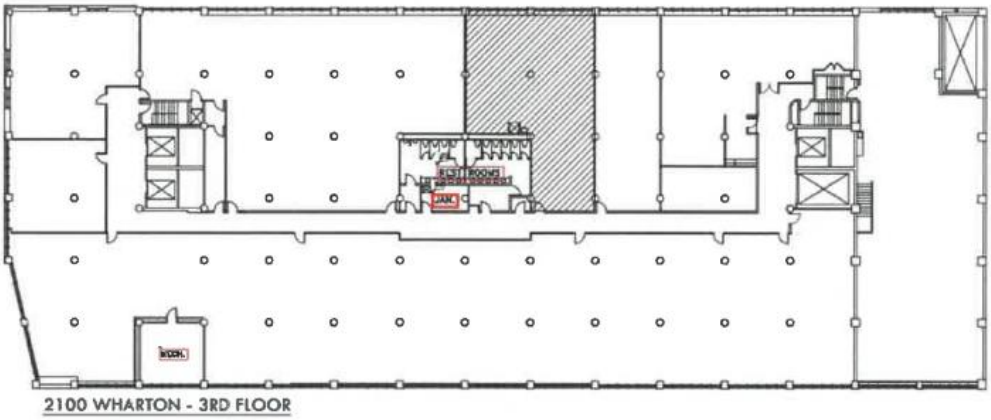
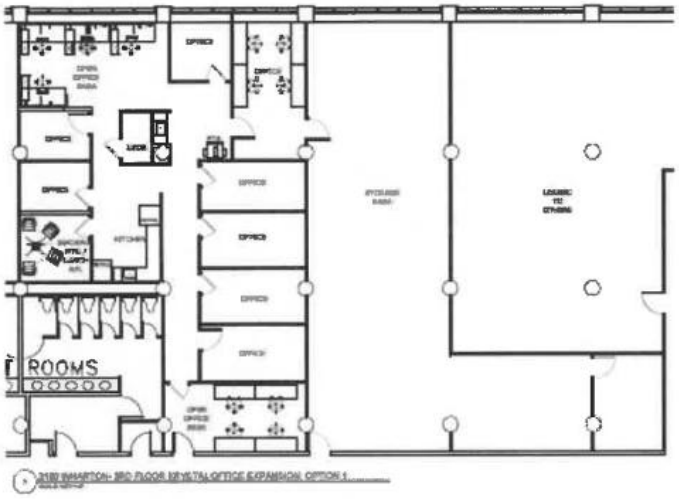


EXHIBIT "B"

Landlord's Third Floor Additional Space Work



Entrance Doors:
Entry door to remain as-is. Signage can be installed by Tenant with the approval of Landlord (which approval shall not be unreasonably withheld or delayed). Tenant shall submit layout and design to Landlord for approval prior to ordering and installation.

Interior Partitions:
Existing partitions to remain with the exception of the ones that are moving. Drywall construction consisting of 3-5/8" steel studs at 24" on-center with one layer 5/8" wall board on each side extending to ceiling grid.

Interior Doors:
Doors shall be reused from demo and reinstalled. Ensure existing doors are in good condition, and repair where needed.

Ceilings:
Existing ceiling grid and tile shall remain. Repair where partitions are demolished.

Lighting:
Remove all existing parabolic and downlights and install new Building Standard 2' x 4' Recessed LED Lights Cree ZR24-40L-35K-10V.

Carpet:
Existing carpet tile shall be removed and new Shaw carpet tile 5T156 Tinge 9" x 36" in color 56861 Tarnished shall be installed.

Base:
New 4" vinyl base shall be installed in a color Burnt Umber.

Paint:
Premises shall receive two (2) coats eggshell finish in colors approved by Tenant. No more than four (4) colors shall be used within the Premises. Colors shall match the Third Floor Additional Space; Blue accent color is Raincheck; General Paint Color is Sherwin Williams SW7004 Snowbound.

Casework:
Existing casework shall remain.

Switches:
Existing switches to remain.

Duplex Outlets/ Floor Outlets:
Existing outlets to remain with the exception on new outlets installed on new partitions and new furniture feed installed for Tenant installed furniture.

Data / Telephone Outlets:
Tenant is responsible for phone and data cabling and system. Tenant-installed phone system must use fire rated telephone cable.

Window Treatment:
All windows to have blinds to match existing. No other type of window cover shall be visible from exterior of the Building. All existing blinds shall be cleaned and made operational.

Plumbing:
Existing sinks shall remain.

HVAC:
Existing ductwork shall remain and be reworked / supplied with new as needed to work with new floor plan.

Fire Protection:
Existing sprinkler system shall remain and be adjusted to work with new floor plan. Concealed sprinkler heads shall be installed in rooms scheduled for a drop acoustical ceiling.

Fire Alarm system:
Fire alarm locations shall be adjusted to work with new floor plan. New locations shall be coordinated with new floor plan and furniture layout.

Notes:

1. A construction supervision fee will be charged for all nonstandard work not identified as part of this Exhibit ("***Non-Standard Additional Work***"), which construtions supervision fee shall not exceed three percent (3%) of the hard costs incurred in connection with such Non-Standard Additional Work.

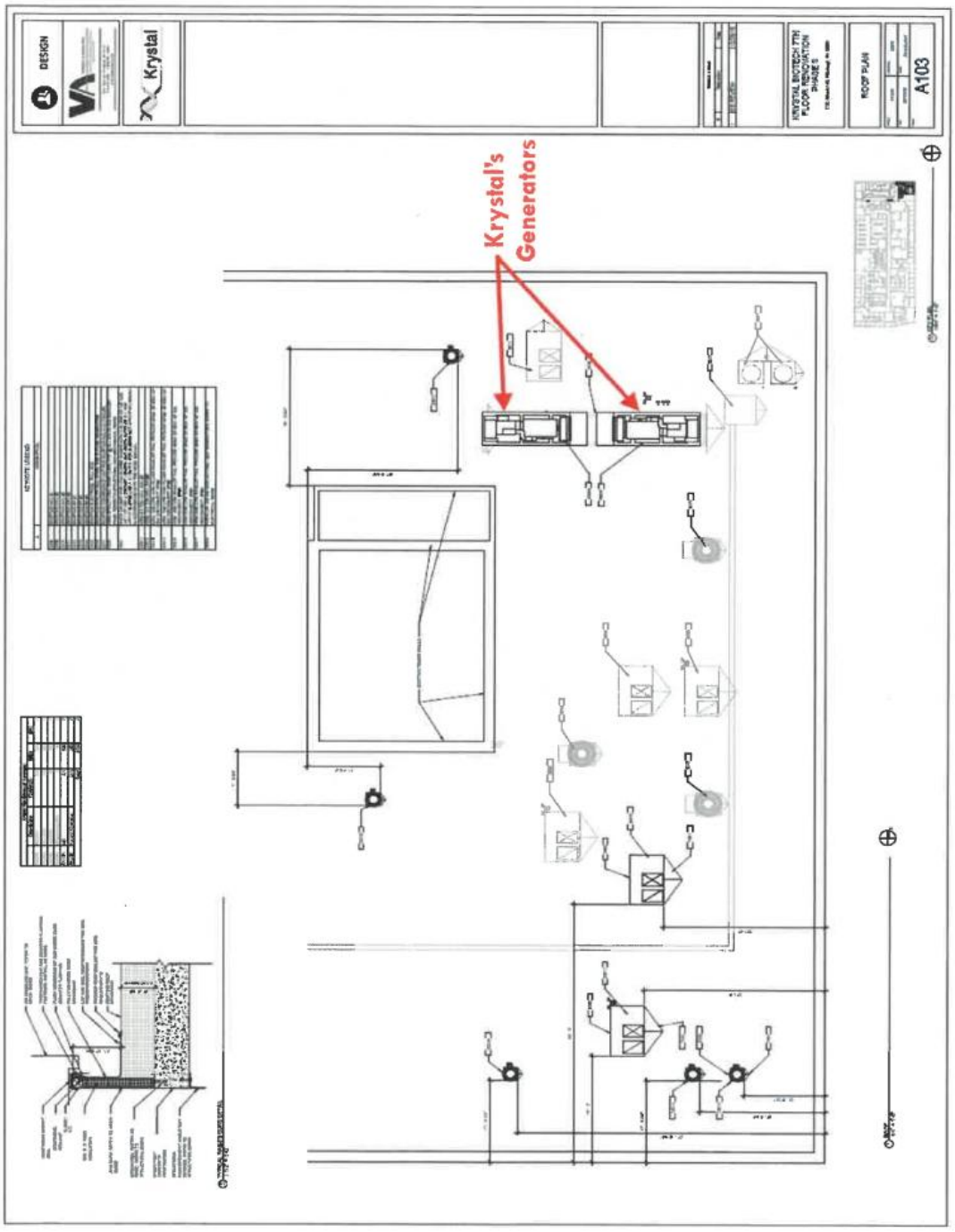
2. No credit will be given for items listed in this Exhibit but not used on the project.

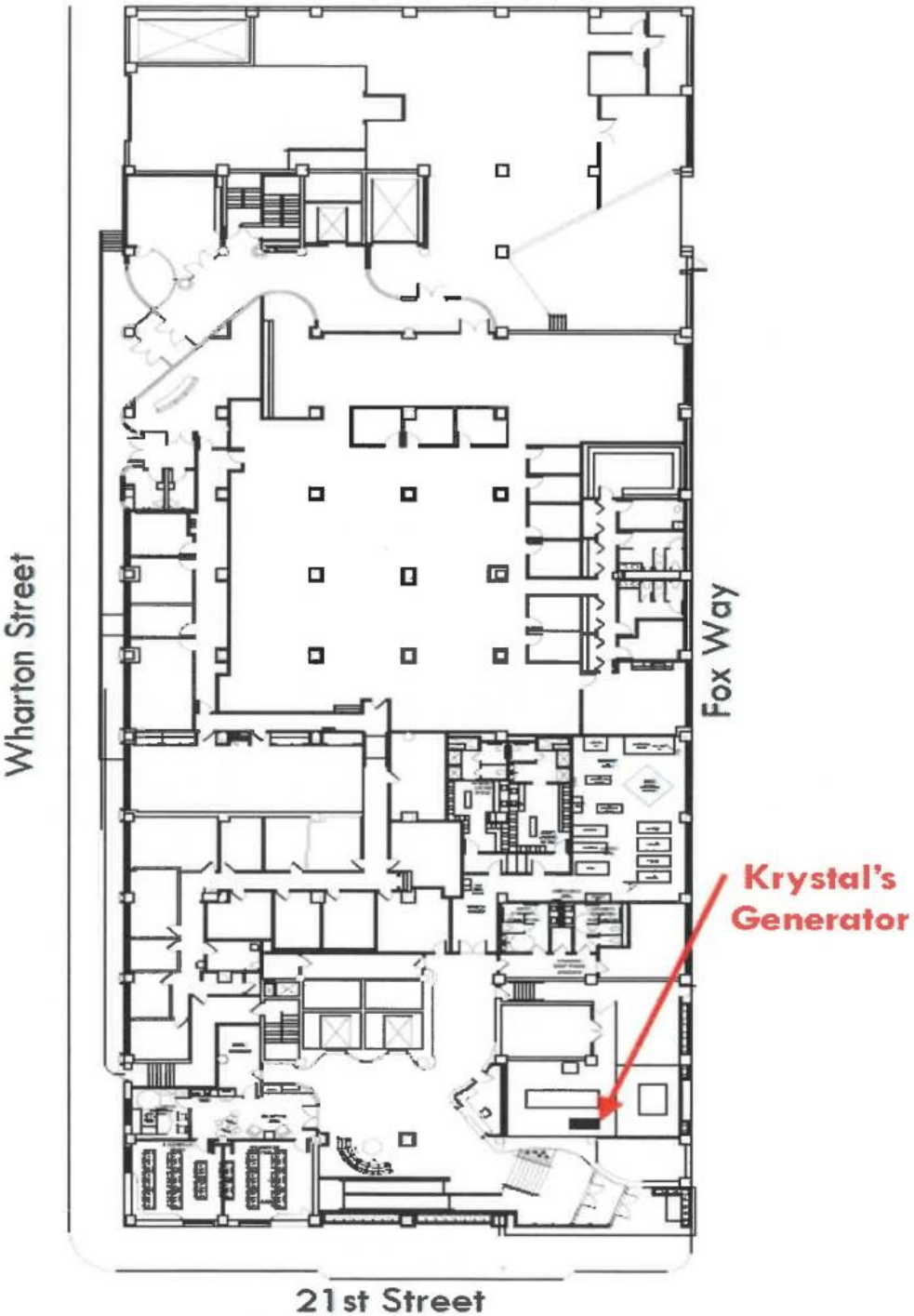
3. Equipment, furniture and workstations are shown on this drawing for reference and coordination purposes only. Except as otherwise expressly set forth in this Exhibit, all equipment, furniture and workstations shall be installed at Tenant's sole cost and expense.

4. Installation of Tenant furnished items (AV, IT, Security) shall be permitted and coordinated during the construction period for Landlord's Third Floor Additional Space Work.

EXHIBIT "C'

Depiction of Tenant's Generators





2100 WHARTON STREET
FIRST FLOOR

SEVENTH AMENDMENT TO LEASE AGREEMENT

THIS SEVENTH AMENDMENT TO LEASE AGREEMENT (this "***Seventh Amendment***") is made as of the 11 day of May 2021 (the "***Effective Date***"), by and between Wharton Lender Associates, LP, a Pennsylvania limited partnership ("***Landlord***"), and Krystal Biotech, Inc., a Delaware corporation, formerly known as Krystal Biotech, LLC, a California limited liability company ("***Tenant***").

WITNESSETH:

WHEREAS, by Lease dated May 26, 2016 (the "***Original Lease***"), as amended by First Amendment to Lease Agreement dated July 26, 2016, Second Amendment to Lease Agreement dated February 27, 2017, Third Amendment to Lease Agreement dated May 31, 2018 (the "***Third Amendment***"), Fourth Amendment to Lease Agreement dated October 22, 2018, (the "***Fourth Amendment***"), Fifth Amendment to Lease Agreement dated December 10, 2018 (the "***Fifth Amendment***") and Sixth Amendment to Lease Agreement/First Amendment to Storage Space Agreement dated January 13, 2021 (the "***Sixth Amendment***") (the Original Lease as amended, collectively, the "***Lease***"), Landlord currently leases to Tenant and Tenant currently leases from Landlord certain premises consisting of a total of 27,870 rentable square feet (the "***Existing Premises***") located in that certain building known as 2100 Wharton Street, Pittsburgh, Pennsylvania (the "***Building***"), being comprised of 10,978 rentable square feet on the 7th Floor of the Building, designated as Suite 701, and 16,892 rentable square feet on the 3rd floor of the Building, designated as Suite 301; and

WHEREAS, by Storage Space Agreement dated April 27, 2020 (the "Storage Space Agreement"), Landlord currently leases to Tenant and Tenant currently leases from Landlord certain storage space consisting of 2,060 square feet on the 3rd Floor of the Building (the "***Storage Space***"); and

WHEREAS, Landlord and Tenant now desire to amend the Lease to: (i) lease to Tenant an additional 7,578 rentable square feet of office space located on the 7th Floor of the Building, designated as Suite 720, as outlined on Exhibit "A" attached hereto and made a part hereof (the "***Seventh Floor Additional Space***"), and 6,003 rentable square feet of office space located on the 6th Floor of the Building, designated as Suite 625, as outlined on Exhibit "B" attached hereto and made a part hereof (the "***Sixth Floor Space***"), thereby increasing Tenant's rentable area of office space in the Building to a total of 41,451 rentable square feet of office space in the Building; (ii) extend the Term of the Lease; and (iii) modify certain other terms of the Lease, all in accordance with the terms and provisions hereof.

NOW THEREFORE, the parties hereto, in consideration of the mutual premises contained herein, and intending to be legally bound hereby, do covenant and agree as follows:

1. Recitals. The foregoing preamble is incorporated by reference herein as if set forth at length. Capitalized terms not otherwise defined herein shall have the meaning given to such terms in the Lease. All references herein to the Lease shall include this Seventh Amendment.

2. Sixth Floor Space.

(a) Commencing as of the Effective Date hereof, the Sixth Floor Space shall become part of the Premises, accordingly, the Term of the Lease for the Sixth Floor Space and Tenant's obligation to pay Fixed Rent and additional rent for the Sixth Floor Space shall commence on the Effective Date hereof. Accordingly, effective as of the Effective Date until the Seventh Floor Additional Space Commencement Date (as defined below), "Premises" shall mean 33,873 rentable square feet in the Building.

(b) Sixth Floor Space Utilities, Janitorial and Cleaning. Notwithstanding anything to the contrary contained in the Lease, Tenant shall be responsible, at Tenant's sole cost and expense, for providing: (i) cleaning and janitorial services in a first class manner and keeping with the standards of the Building, including, but not limited to garbage and rubbish removal on a daily basis and the costs of dumpsters and services thereof for the Sixth Floor Space; and (ii) all extraordinary utilities usage, costs and expenses (e.g., above standard office usage) used in the Sixth Floor Space.

(c) Sixth Floor Space Utilities, Janitorial and Cleaning. Notwithstanding anything to the contrary contained in the Lease, Tenant shall be permitted to use the Sixth Floor Space for general office and/or warehouse use (including inventory storage), and Tenant shall be permitted to install workstations therein, provided that no more than fifty percent (50%) of floor area comprising the Sixth Floor Space shall be used for such workstations, at Tenant's sole cost and expense, subject in all respects to the terms and conditions set forth in the Lease.

3. Seventh Floor Additional Space; Seventh Floor Additional Space Commencement Date.

(a) Effective as of the Seventh Floor Additional Space Commencement Date (as defined below), the Seventh Floor Additional Space shall become part of the Premises. Accordingly, effective as of the Seventh Floor Additional Space Commencement Date, Premises shall mean 41,451 rentable square feet in the Building.

(b) Seventh Floor Additional Space Commencement Date; Expiration Date. The Term of the Lease for the Seventh Floor Additional Space (being 7,578 rentable square feet) and Tenant's obligation to pay Fixed Rent and additional rent for the Seventh Floor Additional Space shall commence on the earlier to occur of the following (as applicable the earlier to occur, the "***Seventh Floor Additional Space Commencement Date***"): (i) the date that Tenant occupies and begins conducting business operations in all or part of the Seventh Floor Additional Space; and (ii) the date that is one hundred and fifty (150) days after Landlord has delivered possession of the Seventh Floor Additional Space. Promptly after the occurrence of the Seventh Floor Additional Space Commencement Date, Landlord and Tenant shall execute a memorandum that memorializes the Seventh Floor Additional Space Commencement Date and the Expiration Date (as extended pursuant to Section 4 below).

(c) Subject to any Force Majeure and any Tenant Delay, and provided that Tenant executes this Seventh Amendment or mutually satisfactory indemnification agreement by

May 11, 2021, time being of the essence, in the event Landlord has not delivered possession of the Seventh Floor Additional Space on or before June 15, 2021 (the "***Outside Delivery Date***"), then Tenant shall be entitled to Fixed Rent abatement for the Seventh Floor Additional Space only equal to (i) two (2) days of Fixed Rent for the Seventh Floor Additional Space only for each one (1) day of actual delay in Landlord's delivery of the Seventh Floor Additional Space beyond the Outside Delivery Date on a day for day basis until June 30, 2021 and (ii) four (4) days of Fixed Rent for the Seventh Floor Additional Space only for each one (1) day of actual delay in Landlord's delivery of the Seventh Floor Additional Space beyond June 30, 2021 on a day for day basis until the Landlord delivers possession of the Seventh Floor Additional Space to Tenant.

4. Extended Term of Lease for Premises. The Term of the Lease for the Premises (as expanded pursuant to this Seventh Amendment) is hereby extended for an additional period commencing on the Seventh Floor Additional Space Commencement Date and ending on the date that is ten (10) years after the Seventh Floor Additional Space Commencement Date (the "***Expiration Date***"). In the event the Seventh Floor Additional Space Commencement Date occurs on a day other than the first day of a calendar month, the Term of this Lease shall be extended by the number of days necessary to cause the Expiration Date to be on the last day of the calendar month.

5. Fixed Rent.

(a) Fixed Rent for the Sixth Floor Space. Commencing on the Effective Date hereof and thereafter until February 28, 2027, Tenant shall pay Landlord Fixed Rent for the Sixth Floor Space pursuant to the terms of the Lease and in accordance with the following table at the annual rates as follows:

LEASE PERIOD	PORTION OF PREMISES	$PER RENTABLE SQ FT	MONTHLY FIXED RENT INSTALLMENT	ANNUAL FIXED RENT AMOUNT
Effective Date hereof – 2/28/22	6,003 rsf Sixth Floor Space	20.00	$10,005.00	$120,060.00
3/1/22 – 2/28/23	6,003 rsf Sixth Floor Space	20.40	$10,205.10	$122,461.20
3/1/23 – 2/29/24	6,003 rsf Sixth Floor Space	20.81	$10,410.20	$124,922.43
3/1/24 – 2/28/25	6,003 rsf Sixth Floor Space	21.23	$10,620.31	$127,443.69
3/1/25 – 2/28/26	6,003 rsf Sixth Floor Space	21.65	$10,830.41	$129,964.95
3/1/26 – 2/28/27	6,003 rsf Sixth Floor Space	22.08	$11,045.52	$132,546.24

(b) Fixed Rent for the Existing Premises. From the Effective Date hereof until February 28, 2027, Tenant shall continue to pay Fixed Rent for the Existing Premises being 27,870 rentable square feet (consisting of 10,978 rentable square feet on the 7th Floor and 16,892 rentable

square feet on the 3rd floor) in accordance with the terms of the Original Lease, Third Amendment, Fourth Amendment, Fifth Amendment and Sixth Amendment.

(c) Fixed Rent for the Seventh Floor Additional Space. Commencing on the Seventh Floor Additional Space Commencement Date and thereafter until February 28, 2027, Tenant shall pay Landlord Fixed Rent for the Seventh Floor Additional Space pursuant to the terms of the Lease and in accordance with the following table at the annual rates as follows:

LEASE PERIOD	PORTION OF PREMISES	$PER RENTABLE SQ FT	MONTHLY FIXED RENT INSTALLMENT	ANNUAL FIXED RENT AMOUNT
Seventh Floor Additional Space Commencement Date – 2/28/22	7,578 rsf Seventh Floor Additional Space	23.41	$14,783.42	$177,400.98
3/1/22 – 2/28/23	7,578 rsf Seventh Floor Additional Space	23.88	$15,080.22	$180,962.64
3/1/23 – 2/29/24	7,578 rsf Seventh Floor Additional Space	24.36	$15,383.34	$184,600.08
3/1/24 – 2/28/25	7,578 rsf Seventh Floor Additional Space	24.85	$15,692.78	$188,313.30
3/1/25 – 2/28/26	7,578 rsf Seventh Floor Additional Space	25.35	$16,008.53	$192,102.30
3/1/26 – 2/28/27	7,578 rsf Seventh Floor Additional Space	25.86	$16,330.59	$195,967.08

(d) Fixed Rent for the Premises.

(i) Fixed Rent for the Existing Premises and the Seventh Floor Additional Space. Commencing on March 1, 2027 and thereafter until the Expiration Date (as defined in Section 4 of this Seventh Amendment), Tenant shall pay Landlord Fixed Rent for the Existing Premises and the Seventh Floor Additional Space (consisting of a total of 35,448 rentable square feet) pursuant to the terms of the Lease and in accordance with the following table at the annual rates as follows:

LEASE PERIOD	PORTION OF PREMISES	$PER RENTABLE SQ FT	MONTHLY FIXED RENT INSTALLMENT	ANNUAL FIXED RENT AMOUNT
3/1/27 – 2/29/28	35,448 rsf Existing Premises and Seventh Floor Additional Space	26.38	$77,926.52	$935,118.24
3/1/28 – 2/28/29	35,448 rsf Existing Premises and Seventh Floor Additional Space	26.91	$79,492.14	$953,905.68
3/1/29 – 2/28/30	35,448 rsf Existing Premises and Seventh Floor Additional Space	27.45	$81,087.30	$973,047.60

3/1/30 – 2/28/31	35,448 rsf Existing Premises and Seventh Floor Additional Space	28.00	$82,712.00	$992,544.00
3/1/31 – Expiration Date	35,448 rsf Existing Premises and Seventh Floor Additional Space	28.56	$84,366.23	$1,012,394.80

(ii) Fixed Rent for the Sixth Floor Space. Commencing on March 1, 2027 and thereafter until the Expiration Date, Tenant shall pay Landlord Fixed Rent for the Sixth Floor Space pursuant to the terms of the Lease and in accordance with the following table at the annual rates as follows:

LEASE PERIOD	PORTION OF PREMISES	$PER RENTABLE SQ FT	MONTHLY FIXED RENT INSTALLMENT	ANNUAL FIXED RENT AMOUNT
3/1/27– 2/29/28	6,003 rsf Sixth Floor Space	22.52	$11,265.63	$135,187.56
3/1/28 – 2/28/29	6,003 rsf Sixth Floor Space	22.97	$11,490.74	$137,888.91
3/1/29 – 2/28/30	6,003 rsf Sixth Floor Space	23.43	$11,720.86	$140,650.29
3/1/30 – 2/28/31	6,003 rsf Sixth Floor Space	23.90	$11,955.98	$143,471.70
3/1/31 – Expiration Date	6,003 rsf Sixth Floor Space	24.38	$12,196.10	$146,353.14

All Fixed Rent shall be payable in equal monthly installments in advance on the first day of each month during the Term without demand, notice, offset or deduction.

6. Tenant's Share; Tenant's Percentage. Commencing as of the Effective Date and continuing until the Seventh Floor Additional Space Commencement Date, "Tenant's Percentage" as defined in Paragraph 1.L. of the Original Lease and "Tenant's Share", as defined in Paragraph 4.A.(ii) of the Original Lease shall mean "14.98%" and all references in the Lease to "Tenant's Share and "Tenant's Percentage" shall mean "14.98%". Commencing on the Seventh Floor Additional Space Commencement Date, "Tenant's Percentage" as defined in Paragraph 1.L. of the Original Lease and "Tenant's Share", as defined in Paragraph 4.A.(ii) of the Original Lease shall mean "18.33%", and all references in the Lease to "Tenant's Share" and "Tenant's Percentage" shall mean "18.33%".

7. Condition of the Premises. Notwithstanding anything contained in the Lease to the contrary: (i) Landlord shall deliver the Sixth Floor Space and the Seventh Floor Additional Space to Tenant and Tenant accepts delivery and possession of the Sixth Floor Space and the Seventh Floor Additional Space in their current "as-is" where is condition with the sole exception that Landlord shall remove the current tenant's property and deliver the Seventh Floor Space to Tenant broom-clean and free of all tenancies; and (ii) Tenant shall perform, at Tenant's sole cost and expense, all other work and modifications to the Premises that is required, necessary or desired, subject to, and in accordance with, the terms of the Lease; and (iii) Tenant's continued possession

of the Existing Premises for the Extended Term shall be in its current "as-is" where is condition, subject to clause (ii) above.

8. New Elevator.

(a) Commencing as of the Effective Date, Tenant shall have the right, upon at least two (2) business days' prior written notice to Landlord to request service of the existing freight elevator serving the Building (the "***Freight Elevator***") after regular business hours and on Saturdays and Sundays in accordance to the terms and conditions of this Section 8.(a). Tenant acknowledges and agrees that the use of the Freight Elevator after regular business hours and on Saturdays and Sundays by tenants of the Building will require the Landlord to employ an operator of the Freight Elevator to provide such service after hours (the "After Hours Elevator Service"). In the event Tenant requires such After Hours Elevator Service, Landlord shall use commercially reasonable efforts to employ such operator of the Freight Elevator to provide such After Hours Elevator Service to the Tenant. . Tenant shall reimburse and pay Landlord, as Additional Rent, the reasonable overtime hourly wages paid to such operator of the After Hours Elevator Service for such After Hours Elevator Service(s) provided to Tenant.

(b) Notwithstanding the foregoing, Tenant shall have the option, exercisable in Tenant's sole discretion, to install an elevator lift system between the Sixth Floor Space and the portion of Tenant's Premises located on the Seventh Floor (the "***New Elevator***") pursuant to the following terms and conditions:

(i) In the event Tenant desires to install the New Elevator, Tenant shall provide written notice to Landlord of its election to do so, together with all proposed specifications, plans and drawings depicting the location and necessary to design and construct the New Elevator (the "***Tenant's Elevator Plans***") for Landlord's review and approval, which shall not be unreasonably withheld, conditioned or delayed. Landlord and Tenant shall cooperate and use good faith efforts to reach agreement on the Tenant's Elevator Plans as promptly and as reasonably possible. Tenant's Elevator Plans shall include fully engineered drawings, that include impact to the structure of the Building and otherwise affecting the Building, prepared and stamped by a structural engineer approved by Landlord and licensed in the Commonwealth of Pennsylvania. Prior to preparation of Tenant's Elevator Plans, Tenant shall provide to Landlord, at Tenant's sole cost and expense, a plan for structural due diligence to be performed on the Building. In furtherance of the foregoing, Landlord shall review and respond to Tenant with any objections or requested modifications to Tenant's Elevator Plans within fifteen (15) business days from receipt of the Tenant's Elevator Plans. Unless Landlord objects in writing within such 15-business day period, Landlord shall be deemed to have approved such Tenant's Elevator Plans. Notwithstanding the foregoing, solely in the event that Tenant retains Steve Bentz, BECS, (steve.bentz.@becsmd.com; 703-402-7121) for the preparation of the foregoing structural plans and Tenant's Elevator Plans, then Landlord's review period shall be reduced to ten (10) business days. In the event Landlord provides a written objection to the location of the New Elevator or otherwise to Tenant's Elevator Plans, together with commercially reasonable justification for such objection, within the aforementioned 15-business day (or 10 business day, as the case may be) period, Tenant shall modify such plans and specifications for the New Elevator and resubmit the same for Landlord's approval, and the aforementioned process shall continue until the plans and specifications for the

New Elevator are agreed to between Landlord and Tenant. Within thirty (30) days after Landlord's invoice therefor together with copies of invoices for the same, Tenant shall reimburse Landlord for its reasonable out-of-pocket third-party costs (including, but not limited to, structural engineer costs) Landlord incurred in reviewing the Tenant's Elevator Plans.

(ii) Tenant and Tenant's contractors and subcontractors shall comply in all respects with the terms of Paragraph 12 of the Original Lease in connection with the performance of the New Elevator work. Tenant shall be solely responsible for all costs and expenses associated with the New Elevator, including, but not limited to the costs of design, permits, approvals, installation, maintenance, utilities, cleaning, power, structural issues, roof warranty compliance (if applicable), repair, removal, liability and operation of and relating to the New Elevator. Tenant shall be solely liable for the New Elevator and any and all matters arising from and/or in connection with the operation of the New Elevator.

(iii) In addition, Tenant agrees to indemnify, defend and hold harmless Landlord and its representatives from and against all claims, actions, losses, liabilities, damages, liabilities, costs and expenses of any nature whatsoever (including attorneys' and other legal fees and costs) arising from or relating to the New Elevator and related equipment, including, but not limited installation, maintenance, replacement, use or removal of the New Elevator and all related facilities and equipment (including, without limitation, for any liabilities or damages related to the New Elevator failing to comply with any applicable laws, regulations or ordinances, or for any damage caused by the New Elevator or as a result of servicing the New Elevator which damages the Building). Except as otherwise expressly set forth herein, Landlord shall maintain responsibility for all maintenance obligations set forth in Paragraph 13 of the Original Lease. For the sake of clarification, Tenant shall be liable for all costs and expenses for all repairs and restoration arising from the New Elevator and/or related facilities and equipment. At any time after the installation of the New Elevator, during the Term, upon Landlord's request, Tenant shall deliver to Landlord a certificate of insurance naming Landlord as additional insured and satisfactory to Landlord covering the New Elevator and Tenant's contractual obligations of indemnification with respect to the New Elevator as set forth in this paragraph. To the maximum extent allowed by applicable law, Landlord and its property manager shall not be responsible or liable for, and Tenant hereby expressly waives all claims against Landlord for, injury to persons caused by the installation and operation of the New Elevator (and the wiring and other equipment related thereto) or damage to the New Elevator or any equipment related thereto . Tenant shall pay all fees to any and all governmental and quasi-governmental authorities relating to or arising from the New Elevator. Following the installation of the New Elevator, Tenant shall, at its sole cost and expense, maintain and operate New Elevator in good, clean and safe condition and repair.

(iv) Upon Landlord's request (the "Landlord' Removal Request"), Tenant shall remove the New Elevator and all related equipment at the expiration or earlier termination of this Lease, provided that such request is delivered to Tenant no later than sixty (60) days after the expiration or earlier termination of this Lease. This Section 8.(b) (iv) shall survive the expiration or earlier termination of this Lease. In the event Landlord provides Tenant with Landlord's Removal Request, Tenant shall be obligated to remove the New Elevator and Tenant shall repair and restore the areas of the Building impacted by the installation or operation of the New Elevator, at Tenant's expense, all to be completed within a reasonable time from receipt of

Landlord's Removal Request, in accordance with this Section 8 and the terms of Paragraphs 11 and 12 of the Original Lease, provided, that in the event of any inconsistency between this Section 8 and Paragraphs 11 and 12 of the Original Lease, this Section 8 shall control. For the sake of clarity, Tenant shall be responsible for all costs and expenses arising from Tenant's installation, maintenance and/or removal of the New Elevator including, but not limited to, all damage to the roof and the Building that is caused by or arising from Tenant's installation, maintenance or removal of the New Elevator and shall comply with all applicable laws and regulations with respect to the New Elevator.

9. Right of First Offer. So long as no event of default by Tenant has occurred under the terms of the Lease beyond the expiration of all applicable notice and cure periods, Tenant shall have a right of first offer for the Offer Space (as hereinafter defined) during the Extended Term of this Lease, such right of first offer to be on the terms and conditions as set forth in this Section 8.

(a) Landlord will provide written notice (the "***Offer Notice***") to Tenant of the availability of the lease for that certain space consisting of approximately 9,190 rentable square feet of space on the 7th Floor of the Building as outlined in Exhibit "C" attached hereto and made a part hereof (the "***Offer Space***"). Tenant will then have the right to lease all (but not less than all) of the Offer Space by giving written notice to Landlord of Tenant's election to do so within fifteen (15) business days following receipt of the Offer Notice. Tenant's lease of the Offer Space shall be in its then current "as-is" where is condition, at the then current rental rate in effect for the Premises (at the time Tenant exercises its right of first offer) for the remainder of the Extended Term, with a proportional increase in Tenant's parking rights. In the event Tenant exercises its option to lease the Offer Space, Tenant shall have the right to terminate its lease with respect to the Additional Third Floor Space (as defined in the Sixth Amendment). Tenant's Share will be adjusted to include the total amount of rentable square feet of the Offer Space that Tenant has exercised its right to lease. After Tenant's exercise of its right of first offer set forth in this Section 8, Landlord and Tenant shall promptly thereafter enter into an amendment to this Lease which memorializes the terms thereof, inclusive of all applicable terms and conditions set forth above.

(b) Time shall be of the essence with regard to this right of first offer, and in the event that Tenant fails to reply in writing within the aforesaid 15-business day period, such failure to reply shall be deemed a waiver by Tenant of its right of first offer of the Offer Space and Tenant shall have no further rights whatsoever to the Offer Space, and this right of first offer, as provided in this Section 9, shall be deemed extinguished, null and void, and of no further effect.

10. Vehicle Parking. Section 7 of the Sixth Amendment is hereby deleted in its entirety and replaced with the following (to be effective as of the Effective Date of this Amendment):

> "Subject to the Parking Rules set forth in Exhibit B to the Original Lease, as modified by Landlord from time to time (the "***Rules***"), Tenant shall be entitled to use up to ninety-five (95) unreserved parking spaces in the parking facility of the Property, at the rate of One Hundred Forty and 00/Dollars ($140.00) per month per parking space. Tenant shall pay Landlord, as additional rent, without demand, notice, offset or deduction, the foregoing rate per parking space per month for each

month of the remainder of the Term hereof for each of the parking spaces utilized by Tenant. Notwithstanding the foregoing, so long as Tenant is not in material default under the terms of the Lease beyond the expiration of all applicable notice and cure periods, if any, twenty-eight (28) of the foregoing unreserved parking spaces shall be provided at no charge. Landlord shall use commercially reasonable efforts to accommodate Tenant's future parking spaces requirements, subject to availability of parking spaces (the "***Additional Spaces***") and pursuant to the Rules, at the then current prevailing rate per month per parking space. Tenant shall pay Landlord, as additional rent, without demand, notice, offset or deduction, the then current prevailing rate(s) per parking space per month for each month of the Term for each of the Additional Spaces used, utilized or requested by Tenant."

11. Roof Repairs.

(a) Subject to any Force Majeure delay and/or Tenant Delay, Landlord, at Landlord's sole cost and expense, will replace that certain portion of the Building's roof located over the Seventh Floor Additional Space (the "***Phase 1 Roof Replacement Area***") on or prior to October 1, 2021. Such Phase 1 Roof Replacement Area is depicted on Exhibit "D-1" attached hereto and made a part hereof. In the event the replacement of the Phase 1 Roof Replacement Area has not been completed by October 31, 2021, subject to any Force Majeure delay or Tenant Delay, and provided that Tenant executes this Seventh Amendment or mutually satisfactory indemnification agreement by May 11, 2021, time being of the essence, commencing on November 1, 2021, Tenant shall be entitled to Fixed Rent abatement solely for the Seventh Floor Additional Space equal to one (1) day of Fixed Rent solely for the Seventh Floor Additional Space for each one (1) day of actual delay in Landlord's completion of the replacement of the Phase 1 Roof Replacement Area beyond October 31, 2021 on a day for day basis until the Landlord completes the replacement of the Phase 1 Roof Replacement Area. Notwithstanding the foregoing, for each day between May 1, 2021 and November 1, 2021 that the Landlord's roofing contractor is not able to perform roofing work that it is scheduled to perform on any particular day during such period of time due to any weather conditions (including, but not limited to, rain) (as applicable, a "***Phase 1 Weather Delay***"), the date of November 1, 2021 shall be extended by each day of Phase 1 Weather Delay.

(b) Subject to any Force Majeure delay and Tenant Delay, in addition to the replacement of the Phase 1 Roof Replacement Area, Landlord, at Landlord's sole cost and expense, will replace that certain portion of the Building's roof (the "***Phase 2 Roof Replacement Area***") that is not a part of the Phase 1 Roof Replacement Area and was not previously replaced during the 2018 calendar year. Such Phase 2 Roof Replacement Area is depicted on Exhibit "D-2" attached hereto and made a part hereof. In the event the replacement of the Phase 2 Roof Replacement Area has not been completed by June 30, 2022, subject to any Force Majeure delay or Tenant Delay, and provided that Tenant executes this Seventh Amendment or mutually satisfactory indemnification agreement by May 11, 2021, time being of the essence, commencing on July 1, 2022, Tenant shall be entitled to Fixed Rent abatement solely for the Seventh Floor Additional Space equal to one (1) day of Fixed Rent solely for the Seventh Floor Additional Space for each one (1) day of actual delay in Landlord's completion of the replacement of the Phase 2 Roof Replacement Area beyond June 30, 2022 on a day for day basis until the Landlord completes

the replacement of the Phase 2 Roof Replacement Area. Notwithstanding the foregoing, for each day between May 1, 2021 and June 30, 2022 that the Landlord's roofing contractor is not able to perform the roofing work that it is scheduled to perform on any particular day during such period of time due to any weather conditions (including, but not limited to, rain) (as applicable, a "***Phase 2 Weather Delay***"), the date of July 1, 2022 shall be extended by each day of Phase 2 Weather Delay.

(c) The replacement of the Phase 1 Roof Replacement Area and Phase 2 Roof Replacement Area are collectively referred to as the "***Roof Replacement Work***". The terms "***Force Majeure***" and "***Tenant Delay***" used herein shall have the same meanings set forth in Section 24.J of the Original Lease and Section 6(b) of the Third Amendment and respectively and as set forth below. Landlord acknowledges that Tenant has certain equipment located on the Building's roof and Tenant may require that certain equipment be relocated or new equipment to be installed on the Building's roof. Accordingly, Landlord and Tenant shall use commercially reasonable efforts to coordinate the phasing and performance of Landlord's Roof Replacement Work to minimize any potential Tenant Delay due any of Tenant's equipment located on the Building's roof. Notwithstanding anything to the contrary in the foregoing, Tenant shall be responsible, at Tenant's sole cost, expense, and liability, to remove all of Tenant's equipment on and in the Phase 1 Roof Replacement Area and/or the Phase 2 Roof Replacement Area (as applicable, "***Tenant's Roof Equipment***") on a timely basis and pursuant to the terms and conditions of Section 10 of the Sixth Amendment. Tenant's failure to timely remove Tenant's Roof Equipment shall be deemed a Tenant Delay. Upon completion of each portion of the work to be performed pursuant to Sections 11(a) and 11(b) above, Tenant may replace Tenant's Roof Equipment located in the applicable portion of the roof pursuant to the terms and conditions of Section 10 of the Sixth Amendment.

12. Broker. Landlord and Tenant each hereby represents and warrants to the other that it has not dealt with any real estate broker, sales person, or finder in connection with this Seventh Amendment except for Landlord's Broker, CBRE, Inc. ("***Broker***"). Landlord shall be responsible for the payment of any commission owed to the Broker based upon Landlord's separate agreement with such Broker. Landlord and Tenant each agree to indemnify and hold harmless the other party and their respective agents and employees, from and against any and all liabilities and claims for commissions and fees arising out of a breach of the foregoing representation (including without limitation, any other broker claiming to have been engaged by such indemnifying party in connection with this Seventh Amendment).

13. Full Force and Effect. Except as specifically set forth herein, the terms, covenants and conditions of the Lease shall remain in full force and effect. The Lease and this Seventh Amendment shall not be further modified or amended, except in writing signed by both Landlord and Tenant. This Seventh Amendment sets forth the entire understanding of the parties with respect to the matters set forth herein and there are no other rights, including but not limited to, any renewals, extensions, expansions, purchases, rights of first refusal, allowances, etc., granted to Tenant other than those expressly set forth in the Lease that have not been deleted or otherwise nullified or this Seventh Amendment. Landlord and Tenant hereby ratify and affirm all of the remaining terms and conditions of the Lease not modified or supplemented by this Seventh

Amendment. Tenant hereby acknowledges that, as of the date of this Seventh Amendment, Landlord is not in default of any of the terms and conditions of the Lease.

14. Provisions Binding. All rights and liabilities herein given to or imposed upon the parties to this Seventh Amendment shall extend to, and be binding upon and inure to the benefit of, the parties hereto and their respective successors and assigns.

15. Confidentiality. Tenant agrees that it shall maintain in confidence and shall not divulge to any third party (except to its employees, brokers, attorneys, accountants or other professional service providers as needed, or as may otherwise be required by the Securities and Exchange Commission or applicable law) any of the items, covenants and conditions of the Lease and this Seventh Amendment, including without limitation, any information related to the rental rate, the length of the Term, and any other terms and conditions thereof. Tenant further agrees to take commercially reasonable precautions to prevent the unauthorized disclosure of any such information to any third parties. Tenant's obligations under this Section 15 shall survive the termination of the Lease.

16. Counterparts; Delivery. This Seventh Amendment may be executed in any number of counterparts, and by each of the parties on separate counterparts, each of which, when so executed, shall be deemed an original, but all of which shall constitute but one and the same instrument provided that all parties execute and deliver a counterpart to the other party. Delivery of an executed counterpart of this Seventh Amendment by electronic delivery shall be equally as effective as delivery of a manually executed counterpart of this Seventh Amendment. Any party delivering an executed counterpart of this Seventh Amendment by electronic delivery shall also endeavor to deliver a manually executed counterpart of this Seventh Amendment, but the failure to deliver a manually executed counterpart shall not affect the validity, enforceability or binding effect of this Seventh Amendment.

[SIGNATURE PAGE FOLLOWS]

IN WITNESS WHEREOF, the parties hereto have executed this Seventh Amendment to Lease Agreement on the day and year set forth below.

LANDLORD:

WHARTON LENDER ASSOCIATES, LP,
a Pennsylvania Limited Partnership

By: WHARTON LENDER PROPERTIES, LLC,
a Pennsylvania Limited Liability Company,
its General Partner

By: _____
Name: Larry Walsh
Title: COO
Date: May 11, 2021

TENANT:

KRYSTAL BIOTECH INC.,
a Delaware corporation

By: DocuSigned by: Kathryn A. Romano
Name: Kathryn A. Romano
Title: Chief Accounting Officer
Date: May 11, 2021

Company Approval:

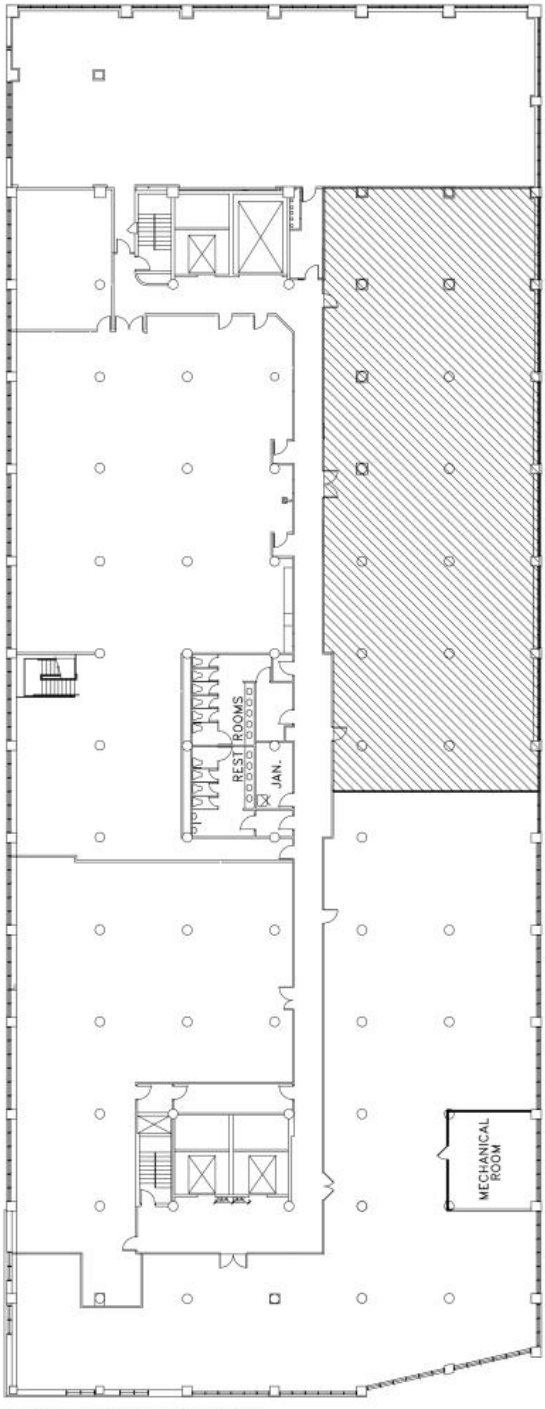
DocuSigned by: Krishi Krishnan — Chairman and CEO

Legal Review:

DocuSigned by: Jon Altman

EXHIBIT "A"

Seventh Floor Additional Space



2100 WHARTON- 7TH FLOOR

EXHIBIT "B"

Sixth Floor Space

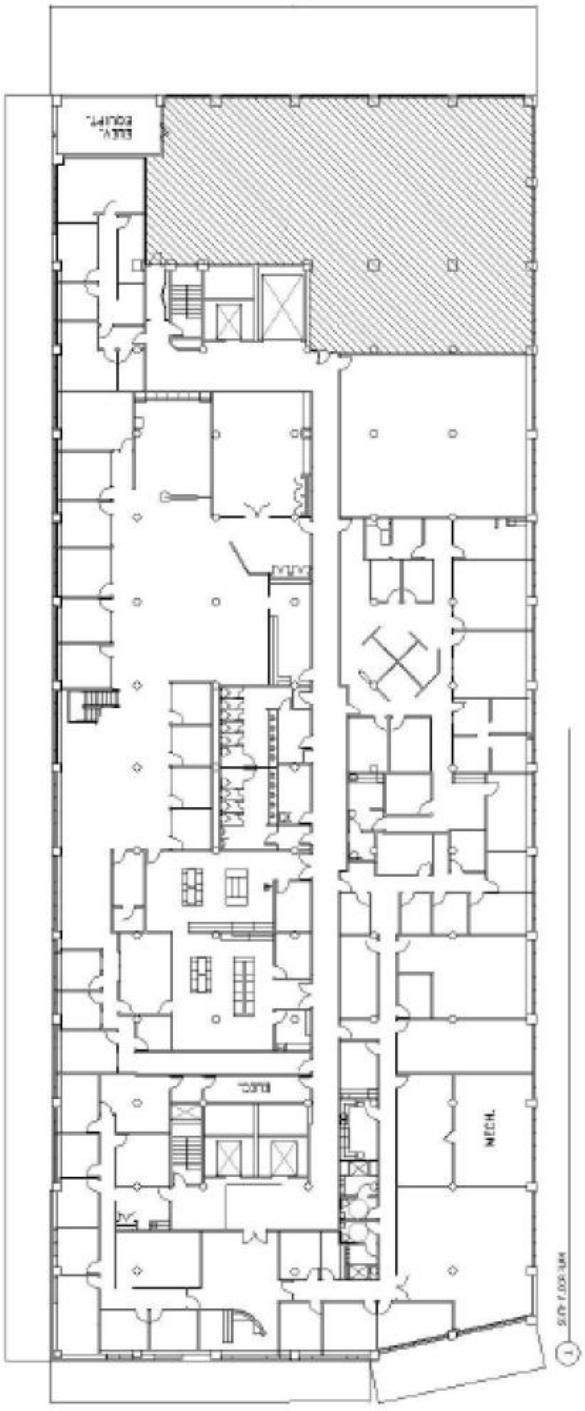
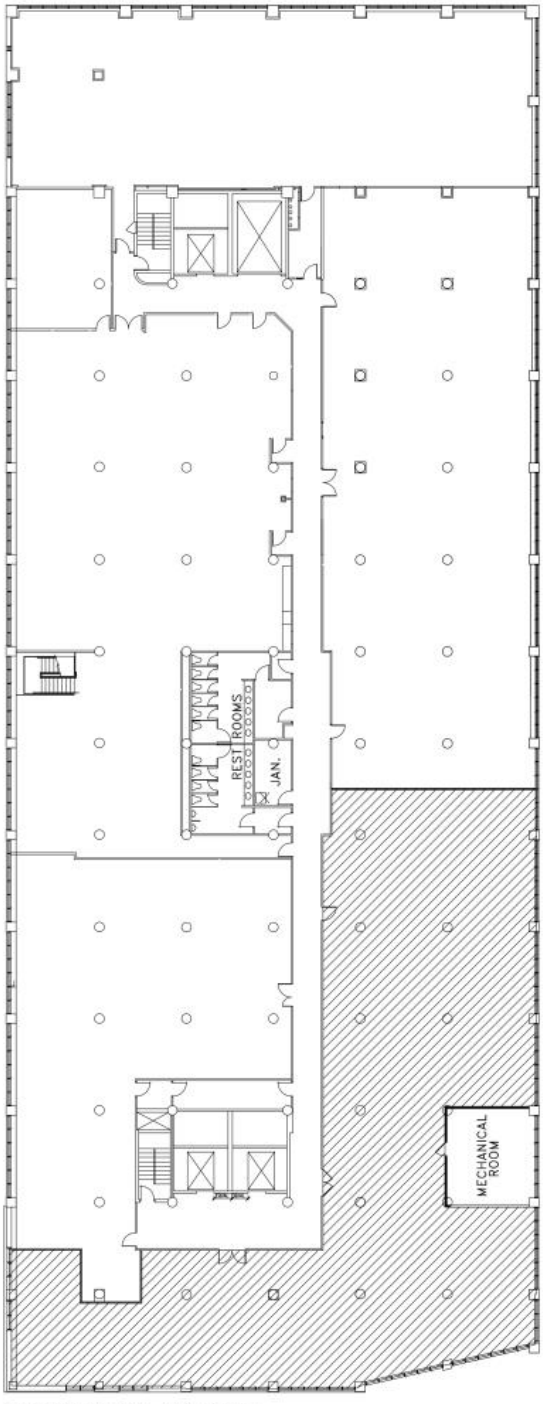


EXHIBIT "C"

Offer Space



2100 WHARTON- 7TH FLOOR

EXHIBIT "D-1"

Phase 1 Roof Replacement Area

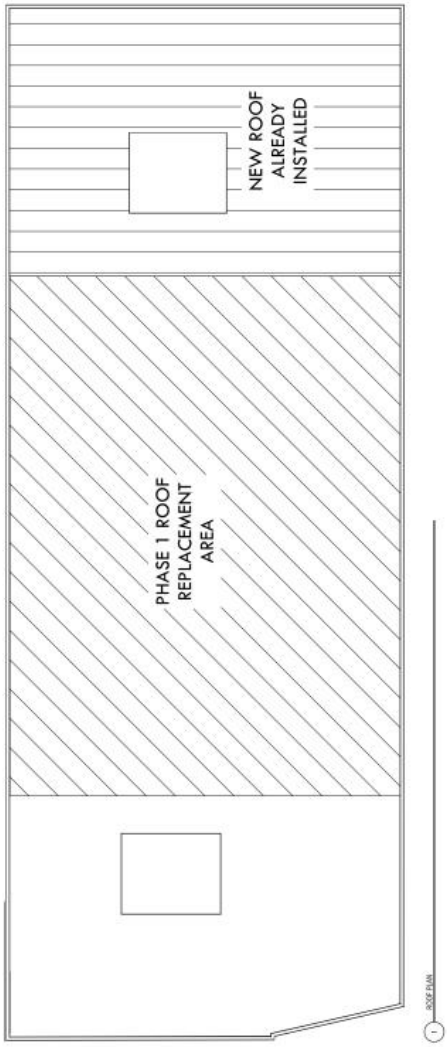
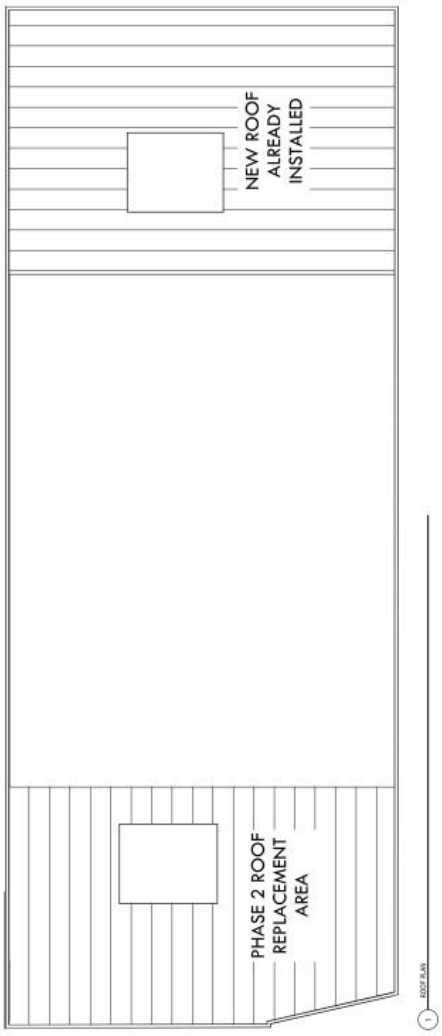


EXHIBIT "D-2"

Phase 2 Roof Replacement Area



EIGHTH AMENDMENT TO LEASE AGREEMENT

THIS EIGHTH AMENDMENT TO LEASE AGREEMENT (this "***Eighth Amendment***") is made as of the 21st day of July 2021 (the "***Effective Date***"), by and between Wharton Lender Associates, LP, a Pennsylvania limited partnership ("***Landlord***"), and Krystal Biotech, Inc., a Delaware corporation, formerly known as Krystal Biotech, LLC, a California limited liability company ("***Tenant***").

WITNESSETH:

WHEREAS, by Lease dated May 26, 2016 (the "***Original Lease***"), as amended by First Amendment to Lease Agreement dated July 26, 2016, Second Amendment to Lease Agreement dated February 27, 2017, Third Amendment to Lease Agreement dated May 31, 2018 (the "***Third Amendment***"), Fourth Amendment to Lease Agreement dated October 22, 2018, (the "***Fourth Amendment***"), Fifth Amendment to Lease Agreement dated December 10, 2018 (the "***Fifth Amendment***"), Sixth Amendment to Lease Agreement/First Amendment to Storage Space Agreement dated January 13, 2021 (the "***Sixth Amendment***") Seventh Amendment to Lease Agreement dated May 11, 2021 (the ***"Seventh Amendment")*** and Reimbursement Agreement dated June 3, 2021 (the "Reimbursement Agreement") (the Original Lease as amended, collectively, the "***Lease***"), Landlord currently leases to Tenant and Tenant currently leases from Landlord certain premises consisting of a total of 33,873 rentable square feet (the "***Current Premises***") located in that certain building known as 2100 Wharton Street, Pittsburgh, Pennsylvania (the "***Building***"), being comprised of 10,978 rentable square feet on the 7th Floor of the Building, and 16,892 rentable square feet on the 3rd floor of the Building, and 6,003 rentable square feet on the 6th Floor of the Building; and

WHEREAS, pursuant to the Seventh Amendment, Tenant has leased from Landlord and Landlord has leased to Tenant an additional 7,578 rentable square feet of office space located on the 7th Floor of the Building (the "***Seventh Floor Additional Space***"): and

WHEREAS, Landlord and Tenant now desire to amend the Lease to: (i) lease to Tenant an additional 2,270 rentable square feet of space located on the 6th Floor of the Building, known as Suite 625A, as outlined on Exhibit "A" attached hereto and made a part hereof (the "***Sixth Floor Additional Space***"), thereby increasing Tenant's rentable area of space in the Building to a total of 43,721 rentable square feet of space in the Building; and (ii) modify certain other terms of the Lease, all in accordance with the terms and provisions hereof.

NOW THEREFORE, the parties hereto, in consideration of the mutual premises contained herein, and intending to be legally bound hereby, do covenant and agree as follows:

1. Recitals. The foregoing preamble is incorporated by reference herein as if set forth at length. Capitalized terms not otherwise defined herein shall have the meaning given to such terms in the Lease. All references herein to the Lease shall include this Eighth Amendment.

2. Sixth Floor Additional Space.

(a) Commencing as of the Effective Date hereof, the Sixth Floor Additional Space shall become part of the Premises, accordingly, the Term of the Lease for the Sixth Floor Additional Space and Tenant's obligation to pay Fixed Rent and additional rent for the Sixth Floor Additional Space shall commence on the Effective Date hereof. Accordingly, effective as of the Effective Date until the Seventh Floor Additional Space Commencement Date (as defined in Section 4 of the Reimbursement Agreement), "Premises" shall mean 36,143 rentable square feet in the Building. Effective as of the Seventh Floor Additional Space Commencement Date, Premises shall mean 43,721 rentable square feet in the Building.

(b) Sixth Floor Additional Space Utilities, Janitorial and Cleaning. Notwithstanding anything to the contrary contained in the Lease, Tenant shall be responsible, at Tenant's sole cost and expense, for providing: (i) cleaning and janitorial services in a first class manner and keeping with the standards of the Building, including, but not limited to garbage and rubbish removal on a daily basis and the costs of dumpsters and services thereof for the Sixth Floor Additional Space; and (ii) all extraordinary utilities usage, costs and expenses (e.g., above standard office usage) used in the Sixth Floor Additional Space.

(c) Use of Sixth Floor Additional Space. Notwithstanding anything to the contrary contained in the Lease, Tenant shall be permitted to use the Sixth Floor Additional Space for general office and/or warehouse use (including inventory storage), and Tenant shall be permitted to install workstations therein, provided that no more than fifty percent (50%) of floor area comprising the Sixth Floor Additional Space shall be used for such workstations, at Tenant's sole cost and expense, subject in all respects to the terms and conditions set forth in the Lease.

3. Fixed Rent.

(a) Fixed Rent for the Sixth Floor Additional Space. Commencing on the Effective Date hereof and thereafter until the Expiration Date (as defined in Section 4 of the Seventh Amendment), Tenant shall pay Landlord Fixed Rent for the Sixth Floor Additional Space pursuant to the terms of the Lease and in accordance with the following table at the annual rates as follows:

LEASE PERIOD	PORTION OF PREMISES	$PER RENTABLE SQ FT	MONTHLY FIXED RENT INSTALLMENT	ANNUAL FIXED RENT AMOUNT
Effective Date hereof – 2/28/22	2,270 rsf Sixth Floor Additional Space	20.00	$3,783.33	$45,400.00
3/1/22 – 2/28/23	2,270 rsf Sixth Floor Additional Space	20.40	$3,859.00	$46,308.00
3/1/23 – 2/29/24	2,270 rsf Sixth Floor Additional Space	20.81	$3,936.56	$47,238.70
3/1/24 – 2/28/25	2,270 rsf Sixth Floor Additional Space	21.23	$4,016.01	$48,192.10
3/1/25 – 2/28/26	2,270 rsf Sixth Floor Additional Space	21.65	$4,095.46	$49,145.50

3/1/26 – 2/28/27	2,270 rsf Sixth Floor Additional Space	22.08	$4,176.80	$50,121.60
3/1/27– 2/29/28	2,270 rsf Sixth Floor Additional Space	22.52	$4,260.03	$51,120.40
3/1/28 – 2/28/29	2,270 rsf Sixth Floor Additional Space	22.97	$4,345.16	$52,141.90
3/1/29 – 2/28/30	2,270 rsf Sixth Floor Additional Space	23.43	$4,432.18	$53,186.10
3/1/30 – 2/28/31	2,270 rsf Sixth Floor Additional Space	23.90	$4,521.08	$54,253.00
3/1/31 – Expiration Date	2,270 rsf Sixth Floor Additional Space	24.38	$4,611.88	$55,342.60

(b) Fixed Rent for the Current Premises. From the Effective Date hereof until the Expiration Date, Tenant shall continue to pay Fixed Rent for the Current Premises being 33,873 rentable square feet (consisting of 10,978 rentable square feet on the 7th Floor and 16,892 rentable square feet on the 3rd floor and 6,003 rentable square feet on the 6th floor) in accordance with the terms of the Original Lease, Third Amendment, Fourth Amendment, Fifth Amendment, Sixth Amendment and Seventh Amendment.

(c) Fixed Rent for the Seventh Floor Additional Space. Commencing on the Seventh Floor Additional Space Commencement Date until the Expiration Date, Tenant shall pay Fixed Rent for the Seventh Floor Additional Space being 7,578 rentable square feet on the 7th floor, in accordance with the terms of the Original Lease and the Seventh Amendment.

All Fixed Rent shall be payable in equal monthly installments in advance on the first day of each month during the Term without demand, notice, offset or deduction.

4. Tenant's Share; Tenant's Percentage. Commencing as of the Effective Date hereof and continuing until the Seventh Floor Additional Space Commencement Date, "Tenant's Percentage" as defined in Paragraph 1.L. of the Original Lease and "Tenant's Share", as defined in Paragraph 4.A.(ii) of the Original Lease shall mean "15.98%" and all references in the Lease to "Tenant's Share and "Tenant's Percentage" shall mean "15.98%". Commencing on the Seventh Floor Additional Space Commencement Date, "Tenant's Percentage" as defined in Paragraph 1.L. of the Original Lease and "Tenant's Share", as defined in Paragraph 4.A.(ii) of the Original Lease shall mean "19.33%", and all references in the Lease to "Tenant's Share" and "Tenant's Percentage" shall mean "19.33%".

5. Condition of the Premises. Notwithstanding anything contained in the Lease to the contrary: (i) Landlord shall deliver the Sixth Floor Additional Space to Tenant and Tenant accepts delivery and possession of the Sixth Floor Additional Space in their current "as-is" where-is condition; and (ii) Tenant shall perform, at Tenant's sole cost and expense, all other work and modifications to the Sixth Floor Additional Space that are required, necessary or desired, subject to, and in accordance with, the terms of the Lease.

6. Vehicle Parking. Section 10 of the Seventh Amendment is hereby deleted in its entirety and replaced with the following (to be effective as of the Effective Date hereof):

> "Subject to the Parking Rules set forth in Exhibit B to the Original Lease, as modified by Landlord from time to time (the "***Rules***"), Tenant shall be entitled to use up to one hundred (100) unreserved parking spaces in the parking facility of the Property, at the rate of One Hundred Forty and 00/Dollars ($140.00) per month per parking space. Tenant shall pay Landlord, as additional rent, without demand, notice, offset or deduction, the foregoing rate per parking space per month for each month of the remainder of the Term hereof for each of the parking spaces utilized by Tenant. Notwithstanding the foregoing, so long as Tenant is not in material default under the terms of the Lease beyond the expiration of all applicable notice and cure periods, if any, twenty-eight (28) of the foregoing unreserved parking spaces shall be provided at no charge. Landlord shall use commercially reasonable efforts to accommodate Tenant's future parking spaces requirements, subject to availability of parking spaces (the "***Additional Spaces***") and pursuant to the Rules, at the then current prevailing rate per month per parking space. Tenant shall pay Landlord, as additional rent, without demand, notice, offset or deduction, the then current prevailing rate(s) per parking space per month for each month of the Term for each of the Additional Spaces used, utilized or requested by Tenant."

7. Broker. Landlord and Tenant each hereby represents and warrants to the other that it has not dealt with any real estate broker, sales person, or finder in connection with this Eighth Amendment except for Landlord's Broker, CBRE, Inc. ("***Broker***"). Landlord shall be responsible for the payment of any commission or other fees owed to the Broker based upon Landlord's separate agreement with such Broker. Landlord and Tenant each agree to indemnify and hold harmless the other party and their respective agents and employees, from and against any and all liabilities and claims for commissions and fees arising out of a breach of the foregoing representation (including without limitation, any other broker claiming to have been engaged by such indemnifying party in connection with this Eighth Amendment).

8. Full Force and Effect. Except as specifically set forth herein, the terms, covenants and conditions of the Lease shall remain in full force and effect. The Lease and this Eighth Amendment shall not be further modified or amended, except in writing signed by both Landlord and Tenant. This Eighth Amendment sets forth the entire understanding of the parties with respect to the matters set forth herein and there are no other rights, including but not limited to, any renewals, extensions, expansions, purchases, rights of first refusal, allowances, etc., granted to Tenant other than those expressly set forth in the Lease that have not been deleted or otherwise nullified or this Eighth Amendment. Landlord and Tenant hereby ratify and affirm all of the remaining terms and conditions of the Lease not modified or supplemented by this Eighth Amendment.

9. Provisions Binding. All rights and liabilities herein given to or imposed upon the parties to this Eighth Amendment shall extend to and be binding upon and inure to the benefit of, the parties hereto and their respective successors and assigns.

10. Confidentiality. Tenant agrees that it shall maintain in confidence and shall not divulge to any third party (except to its employees, brokers, attorneys, accountants or other professional service providers as needed, or as may otherwise be required by the Securities and Exchange Commission or applicable law) any of the items, covenants and conditions of the Lease and this Eighh Amendment, including without limitation, any information related to the rental rate, the length of the Term, and any other terms and conditions thereof. Tenant further agrees to take commercially reasonable precautions to prevent the unauthorized disclosure of any such information to any third parties. Tenant's obligations under this Section 10 shall survive the termination of the Lease.

11. Counterparts; Delivery. This Eighth Amendment may be executed in any number of counterparts, and by each of the parties on separate counterparts, each of which, when so executed, shall be deemed an original, but all of which shall constitute but one and the same instrument provided that all parties execute and deliver a counterpart to the other party. Delivery of an executed counterpart of this Eighth Amendment by electronic delivery shall be equally as effective as delivery of a manually executed counterpart of this Eighth Amendment.

[SIGNATURE PAGE FOLLOWS]

IN WITNESS WHEREOF, the parties hereto have executed this Eighth Amendment to Lease Agreement on the day and year set forth below.

LANDLORD:

WHARTON LENDER ASSOCIATES, LP,
a Pennsylvania Limited Partnership

By: WHARTON LENDER PROPERTIES, LLC,
a Pennsylvania Limited Liability Company,
its General Partner

By: _____
Name: Larry Walsh
Title: COO
Date: July 22, 2021

TENANT:

KRYSTAL BIOTECH INC.,
a Delaware corporation

By: DocuSigned by: Kathryn Romano
Name: Kathryn Romano
Title: Chief Accounting Officer
Date: July 21, 2021

DS AP

EXHIBIT "A"

Sixth Floor Additional Space

2100 WHARTON- SIXTH FLOOR PLAN
MECH.
ELEC.
JAN.
RESTROOMS
ELEV. EQUIPT.
2,270 R.S.F.

NINTH AMENDMENT TO LEASE AGREEMENT

THIS NINTH AMENDMENT TO LEASE AGREEMENT (this "Ninth Amendment") is made as of the 4th day of January 2022, by and between Wharton Lender Associates, LP, a Pennsylvania limited partnership ("Landlord"), and Krystal Biotech, Inc., a Delaware corporation ("Tenant").

WITNESSETH:

WHEREAS, by Lease dated May 26, 2016 (the "Original Lease"), as amended by First Amendment to Lease Agreement dated July 26, 2016, Second Amendment to Lease Agreement dated February 27, 2017, Third Amendment to Lease Agreement dated May 31, 2018, Fourth Amendment to Lease Agreement dated October 22, 2018, Fifth Amendment to Lease Agreement dated December 10, 2018, Sixth Amendment to Lease Agreement/First Amendment to Storage Space Agreement dated January 13, 2021 (the "Sixth Amendment"), Seventh Amendment to Lease Agreement dated May 11, 2021 (the "Seventh Amendment"), Reimbursement Agreement dated June 3, 2021 and Eighth Amendment to Lease Agreement dated July 21, 2021 (the Original Lease as amended, collectively, the "Lease"), Landlord currently leases to Tenant and Tenant currently leases from Landlord certain premises consisting of a total of 43,721 rentable square feet (the "Existing Premises") located in that certain building known as 2100 Wharton Street, Pittsburgh, Pennsylvania (the "Building"), being comprised of 18,556 rentable square feet on the 7th Floor of the Building, and 16,892 rentable square feet on the 3rd floor of the Building, and 8,273 rentable square feet on the 6th Floor of the Building; and

WHEREAS, Landlord and Tenant now desire to amend the Lease to: (i) lease to Tenant an additional 3,507 rentable square feet of office space located on the 6th Floor of the Building, known as Suite 620, as outlined on Exhibit "A" attached hereto and made a part hereof (the "Sixth Floor Expansion Space"), thereby increasing Tenant's rentable area of space in the Building to a total of 47,228 rentable square feet of space in the Building; and (ii) modify certain other terms of the Lease, all in accordance with the terms and provisions hereof.

NOW THEREFORE, the parties hereto, in consideration of the mutual promises contained herein, and intending to be legally bound hereby, do covenant and agree as follows:

1. Recitals. The foregoing preamble is incorporated by reference herein as if set forth at length. Capitalized terms not otherwise defined herein shall have the meaning given to such terms in the Lease. All references herein to the Lease shall include this Ninth Amendment.

2. Sixth Floor Expansion Space; Sixth Floor Expansion Space Commencement Date.

(a) Effective as of the Sixth Floor Expansion Space Commencement Date (as defined below), the Sixth Floor Expansion Space shall become part of the Premises. Accordingly, effective as of the Sixth Floor Expansion Space Commencement Date, Premises shall mean 47,228 rentable square feet in the Building.

(b) Sixth Floor Expansion Space Commencement Date; Expiration Date. The Term of the Lease for the Sixth Floor Expansion Space and Tenant's obligation to pay Fixed Rent and additional rent for the Sixth Floor Expansion Space shall commence on the date (the "Sixth Floor Expansion Space Commencement Date") which is the earlier to occur of: (i) the date that Landlord has Substantially Completed Landlord's Sixth Floor Expansion Space Work (which will not be earlier than January 3, 2022); or (ii) the date Tenant first occupies and begins conducting business operations in all or part of the Sixth Floor Expansion Space, which may be prior to Substantial Completion of Landlord's Sixth Floor Expansion Space Work but not earlier than January 3, 2022; provided however, that should the Sixth Floor Expansion Space Commencement Date fall on any day other than the first day of the month, the anniversary of the Sixth Floor Expansion Space Commencement Date shall be deemed after the completion of twelve full calendar months following the Sixth Floor Expansion Space Commencement Date. For the avoidance of doubt, the parties agree that the Sixth Floor Expansion Space Commencement Date shall be no earlier than January 3, 2022. The expiration date of the Term of the Lease for the Sixth Floor Expansion Space shall be the Expiration Date set forth in the Lease for the Existing Premises which the parties agree is October 31, 2031. Upon Landlord's Sixth Floor Expansion Space Work being Substantially Completed, Tenant shall, upon Landlord's request, promptly execute a Sixth Floor Expansion Space Commencement Date Agreement, which shall specify the Sixth Floor Expansion Space Commencement Date.

5. Fixed Rent for the Sixth Floor Expansion Space. Commencing on the Sixth Floor Expansion Space Commencement Date, Tenant shall pay Landlord Fixed Rent for the Sixth Floor Expansion Space pursuant to the terms of the Lease and in accordance with the following table at the rates as follows:

LEASE PERIOD	PORTION OF PREMISES	$PER RENTABLE SQ FT	MONTHLY FIXED RENT INSTALLMENT	ANNUAL FIXED RENT AMOUNT
Sixth Floor Expansion Space Commencement Date – 2/28/22	3,507 rsf Sixth Floor Expansion Space	23.41	$6,841.57	$82,098.87
3/1/22 – 2/28/23	3,507 rsf Sixth Floor Expansion Space	23.88	$6,978.93	$83,747.16
3/1/23 – 2/29/24	3,507 rsf Sixth Floor Expansion Space	24.36	$7,119.21	$85,430.52
3/1/24 – 2/28/25	3,507 rsf Sixth Floor Expansion Space	24.85	$7,262.41	$87,148.95
3/1/25 – 2/28/26	3,507 rsf Sixth Floor Expansion Space	25.35	$7,408.54	$88,902.45
3/1/26 – 2/28/27	3,507 rsf Sixth Floor Expansion Space	25.86	$7,557.59	$90,691.02
3/1/27 – 2/29/28	3,507 rsf Sixth Floor Expansion Space	26.38	$7,709.56	$92,514.66
3/1/28 – 2/28/29	3,507 rsf Sixth Floor Expansion Space	26.91	$7,864.45	$94,373.37
3/1/29 – 2/28/30	3,507 rsf Sixth Floor Expansion Space	27.45	$8,022.26	$96,267.15

3/1/30 – 2/28/31	3,507 rsf Sixth Floor Expansion Space	28.00	$8,183.00	$98,196.00
3/1/31 – 10/31/31	3,507 rsf Sixth Floor Expansion Space	28.56	$8,346.66	$100,159.92

All Fixed Rent shall be payable in equal monthly installments in advance on the first day of each month during the Term without demand, notice, offset or deduction.

6. Tenant's Share; Tenant's Percentage. Commencing on the Sixth Floor Expansion Space Commencement Date, "Tenant's Percentage" as defined in Paragraph 1.L. of the Original Lease and "Tenant's Share", as defined in Paragraph 4.A.(ii) of the Original Lease shall mean "20.88%", and all references in the Lease to "Tenant's Share" and "Tenant's Percentage" shall mean "20.88%".

7. Landlord's Sixth Floor Expansion Space Work.

A. Notwithstanding anything contained in the Lease to the contrary, Landlord shall deliver the Sixth Floor Expansion Space to Tenant and Tenant accepts delivery and possession of the Sixth Floor Expansion Space in its current "as-is" where is condition with the sole exception that Landlord agrees to do or otherwise perform that certain work in or relating to the Sixth Floor Expansion Space described in Exhibit "B" (the "Landlord's Sixth Floor Expansion Space Work"). In no event and under no circumstances will Landlord's Sixth Floor Expansion Space Work entail or will Landlord be obliged to perform any work or supply any materials in excess of the work and materials described with particularity in Exhibit "B". All work in the Sixth Floor Expansion Space other than Landlord's Sixth Floor Expansion Space Work shall be performed by Landlord or Landlord's contractors at Tenant's sole cost and expense.

B. The Landlord's Sixth Floor Expansion Space Work shall be deemed to be Substantially Completed when the work shown on Exhibit "B" has been completed, which Landlord estimates shall be substantially completed approximately thirty (30) days from the date hereof, subject to Force Majeure and Tenant Delay except for: (i) any improvements or work to be performed by Tenant; and (ii) such items of finishing and construction of a nature which are not necessary to make the Sixth Floor Expansion Space reasonably tenantable for Tenant's use as stated herein; and (iii) items not completed because of delay by Tenant in furnishing or receiving any drawings or approvals or within the time set forth in any agreement between Landlord and Tenant; and (iv) changes in the work to be performed by Landlord which are requested by Tenant after Landlord's approval of Tenant's plans; or (v) the performance of any work or activity in the Sixth Floor Expansion Space by Tenant or any of its employees, agents or contractors.

The following shall be deemed Tenant's Delay: (i) Tenant fails to timely provide the necessary approvals to Landlord's drawings; or (ii) Tenant otherwise unreasonably delays the Substantial Completion of Landlord's Sixth Floor Expansion Space Work. If a Tenant Delay occurs, Rent for the Sixth Floor Expansion Space shall commence on the date upon which Landlord's Sixth Floor Expansion Space Work would have been Substantially Completed had the above-described delays by Tenant not occurred.

C. Notwithstanding anything contained in the Lease to the contrary, Tenant's continued possession of the Premises shall be in its current "as-is" where is condition and, except as otherwise specifically set forth herein, any and all costs for work required in the Premises shall be at Tenant's sole cost and expense.

9. Seventh Floor HVAC. Tenant shall purchase and install, at Tenant's sole cost and expense, except as otherwise specifically set forth in this Paragraph 9, upon the terms and conditions in this Paragraph 9 a new HVAC unit for the 7th Floor, such unit shall be either the exact York unit or exact Rheem unit specified and set forth in Exhibit "C" attached hereto and made a part hereof(the "Seventh Floor HVAC Unit").

(a) Tenant's Plans. Tenant shall provide, at Tenant's sole cost and expense, all of the plans, specifications and drawings for the Seventh Floor HVAC Unit necessary to design and install the Seventh Floor HVAC Unit in Exhibit "C" (the "Tenant's HVAC Work"), including all required mechanical, electrical and plumbing drawings, the location and installation of all equipment, risers, disconnects, ducts, utility and HVAC distribution, and other Tenant installations (collectively, the "Tenant's Plans"). For the sake of clarity, the Tenant's Plans shall include all the plans, specifications and drawings for either the Rheem or York unit that is specified in Exhibit C. Tenant's Plans shall be prepared by Tenant and shall be subject to the prior written approval of Landlord, which shall not be unreasonably withheld or delayed. Landlord's review of Tenant's Plans shall not impose any obligation or liability on Landlord, its agents or representatives, and Landlord's approval of Tenant's Plans shall not serve as a representation or warranty as to the accuracy of Tenant's Plans or as to compliance with any laws, codes, regulations or ordinances. Landlord shall approve Tenant's Plans prior to Tenant commencing any of Tenant's HVAC Work.

(b) Tenant's HVAC Work shall be performed, at Tenant's sole cost and expense, by a bona fide union general contractor and bona fide union subcontractors, architects and engineers selected by Tenant. Landlord shall have the right to approve all contractors and subcontractors, and the performance of Tenant's HVAC Work, and all such contractors and subcontractors performing such work, shall comply in all respects with all applicable laws, codes and regulations and with the terms of this Paragraph 9 and the terms of Paragraph 12 of the Original Lease, Tenant's Plans, and with the rules and regulations attached to the Lease; provided, however, that Landlord will not unreasonably withhold approval of said contractors and subcontractors if proof of proper licensure and insurance is demonstrated to Landlord. Tenant's HVAC Work shall not interfere with or affect the common areas or structural components of the Building or any Building mechanical systems, HVAC, electrical, plumbing, gas, elevator or other Building operating systems serving other tenants and occupants of the Building. Tenant shall perform or cause to be performed Tenant's HVAC Work in a manner which shall not interfere with or interrupt the business operations or premises of other tenants in the Building, except as may be approved by Landlord, which approval shall not be unreasonably withheld or delayed. Tenant shall diligently pursue the performance and completion Tenant's HVAC Work following Landlord's written approval of Tenant's Plans therefor and the parties will agree on a schedule for the completion of Tenant's HVAC Work upon Landlord's approval of Tenant's Plans, provided, however, that in no event shall Tenant's HVAC Work be completed later than March 10, 2022, time being of the essence. All of the cost and expense of and relating to Tenant's HVAC Work and installations thereof shall be borne by Tenant except solely as follows:

(i) Tenant shall provide Landlord with receipt of the cost of the Seventh Floor HVAC Unit and Landlord shall promptly, within (30) days of receipt of Tenant's invoice therefor, reimburse Tenant for an amount up to the cost of the Seventh Floor HVAC Unit that Landlord would have paid and that the parties agree is the amount of Ten Thousand Nine Hundred Sixty-nine and 87/100 Dollars ($10,969.87) ; and (ii) Tenant, at Tenant's sole cost and expense, shall perform and manage the installation of the Seventh Floor HVAC Unit and purchase all associated controls; all such work and controls shall be subject to Landlord's prior written approval (not to be unreasonably withheld, conditioned or delayed); provided, however, that Landlord will contribute Twenty Thousand and 00/100 Dollars ($20,000.00) towards the cost of installation of the Seventh Floor HVAC Unit within fifteen (15) days after Tenant provides proof of payment and completes the installation of the HVAC Unit; and (iii) Landlord agrees to install a controls system for the Seventh Floor HVAC Unit, at the Tenant's sole cost and expense with the sole exception that the Landlord shall pay the lower of: (i)Two Thousand Five Hundred and 00/100 Dollars ($2,500.00); or (ii) fifty percent of the installation cost of installation of the controls (the "Controls Cost"), and the Tenant shall pay the remaining amount of the Controls Cost to Landlord as additional rent within fifteen (15) days of receipt of Landlord's invoice therefor; (iv) if Tenant leases the Offer Space (as defined in the Seventh Amendment), then commencing with the first Rent payment for the Offer Space, Landlord agrees to provide a Rent abatement to Tenant in an amount equal to Twenty Five Thousand and 00/100 ($25,000).

10. Vehicle Parking. Effective as of the Sixth Floor Expansion Space Commencement Date, Paragraph 6 of the Eighth Amendment is hereby deleted in its entirety and replaced with the following:

> "Subject to the Parking Rules set forth in Exhibit B to the Original Lease, as modified by Landlord from time to time (the "Rules"), Tenant shall be entitled to use up to one hundred eight (108) unreserved parking spaces in the parking facility of the Property, at the rate of One Hundred Forty and 00/Dollars ($140.00) per month per parking space. Tenant shall pay Landlord, as additional rent, without demand, notice, offset or deduction, the foregoing rate per parking space per month for each month of the remainder of the Term hereof for each of the parking spaces utilized by Tenant. Notwithstanding the foregoing, so long as Tenant is not in material default under the terms of the Lease beyond the expiration of all applicable notice and cure periods, if any, twenty-eight (28) of the foregoing unreserved parking spaces shall be provided at no charge. Landlord shall use commercially reasonable efforts to accommodate Tenant's future parking spaces requirements, subject to availability of parking spaces (the "Additional Spaces") and pursuant to the Rules, at the then current prevailing rate per month per parking space. Tenant shall pay Landlord, as additional rent, without demand, notice, offset or deduction, the then current prevailing rate(s) per parking space per month for each month of the Term for each of the Additional Spaces used, utilized or requested by Tenant."

11. Additional Modifications to Lease. Paragraph 9 of the Seventh Amendment shall be amended so as to delete the sentence "In the event Tenant exercises its option to lease the Offer Space, Tenant shall have the right to terminate its lease with respect to the Additional Third Floor Space (as defined in the Sixth Amendment)" (in sub-section 9(a) of the Seventh Amendment) shall

be deleted in its entirety, null and void and of no further force or effect. Tenant specifically acknowledges and agrees that Tenant does not have any rights to terminate the lease of the Additional Third Floor Space (as defined in the Sixth Amendment) whatsoever. The following sentence is added to the end of Section 9 (a) of the Seventh Amendment: If Tenant exercises its option to lease the Offer Space pursuant to this Section 9(a), Landlord agrees to provide a Fixed Rent abatement to Tenant in an amount equal to Twenty Five Thousand and 00/100 ($25,000) to be credited against the Fixed Rent due for the Offer Space as Tenant's sole and exclusive abatement, improvement allowance and/or other credit for the Offer Space whatsoever. Notwithstanding anything to the contrary in the foregoing and/or the Lease, Tenant shall have no right whatsoever to terminate the lease of the Additional Third Floor Space whatsoever.

12. Broker. Landlord and Tenant each hereby represents and warrants to the other that it has not dealt with any real estate broker, sales person, or finder in connection with this Ninth Amendment except for Landlord's Broker, CBRE, Inc. ("Broker"). Landlord shall be responsible for the payment of any commission owed to the Broker based upon Landlord's separate agreement with such Broker. Landlord and Tenant each agree to indemnify and hold harmless the other party and their respective agents and employees, from and against any and all liabilities and claims for commissions and fees arising out of a breach of the foregoing representation (including without limitation, any other broker claiming to have been engaged by such indemnifying party in connection with this Ninth Amendment).

13. Full Force and Effect. Except as specifically set forth herein, the terms, covenants and conditions of the Lease shall remain in full force and effect. The Lease and this Ninth Amendment shall not be further modified or amended, except in writing signed by both Landlord and Tenant. This Ninth Amendment sets forth the entire understanding of the parties with respect to the matters set forth herein and there are no other rights, including but not limited to, any renewals, extensions, expansions, purchases, rights of first refusal, allowances, etc., granted to Tenant other than those expressly set forth in the Lease that have not been deleted or otherwise nullified or this Ninth Amendment. Landlord and Tenant hereby ratify and affirm all of the remaining terms and conditions of the Lease not modified or supplemented by this Ninth Amendment. Tenant hereby acknowledges that, as of the date of this Ninth Amendment, Landlord is not in default of any of the terms and conditions of the Lease.

14. Provisions Binding. All rights and liabilities herein given to or imposed upon the parties to this Ninth Amendment shall extend to, and be binding upon and inure to the benefit of, the parties hereto and their respective successors and assigns.

15. Confidentiality. Tenant agrees that it shall maintain in confidence and shall not divulge to any third party (except to its employees, brokers, attorneys, accountants or other professional service providers as needed, or as may otherwise be required by the Securities and Exchange Commission or applicable law) any of the items, covenants and conditions of the Lease and this Ninth Amendment, including without limitation, any information related to the rental rate, the length of the Term, and any other terms and conditions thereof. Tenant further agrees to take commercially reasonable precautions to prevent the unauthorized disclosure of any such information to any third parties. Tenant's obligations under this Section 15 shall survive the termination of the Lease.

16. Counterparts; Delivery. This Ninth Amendment may be executed in any number of counterparts, and by each of the parties on separate counterparts, each of which, when so executed, shall be deemed an original, but all of which shall constitute but one and the same instrument provided that all parties execute and deliver a counterpart to the other party. Delivery of an executed counterpart of this Ninth Amendment by electronic delivery shall be equally as effective as delivery of a manually executed counterpart of this Ninth Amendment. Any party delivering an executed counterpart of this Ninth Amendment by electronic delivery shall also endeavor to deliver a manually executed counterpart of this Ninth Amendment, but the failure to deliver a manually executed counterpart shall not affect the validity, enforceability or binding effect of this Ninth Amendment.

[SIGNATURE PAGE FOLLOWS]

IN WITNESS WHEREOF, the parties hereto have executed this Ninth Amendment to Lease Agreement on the day and year set forth below.

LANDLORD:

WHARTON LENDER ASSOCIATES, LP,
a Pennsylvania Limited Partnership

By: WHARTON LENDER PROPERTIES, LLC,
a Pennsylvania Limited Liability Company,
its General Partner

DocuSigned by:
By: _____
89B6BB986FD4454...
Name: Larry Walsh
Title: COO
Date: January 4, 2022

TENANT:

KRYSTAL BIOTECH, INC.,
a Delaware corporation

DocuSigned by:
By: Kathryn Romano
9FB32765999540D...
Name: Kathryn Romano
Title: Chief Accounting Officer
Date: January 4, 2022

DS
ASP

EXHIBIT "A"

Sixth Floor Expansion Space

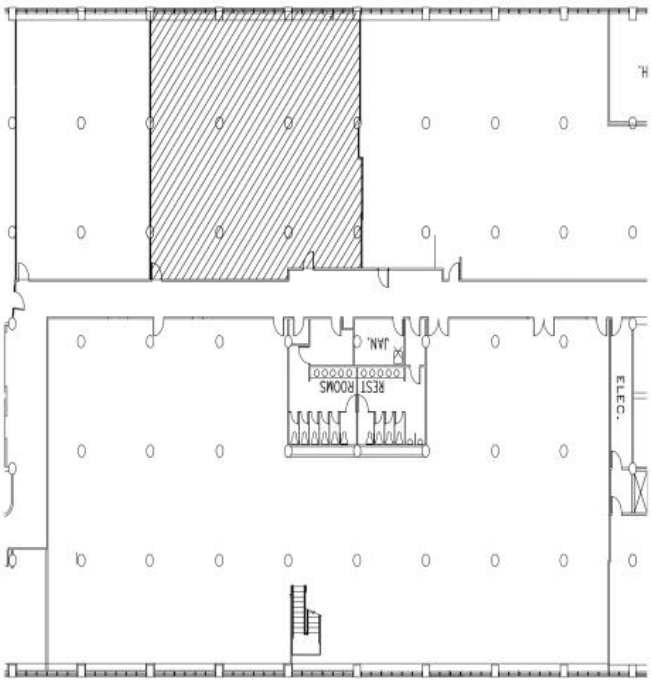
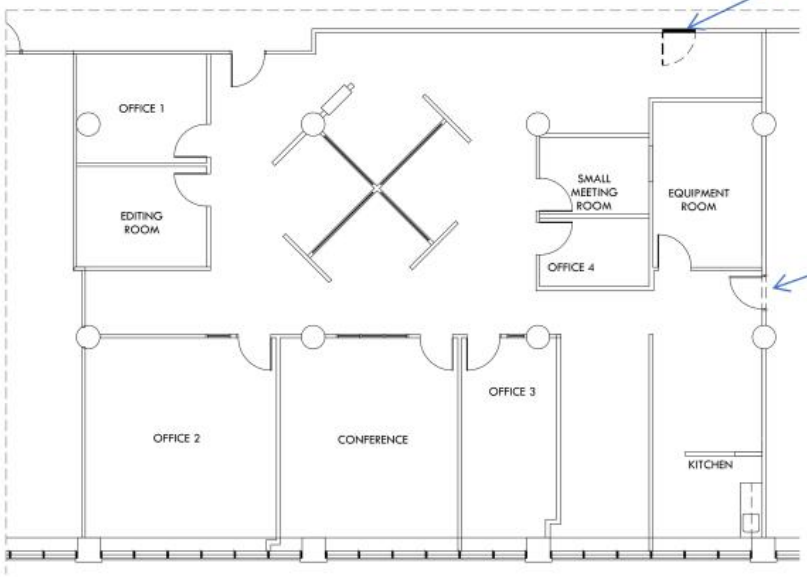


EXHIBIT "B"

Landlord's Sixth Floor Expansion Space Work



Demo Door- infill with metal studs and drywall- finish, paint and install base to match; both sides

Demo section of existing partition and install a new hollow metal door frame with wood door to match expansion space with clear tempered glass lite. Install locking hardware. Tenant shall install electric strike & card reader/ card access system.

Landlord will deliver the Expansion Space in its existing 'as-is' 'where-is' condition with all of the current tenant's property removed and in broom-clean condition with all lights and plugs in good working order, plus complete the below work using building standard materials at no cost to Tenant.

- Cove base will be repaired where needed
- Broken ceiling tiles will be replaced
- Walls will be painted a maximum of 2 colors selected by Tenant
- ☐ Existing partitions and doors will remain in their current locations and conditions except for:
  - Any damaged dry wall will be patched and repaired
  - 2nd door to the floor corridor (not the main entrance door) will be removed and replaced with dry wall to seal the opening
  - New door created between the Expansion Space and Suite 625A (already part of Tenant's Premises). Door will have a hollow metal frame, wood door to match with a tempered glass insert with a lock and the ability to accommodate key fob locking mechanism supplied by tenant.

Exhibit C

Date
11/13/2019
Project Name
ZXG12 460v 3ph down
Project Number
Client / Purchaser

YORK®

Submittal Summary Page

Qty	Tag #	Model #	Description
1		ZXG12E4B3AA1A111A2	10 Ton, Two Stage Cooling, York Sun Core Single Packaged R-410A Air Conditioner, 11.0 EER, 220 MBH Two Stage Input Medium Heat Aluminized Gas, Gas Heat, 460-3-60 • VFD IntelliSpeed • Medium Static Belt Drive Blower • Smart Equipment Controller including Discharge Air, Return Air, and Outdoor Air Temperature Sensors. • Microchannel All Aluminum Condenser Coil, Copper tube/Aluminum fin Evaporator Coil
1		1RC0457	Curb Rigid 14" (356 mm) Large Footprint
1		2EE04706824	Economizer, DB, Vertical Flow, Large Footprint (with Barometric Relief)

Equipment start-up and commissioning by a factory trained technician is recommended.
Contact your supplying distributor or sales representative for additional information & guidance.

⚠ WARNING: Cancer and Reproductive Harm - www.P65Warnings.ca.gov

YORK®

Direct Fit (3-12.5 Ton Package) L526

Single Package R-410A Air Conditioner

Project Name: **ZXG12 460v 3ph down** Unit Model #: **ZXG12E4B3AA1A111A2**

Quantity: **1** System: **ZXG12E4B3AA1A111A2**

Cooling Performance	
Total gross capacity	133.0 MBH
Sensible gross capacity	93.0 MBH
Efficiency (at ARI)	11.00 EER
Integrated eff. (at ARI)	14.40 IEER
Ambient DB temp.	95.0 °F
Entering DB temp.	80.0 °F
Entering WB temp.	67.0 °F
Leaving DB temp.	58.5 °F
Leaving WB temp.	56.5 °F
Power input (w/o blower)	9.21 kW
Sound power	84 dB(A)

Refrigerant	
Refrigerant type	R-410A
Sys1	5 lbs 12 oz
Sys2	5 lbs 12 oz

Gas Heating Performance	
Entering DB temp.	60 °F
Heating output capacity (Max)	176 MBH
Supply air	4000 CFM
Heating input capacity (Max)	220 MBH
Leaving DB temp.	100.7 °F
Air temp. rise	40.7 °F
SSE	80.0 %
Stages	2

Supply Air Blower Performance	
Supply air	4000 CFM
Ext. static pressure	0.4 IWG
Addl. Unit Losses (Options/Accessories)	0.38 IWG
Blower speed	882 RPM
Max BHP of Motor (including service factor)	3.70 HP
Duct location	Bottom
Motor rating	3.70 HP
Actual required BHP	2.41 HP
Power input	2.14 kW
Elevation	0 ft.
Drive type	BELT

Electrical Data	
Power supply	460-3-60
Unit min circuit ampacity	24.9 Amps
Unit min over-current protection	25 Amps
Unit max over-current protection	30 Amps

Dimensions & Weight					
Hgt	49 in.	Len	87 in.	Wth	62 in.
Weight with factory installed options					995 lbs.

Clearances					
Right	18 in.	Front	48 in.	Back	18 in.
Top	72 in.	Bottom	1 in.	Left	12 in.

Note: Please refer to the tech guide for listed maximum static pressures

10 Ton

- All units are manufactured at an ISO 9001 registered facility and each rooftop is completely computer-run tested prior to shipment.

Unit Features

- Two Stage Cooling
- 220 MBH Two Stage Input Medium Heat Aluminized Gas
- Full perimeter base rails with built in rigging capabilities
- Either supply and/or return can be field converted from vertical to horizontal configuration without cutting panels.
- Unit Cabinet Constructed of Powder Painted Steel, Certified At 750 Hours Salt Spray Test (ASTM B-117 Standards)
- Scroll Compressors
- Medium Static Belt Drive Blower
- Solid Core Liquid Line Filter Driers
- Unit Ships with 2" Throwaway Filters
- Replacement Filters: 4 - (20" x 20"). Unit accepts 2" or 4" wide filters.
- Short Circuit Current: 5kA RMS Symmetrical
- Single Point Power Connection
- Microchannel All Aluminum Condenser Coil, Copper tube/Aluminum fin Evaporator Coil

BAS Controller

- Smart Equipment Controller including Discharge Air, Return Air, and Outdoor Air Temperature Sensors.

Standard Unit Controller: Smart Equipment Control Board

- Safety Monitoring - Monitors the high and low-pressure switches, the freezestats, the gas valve, if applicable, and the temperature limit switch on gas and electric heat units. The unit control board will alarm on ignition failures, safety lockouts and repeated limit switch trips.
- An Integrated Low-Ambient Control, Anti-Short Cycle Protection, Lead-Lag, Fan On and Fan off Delays, Low Voltage Protection, On-Board Diagnostic and Fault Code Display. Allows all units to operate in the cooling mode down to 0 °F outdoor ambient without additional components or intervention.

Warranty

- One (1) Year Limited Warranty on the Complete Unit
- Five (5) Year Warranty - Compressors
- Ten (10) Year Warranty - Aluminized Steel Tubular Heat Exchangers

YORK®

Direct Fit (3-12.5 Ton Package) L526

Single Package R-410A Air Conditioner

Project Name: **ZXG12 460v 3ph down** Unit Model #: **ZXG12E4B3AA1A111A2**

Quantity: 1 System: **ZXG12E4B3AA1A111A2**

Factory Installed Options

ZXG12E4B3AA1A111A2

Equipment Options		Option(s) Selected
Product Category:	ZX	York Sun Core Single Packaged R-410A Air Conditioner
Heat Type:	G	Gas Heat
Nominal Cooling Capacity:	12	10 Ton Two Stage Cooling 11.0 EER
Heat Size:	E	220 MBH Two Stage Input Medium Heat Aluminized Gas
Voltage:	4	460-3-60
Airflow:	B	Medium Static Belt Drive Blower
Airflow Options:	3	VFD IntelliSpeed
Coil Options:	A	Microchannel All Aluminum Condenser Coil, Copper tube/Aluminum fin Evaporator Coil
Controls:	A	Smart Equipment Controller including Discharge Air, Return Air, and Outdoor Air Temperature Sensors.
Sensor Options:	1	
Economizer / Damper:	A	
Convenience Outlet:	1	
Electrical Options:	1	
Cabinet Options:	1	
Special Options:	A	
Product Generation:	2	

Field Installed Accessories

- 1RC0457 - Curb Rigid 14" (356 mm) Large Footprint (135.0 lbs)
- 2EE04706824 - Economizer, DB, Vertical Flow, Large Footprint (with Barometric Relief) (96.0 lbs)

Equipment list for project: Krystal - Dated: Nov 5 2021

Units

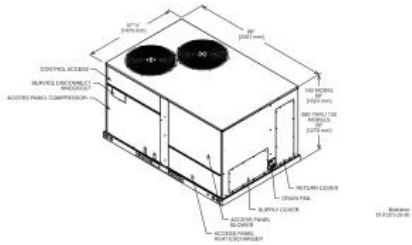
Tag No	Model No	Qty	Description
RTU - 1	RACDZT120ACG000CAAA1	1	RACD w/ VFD: New platform air conditioner small commercial packages, with VFD Voltage: 208-230V - 3PH - 60Hz Factory Options: Clear Control Economizer: Economizer

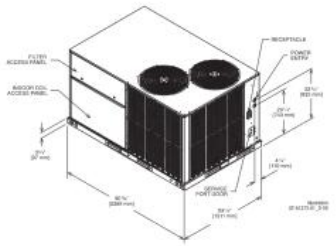
Accessories

Tag No	Field Model	Description
RTU - 1	RXRX-AY01	BACnet Communication Card
RTU - 1	RXKG-DDD14	Roofcurb 14"

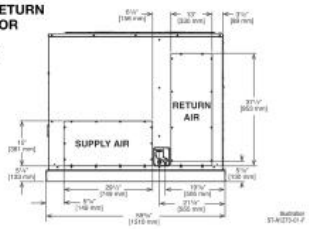
Notes

Model: RACDZT120ACG000CAAA1

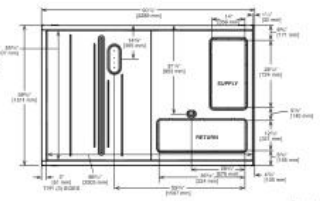




SUPPLY AND RETURN DIMENSIONS FOR HORIZONTAL APPLICATIONS



SUPPLY AND RETURN DIMENSIONS FOR DOWNFLOW APPLICATIONS



[ ] Designates Metric Conversions

Accessory
Economizer w/Single Enthalpy (Downflow)
Economizer w/Single Enthalpy (Horizontal)
Economizer-w/Single Enthalpy (Downflow) DDC
Economizer w/Single Enthalpy (Horizontal) DDC
Dual Enthalpy Kit
Dual Enthalpy Kit DDC
Carbon Dioxide Sensor (Wall Mount)
Power Exhaust
Power Exhaust
Manual Fresh Air Damper
Motorized Fresh Air Damper
Motorized Fresh Air Damper (DDC)
Roofcurb, 14"
Roofcurb, 24"
Roofcurb Adapter
Concentric Diffuser 7.5/8.5 Ton Flush
Concentric Diffuser 10.0 Ton Flush
Concentric Diffuser 12.5 Ton Flush
Concentric Diffuser 7.5/8.5 Ton Drop
Concentric Diffuser 10.0 Ton Drop

Accessory
Concentric Diffuser 12.5 Ton Drop
Concentric Adapter 7.5/8.5 Ton Drop
Concentric Adapter 10 Ton Drop
Concentric Adapter 12.5 Ton Drop
Outdoor Coil Louver Kit - ACD/090/102/120
Outdoor Coil Louver Kit - ACD150
Unwired Convenience Outlet
Unfused Service Disconnect
Comfort Alert (1 Per Compressor)
Comfort Alert (1 Per Compressor)
BACnet Communication Card
LonWorks Communication Card
Room Humidity Sensor
Room Temperature and Relative Humidity Sensor
Low-Ambient Control Kit
Freeze Stat Kit
Variable Frequency Drive Kit* *See model number break down below
Electric Heater Kits
Single Point Wiring Kit*

Before proceeding with installation, refer to installation instructions packaged with each model, as well as complying with all Federal, State, Provincial, and Local codes, regulations, and practices.

Rheem Sales Company, Inc.
P.O. Box 17010, Fort Smith, AR 72917

"In keeping with its policy of continuous progress and product improvement, Rheem reserves the right to make changes without notice."

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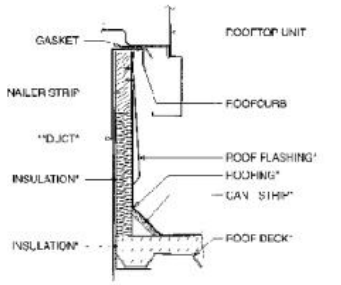
RXKG-DDD14 - Roofcurb 14"

ROOFCURBS (Full Perimeter)

- Rheem's roofcurb design can be utilized on all 7.5-12.5 ton [26.4-44.0 kW] RACD.
- Two available heights (14" [356 mm] and 24" [610 mm]) for ALL models.
- Quick assembly corners for simple and fast assembly.
- Opening provided in bottom pan to match the "Thru the Curb" electrical connection opening provided on the unit base pan.
- 1" [25 mm] x 4" [102 mm] Nailer provided.
- Insulating panels not required because of insulated outdoor base pan.
- Sealing gasket (40' [12.2 m]) provided with Roofcurb.
- Packaged for easy field assembly.

Roofcurb Model	Height of Curb
RXKG-DDD14	14" [356 mm]
RXKG-DDD24	24" [610 mm]



*BY CONTRACTOR

**FOR INSTALLATION OF DUCT AS SHOWN, USE RECOMMENDED DUCT SIZES FROM ROOFCURB INSTALLATION INSTRUCTIONS. FOR DUCT FLANGE ATTACHMENT TO UNIT, SEE UNIT INSTALLATION INSTRUCTIONS FOR RECOMMENDED DUCT SIZES.

Illustration
SI-A0743-02

ROOFCURB INSTALLATION

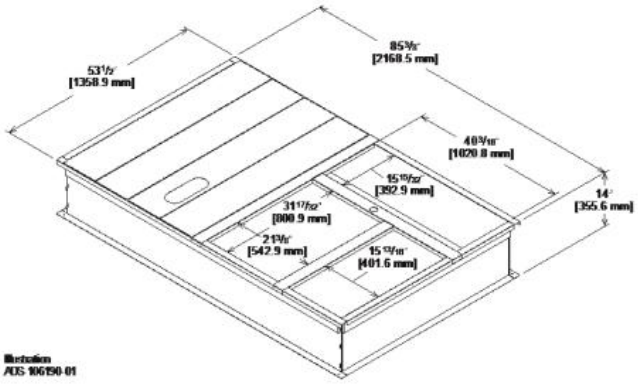


Illustration
AUS 10G190-01

[ ] Designates Metric Conversions

Exhibit 21.1

SUBSIDIARIES OF KRYSTAL BIOTECH, INC. AS OF DECEMBER 31, 2021

Name	Direct Parent	Ownership	Jurisdiction of Incorporation
Krystal Australia Pty Ltd	Krystal Biotech, Inc.	100%	Australia
Jeune, Inc.	Krystal Biotech, Inc.	100%	Delaware

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in Registration Statements on Form S-8 (Nos. 333-220589, 333-252351, 333-262825) and Form S-3-ASR (No. 333-237983) of our report dated February 28, 2022, with respect to the consolidated financial statements of Krystal Biotech, Inc. as of December 31, 2021 and 2020 and for the two years then ended, included in this annual report on Form 10-K of Krystal Biotech, Inc. as of and for the years ended December 31, 2021 and 2020.

/s/ Mayer Hoffman McCann P.C.

San Diego, California
February 28, 2022

Exhibit 31.1

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Krish S. Krishnan, certify that:

1. I have reviewed this Annual Report on Form 10-K of Krystal Biotech, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the small business issuer as of, and for, the periods presented in this report;

4. The small business issuer's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the small business issuer and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the small business issuer, including its subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the small business issuer's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the small business issuer's internal control over financial reporting that occurred during the small business issuer's most recent fiscal quarter (the small business issuer's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the small business issuer's internal control over financial reporting; and

5. The small business issuer's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the small business issuer's auditors and the audit committee of the small business issuer's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the small business issuer's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the small business issuer's internal control over financial reporting.

Date: February 28, 2022 By: /s/ Krish S. Krishnan

Krish S. Krishnan
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Kathryn A. Romano, certify that:

1. I have reviewed this Annual Report on Form 10-K of Krystal Biotech, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the small business issuer as of, and for, the periods presented in this report;

4. The small business issuer's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the small business issuer and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the small business issuer, including its subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the small business issuer's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the small business issuer's internal control over financial reporting that occurred during the small business issuer's most recent fiscal quarter (the small business issuer's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the small business issuer's internal control over financial reporting; and

5. The small business issuer's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the small business issuer's auditors and the audit committee of the small business issuer's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the small business issuer's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the small business issuer's internal control over financial reporting.

Date: February 28, 2022 By: /s/ Kathryn A. Romano

Kathryn A. Romano
Chief Accounting Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Krystal Biotech, Inc. (the "Company") on Form 10-K for the period ending December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: February 28, 2022 By: /s/ Krish S. Krishnan

Krish S. Krishnan
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Krystal Biotech, Inc. (the "Company") on Form 10-K for the period ending December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: February 28, 2022 By: /s/ Kathryn A. Romano

Kathryn A. Romano
Chief Accounting Officer
(Principal Financial and Accounting Officer)