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, 2023

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 Global Select Market

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

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

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 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 ☐

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

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, 2023 as reported by The Nasdaq Stock Market, was $2.8 billion.

The number of shares of Registrant's common stock outstanding as of February 19, 2024 was 28,292,616.

Portions of the Registrant's definitive proxy statement relating to its 2024 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.

Table of Contents

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:

- our commercialization plans in the United States for our first commercial product, VYJUVEK® (beremagene geperpavec-svdt, or B-VEC; referred to as B-VEC outside the U.S.), which was approved by the United States Food and Drug Administration ("FDA") in May 2023 for the treatment of dystrophic epidermolysis bullosa ("DEB");
- our expectations regarding reimbursement of VYJUVEK in the U.S., including coverage determinations and the timing thereof from commercial health plans and Medicaid;
- the timing, scope and results of our regulatory filings and potential approvals for marketing authorizations for B-VEC in the European Union and Japan,
- our expectations regarding the timing of completion of our open label extension study of B-VEC in Japanese patients, and our plans and expected timing of commercial launch in Europe and Japan;
- our plans for commercialization of B-VEC outside of Germany, France, Italy, Spain, the United Kingdom, and Japan;
- the potential clinical development path for ophthalmic B-VEC for the treatment of ocular complications of DEB;
- the initiation, timing, progress and results of clinical trials for KB407, KB408, KB707 (intratumoral and inhaled), KB105, KB104, KB301, 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, the timing of our disclosure of study data, and our research and development programs;
- the timing, scope or results of regulatory filings and approvals, marketing and other regulatory approval of our product candidates;
- our ability to achieve certain accelerated, orphan drug, and other designations from the FDA or other regulatory authorities;
- our estimates regarding the potential market opportunity for any of our 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 beliefs about our proprietary HSV-1 based vector platform, including its ability to deliver multiple genes and other effectors, which could enable development of therapies for more common conditions that are not necessarily the result of an inherited genetic defect;
- 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 VYJUVEK and 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;
- our estimates regarding expenses, revenue, capital requirements and needs for or ability to obtain additional capital;
- developments and projections relating to our competitors and our industry;
- our ability to establish and maintain collaborations;
- our ability to successfully resolve any intellectual property or other claims that may be brought against us;
- the impact of laws and regulations; and
- any statements regarding U.S. or global economic conditions 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. You should read this Annual Report completely and with the understanding that our actual future results may be materially different from what we expect.

Forward-looking statements represent our management's beliefs and assumptions only as of the date of this Annual Report. Except as required by law, we assume no obligation to update or revise these forward-looking statements publicly as a result of subsequent events, developments or otherwise, 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.

This Annual Report on Form 10-K also contains estimates and other statistical data made by independent parties and by the Company that involves a number of assumptions and limitations. Neither the Company nor any other person makes any representation as to the accuracy or completeness of such data or undertakes any obligation to update such data after the date of this Annual Report.

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 are substantially dependent on the commercial success of VYJUVEK.
- 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 VYJUVEK or our product candidates, if approved.
- If any product liability lawsuits are successfully brought against us, we may incur substantial liabilities and may be required to limit commercialization of VYJUVEK or our product candidates.
- Healthcare legislative reform measures may have a material adverse effect on our business and results of operations.

- We are subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws and health information privacy and security laws, and if we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.
- Our internal computer systems, or those of our collaborators or other contractors or consultants, may fail or suffer a cyber-security incident, such as a data breach or computer virus, which could harm our business by damaging our reputation, exposing us to liability, or materially disrupting our operations, including production of VYJUVEK or our product development programs.
- Our international operations may expose us to business, regulatory, political, operational, financial, pricing and reimbursement and economic risks associated with doing business outside of the United States.
- 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 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 products may cause undesirable side effects or have other properties that could delay or prevent regulatory approval, limit the commercial potential or result in significant negative consequences following any potential marketing approval.
- We rely on third parties to conduct certain aspects of our preclinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or comply with regulatory requirements, we may not be able to obtain regulatory approval for, or commercialize, our product candidates.
- 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.
- VYJUVEK and our product candidates remain subject to regulatory oversight even after regulatory approval. 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 VYJUVEK or any of our product candidates that obtain regulatory approval to lose that approval.
- Even though we have obtained FDA approval of VYJUVEK and 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.
- Delays in obtaining regulatory approvals of the process and facilities needed to manufacture our product candidates or disruptions in our manufacturing process may disrupt our production of VYJUVEK or delay or disrupt our development and commercialization efforts with respect to our product candidates.
- Although we have established our own manufacturing facilities for VYJUVEK and our product candidates, we may also utilize third parties to conduct our product manufacturing or components thereof. Therefore, we are subject to the risk that these third parties may not perform satisfactorily.
- 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 ability to produce VYJUVEK for commercial supply or any product candidate for clinical development.
- We have limited experience as a commercial company and the sales, marketing, and distribution of VYJUVEK or any future approved products may be unsuccessful or less successful than anticipated.
- If we are unable to maintain our agreements with third parties to distribute VYJUVEK to patients in the United States, our results of operations and business could be adversely affected.
- If we are unable to expand our medical affairs, marketing, market access, sales, and distribution capabilities or collaborate with third parties to market and sell our product candidates for which we obtain marketing approval, we may be unable to generate sufficient product revenue.
- If the market opportunities for VYJUVEK or our product candidates are smaller than we believe they are, our product revenue may be adversely impacted, and our business may suffer.
- Government price controls or other changes in pricing regulation could restrict the amount that we are able to charge for VYJUVEK and our product candidates, if approved, which would adversely affect our 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 VYJUVEK or our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate product revenue.
- If we are unable to obtain and maintain adequate United States and foreign patent protection for VYJUVEK, our current product candidates, 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 VYJUVEK, 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 rights and regulatory exclusivity rights do not necessarily address all potential threats.
- Risks related to our financial position and need for additional capital.
- Our Chief Executive Officer and Chairman of the Board of Directors and our founder, President of R&D and director will have the ability to substantially influence all matters submitted to stockholders for approval.

Item 1. Business.

Overview

We are a fully integrated, commercial-stage biotechnology company focused on the discovery, development, and commercialization of genetic medicines to treat diseases with high unmet medical needs. Our first commercial product, VYJUVEK®, was approved by the FDA on May 19, 2023 for the treatment of DEB, and we subsequently initiated our U.S. commercial launch. VYJUVEK is the first medicine approved by the FDA for the treatment of DEB.

Using our patented gene therapy technology 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 healthcare professional's office or 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 and serious diseases. Our innovative technology platform is supported by an in-house, FDA-inspected commercial scale Current Good Manufacturing Practice ("CGMP") manufacturing facility and a second, completed and qualified, commercial scale CGMP facility to support future expansion.

Our development pipeline includes multiple clinical stage programs for rare and serious diseases, and we are investing in research and development to advance and grow this pipeline. We possess exclusive rights to develop, manufacture, and commercialize our FDA approved product and our pipeline candidates throughout the world.

While our focus is on the development of gene therapies to treat patients with severe, life-threatening, or rare diseases with high unmet medical needs, we are also evaluating the potential of our platform to address more prevalent and/or non-genetic conditions. To that end, in April 2019, we incorporated Jeune Aesthetics, Inc. ("Jeune Aesthetics"), a wholly-owned subsidiary, for the purposes of undertaking preclinical and clinical studies for aesthetic skin conditions.

Our Redosable Gene Therapy Platform

We believe that certain inherent features of the 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 and represents an opportunity to generate a portfolio of highly differentiated and potentially first-in-class or best-in-class genetic medicines. Advantages of our gene therapy technology platform include 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 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 wild-type virus will not limit the number of patients who may be amenable to treatment with VYJUVEK or 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-based 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 35 Kb or greater without any significant impact on yield or titer. In VYJUVEK, we have successfully inserted two functional copies of the complete ~9 Kb human *COL7A1* gene. In contrast, packaging capacity for most other vectors being used is at or under ~10 Kb, 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, we believe our vector penetrates and delivers its payload much more efficiently than other vectors,

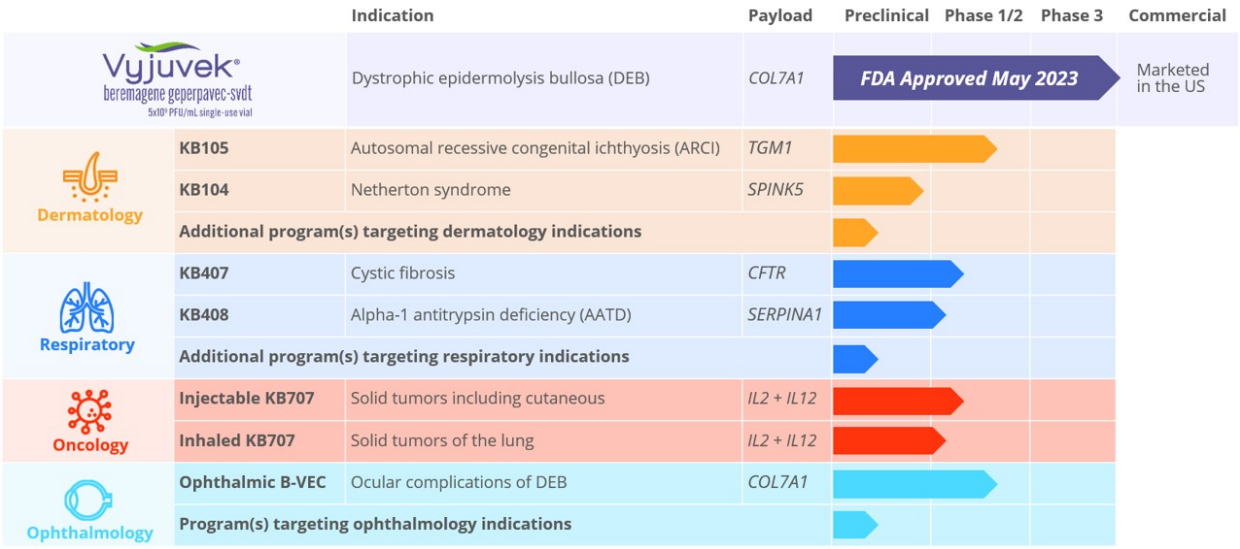
resulting in transduction efficiencies or cell penetration as high as 95% in cell-based studies. The greater payload capacity of our vector and the high transduction efficiencies achieved allow us to deliver a full gene (or genes) directly to any patient's tissues for off-the-shelf, *in vivo* gene expression 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 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 facilitates our ability to ship VYJUVEK and our product candidates 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 commercial manufacturing. Our scientific team's collective decades of experience and expertise in HSV engineering and purification has allowed us to successfully optimize our engineered HSV-1 vector production process and develop in-house Chemistry, Manufacturing and Control ("CMC") capabilities.
- **First Approval for Platform Builds on 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 for chronic administration, it created a regulatory precedent for approval of an HSV-1-based chronic gene therapy. Now, with the FDA approval our first platform product, VYJUVEK, regulatory precedent for our proprietary HSV-1-based platform has also been established, and regulator familiarity with HSV-1 and our platform continues to grow.

The above listed benefits of our innovative platform, and compatibility with formulation for topical, injectable, and inhaled delivery, make it the ideal choice to treat diseases and conditions of the skin, lung, and eye.

Our FDA Approved Product and Pipeline

The following table summarizes information regarding our FDA approved product, VYJUVEK, and product candidates in various stages of clinical and preclinical development as of the date of this Annual Report:



Our FDA Approved Commercial Product

VYJUVEK (beremagene geperpavec-svdt, or B-VEC; referred to as B-VEC outside the U.S.)

Disease Background

DEB is a rare and severe monogenic skin disease. DEB affects the skin and mucosal tissues and is caused by one or more mutations in a gene called *COL7A1*, which is responsible for the formation of the protein type VII collagen ("COL7"). COL7 forms anchoring fibrils that bind the dermis (inner layer of the skin) to the epidermis (outer layer of the skin). In DEB patients, the genetic defect in *COL7A1* results in loss or malfunctioning of these anchoring fibrils, leading to extremely fragile skin that blisters and tears from minor friction or trauma. Those who are born with DEB are sometimes called "butterfly children," because their skin is likened to be as fragile as the wings of a butterfly. DEB patients may suffer from open wounds, skin infections, fusion of fingers and toes, ocular complications that can result in severe vision loss, 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 DEB patients in the United States and approximately 9,000 worldwide. Prior to the approval of VYJUVEK, the standard of care for DEB patients had been limited to palliative measures that seek to provide relief from some of the symptoms of DEB but do not meaningfully impact disease outcomes.

B-VEC

B-VEC 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 previous standard of care, B-VEC treats DEB 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. B-VEC was specifically designed to be easily administered by a healthcare professional in a doctor's office or at the patient's home. B-VEC was approved by the FDA in May 2023 and is marketed as VYJUVEK in the United States.

We believe our approach to treating DEB is positively differentiated relative to palliative approaches, which do not address the underlying genetic cause of DEB or impact the durability of wound closure, and 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.

Commercial Launch

We launched VYJUVEK, the first FDA approved treatment for DEB and the first and only corrective therapy for DEB globally, in the United States in the second quarter of 2023. We estimate that there are approximately 3,000 patients in the United States suffering from DEB, of which 1,200 were identified at launch through claims analytics and pre-launch patient identification activities conducted by our commercial field force. Since our commercial launch of VYJUVEK in the United States in the second quarter of 2023, we have reported $50.7 million in net product revenue.

Commercial readiness efforts had been underway over two years prior to the FDA approval of VYJUVEK. In the United States, prior to FDA approval and VYJUVEK launch, as part of our disease awareness program, our medical science liaisons had been interacting with and educating health care professionals ("HCPs") on DEB and the importance of genetic testing in ensuring an accurate diagnosis. We also built-out Krystal Connect™, our U.S. in-house patient services call center staffed with Krystal employees, which was launched subsequent to FDA approval to assist patients, caregivers and HCPs interested in accessing VYJUVEK. Additionally, we hired, trained and deployed commercial field teams to educate on DEB and to prepare for launch of VYJUVEK. Our field force has been fully deployed since launch and is covering both centers of excellence and community physicians treating patients with DEB.

Our market access team had successfully secured positive policies or coverage decisions from plans covering over 93% of commercial and Medicaid lives in the United States, including positive coverage determinations from all major commercial national health plans and several regional health plans. In January 2024, we announced that the United States Centers for Medicare & Medicaid Services ("CMS") had assigned a permanent and product-specific J-code (J3401) for VYJUVEK, effective on January 1, 2024.

VYJUVEK is distributed in the U.S. through a limited network of specialty pharmacy providers that administer the medication to patients in their homes and specialty distributors that distribute VYJUVEK for administration to patients at the site of care.

Preparations and infrastructure buildout are underway in Europe and Japan to support direct commercial launch by Krystal in these regions, which is expected by 2025. We have also initiated a named patient program in Europe to provide initial access to VYJUVEK. Outside of Germany, France, Italy, Spain, the United Kingdom, and Japan, our strategy is to enter into distribution arrangements with local distributors to commercialize VYJUVEK.

Regulatory Status

On May 19, 2023, the FDA approved VYJUVEK, the first ever redosable gene therapy, for treating patients, six months of age or older, suffering from DEB. No clinical post-marketing commitments or Risk Evaluation and Mitigation Strategies program were required by the FDA. With the approval, the FDA issued a Rare Pediatric Disease Priority Review Voucher ("PRV"), which confers priority review to a subsequent drug application that would not otherwise qualify for priority review. We sold the PRV in the third quarter of 2023 for $100.0 million.

The FDA had previously granted B-VEC Orphan Drug Designation ("ODD"), Fast Track Designation, Rare Pediatric Designation, and granted Regenerative Medicine Advanced Therapy to B-VEC for the treatment of DEB.

In September 2023, we received a positive opinion from the EMA Pediatric Committee on the Pediatric Investigation Plan for B-VEC for the treatment of DEB. Based on this positive opinion, we expect to be eligible for up to an additional two years of marketing exclusivity in the European Union ("EU"), on top of the ten-year EU market exclusivity after market approval in the EU. The European regulatory authorities have also granted B-VEC Orphan Designation and PRIority MEdicines eligibility for B-VEC to treat DEB.

In October 2023, we submitted a marketing authorization application ("MAA") to the EMA for B-VEC for the treatment of DEB in patients from birth. In November 2023, we were notified that the MAA had been validated and was now under Committee for Medicinal Products for Human Use review. We currently expect an EMA decision on our MAA in the second half of 2024.

In December 2023, B-VEC was granted ODD status for the treatment of DEB by the Japan Ministry of Health, Labour and Welfare, a designation which confers specific benefits for orphan drug development including priority review of applications, extended registration validity, and reduced development costs. We anticipate filing our Japan New Drug Application with Japan's Pharmaceuticals and Medical Devices Agency ("PMDA") in the second half of 2024 enabling a potential authorization in 2025.

Clinical Development

We initiated Phase 1 testing of a topical formulation of B-VEC 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. In March 2022, results from the complete Phase 1/2 study of topical B-VEC for the treatment of DEB were published in *Nature Medicine.*

We initiated a pivotal Phase 3 trial ("GEM-3 trial") in July 2020. The GEM-3 trial of topical B-VEC for the treatment of DEB was a randomized, double-blind, intra-patient placebo-controlled multicenter study designed to evaluate the efficacy and safety of B-VEC for patients suffering from both recessive and dominant forms of DEB. The trial enrolled 31 participants with DEB, 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 B-VEC 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. 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. We announced positive results from the GEM-3 trial in November 2021 and in December 2022 full results from the GEM-3 trial were published in the *New England Journal of Medicine.*

Following completion of the GEM-3 trial, we initiated an open label extension study ("OLE") to provide extension of B-VEC treatment for participants who completed study GEM-3 ("rollover participants") and B-VEC treatment for newly enrolling ("naïve participants") participants with DEB. The OLE was a multi-center, open-label study of B-VEC for the topical treatment of DEB wounds. The study enrolled 47 participants in total, comprising of 24 rollover participants and 23 naïve participants, at five sites in the United States. In April 2022, following feedback from the FDA, we announced that patients enrolled in the OLE study would have the option to be dosed in their homes by a health care professional. The primary study objective was the assessment of safety and tolerability of extended dosing with B-VEC in a broader patient population. Various quality of life and participant satisfaction metrics were also assessed. The OLE study was concluded in the third quarter of 2023, and the safety profile continued to support the overall benefit-risk of B-VEC, with no new safety concerns noted with extended duration of dosing of B-VEC. We expect to disclose detailed study data at upcoming scientific meetings or in scientific publications.

In July 2023, the PMDA in Japan officially accepted our OLE study of B-VEC in Japanese patients (the "Japan OLE"). Following that acceptance, we initiated the Japan OLE study and completed study enrollment. A total of 5 Japanese DEB patients have been enrolled. Details of the study can be found at jrct.niph.go.jp under JRCT ID jRCT2053230075. Nothing

included on this website shall be deemed incorporated by reference into this Annual Report on Form 10-K. We expect to complete the study in 2024.

Our Pipeline Programs

Ophthalmology

Ophthalmic B-VEC for Ocular Complications of DEB

Disease Background

DEB is a rare and severe monogenic blistering disease that affects not only the skin, but also mucosal tissues dependent on COL7 anchoring fibrils for maintaining epithelial lining integrity. This includes the eye, where COL7 anchors the corneal epithelium. For a meaningful proportion of DEB patients, the genetic defect in *COL7A1* results in loss or malfunctioning of these anchoring fibrils causing ocular complications, such as corneal erosions, abrasions, blistering and scarring, that can lead to progressive vision loss.

Over 50% of patients with recessive form of DEB are thought to suffer from ocular complications. Correspondingly, we believe there are over 750 patients in the United States and over 2,000 worldwide that are affected. Disease management varies from supportive care and wound management to surgical interventions to remove scar tissue. No corrective or FDA approved therapies are presently available.

Ophthalmic B-VEC

Ophthalmic B-VEC is a redosable eye drop formulation of B-VEC, designed to deliver two copies of the *COL7A1* transgene to the epithelial cells in a patient's eye to produce COL7 protein. As with VYJUVEK, the goal of therapy with ophthalmic B-VEC is to treat the disease locally, at the molecular level, by providing the patient's epithelial cells of the eye the template to make normal COL7 protein, and thereby address the fundamental disease-causing mechanism. In preclinical studies, single and repeated topical B-VEC administration to the eye in a mouse corneal lesion model resulted in localized *COL7A1* expression with no adverse effects noted histologically.

Ophthalmic B-VEC has been applied topically to the eye of one DEB patient under a compassionate use protocol. The clinical observations of this compassionate use case were published in the *New England Journal of Medicine* in February 2024. The patient presented with severe cicatrizing conjunctivitis secondary to DEB. Surgical symblepharon lysis of the patient's right eye with pannus removal was conducted and regular administration of B-VEC as an eye drop directly to the eye (5×10^9 PFU/mL) were added to routine post-surgical care, three times weekly for the first two weeks and then once weekly. B-VEC application frequency was further decreased to once monthly once the corneal epithelium was healed. B-VEC was well tolerated with no drug related adverse events noted. Full corneal healing was observed at 3 months, as well as significant visual acuity improvement from hand motion to 20/25 by 8 months.

In February 2024, the FDA agreed with our proposed single arm, open label study in approximately 10 patients to enable approval of B-VEC eyedrops to treat ocular complications secondary to DEB. We plan to initiate this study in the second half of 2024.

Respiratory

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 36.6 years in 2022. 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%-15% of patients with CF who have genetic mutations non-amenable to currently approved CFTR small molecule "modulators". The CFF estimates that there are close to 40,000 children and adults living with CF in the United States, and an estimated 105,000 people diagnosed with CF across 94 countries. People of every racial and ethnic group are affected by this debilitating disease.

KB407

KB407 is a redosable off the-shelf gene therapy designed to deliver two copies of the full-length *CFTR* transgene 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 granted KB407 ODD and Orphan Designation, respectively, 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 July 2023, we announced that we had dosed the first patient in our Phase 1 CORAL-1 study evaluating KB407, delivered via a nebulizer, for the treatment of patients with CF. The CORAL-1 study is a multi-center, dose-escalation trial of KB407 in patients with CF, regardless of their underlying genotype. In the fourth quarter of 2023, we completed the first cohort of the CORAL-1 study with no severe or serious adverse events and, in January 2024, we initiated dosing in the second of three cohorts. Details of the Phase 1 study can be found at www.clinicaltrials.gov under NCT identifier NCT05504837. Nothing included on this website shall be deemed incorporated by reference into this Annual Report on Form 10-K.

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 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.

We estimate that there are over 60,000 patients in the United States and over 250,000 patients globally suffering from severe AATD. 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 proprietary vector, designed to deliver two copies of the *SERPINA1* transgene that encodes functional, full-length human AAT protein, for the treatment of AATD. Preclinical studies 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.

In September 2023, the FDA granted KB408 ODD for the treatment of AATD.

Clinical Development of KB408

In September 2023, we announced that the FDA had accepted our Investigational New Drug ("IND") application to evaluate KB408, delivered via a nebulizer, in a clinical trial to treat patients with AATD. In February 2024, the Company dosed the first patient in the KB408 Phase 1 SERPENTINE-1 study for the treatment of Alpha-1 Antitrypsin Deficiency. SERPENTINE-1 is a Phase 1 open-label, single dose escalation study in adult patients with AATD with a PI*ZZ genotype. Three planned dose levels of KB408 will be evaluated in up to 12 patients to evaluate the safety, tolerability, and proof-of-mechanism of KB408. Cohorts 1 and 2 will focus predominantly on safety with dose escalation and pharmacodynamic activity in the lung will be assessed at the highest dose by bronchoscopy in Cohort 3. The Company is working closely with the Alpha-1 Foundation and their Therapeutic Development Network on the SERPENTINE-1 study and intends to announce interim data from the study in the second half of 2024. Details about the Phase 1 study can be found at www.clinicaltrials.gov under NCT

identifier: NCT06049082. Nothing included on this website shall be deemed incorporated by reference into this Annual Report on Form 10-K.

Oncology

KB707 for Solid Tumors

Disease Background

Cancer is progressive and typically fatal disease for which adequate treatment options are lacking. Despite recent advancements, the treatment of locally advanced or metastatic solid tumors remains particularly difficult and long-term outcomes are poor. Standard of care treatments are rarely curative, therapeutic benefits are transient, and the majority of patients with locally advanced or metastatic solid tumors are either ineligible for, or will eventually exhaust, currently available therapies. Many available therapies are also highly toxic and poorly tolerated by patients.

Cancer imposes a heavy burden on patients worldwide. The World Health Organization lists cancer as a leading cause of death globally and estimates that the disease was responsible for nearly 10 million deaths in 2020. Of these, an estimated 5 million deaths were attributed to solid tumor malignancies of the lung, colon and rectum, liver, stomach, and breast alone. Solid tumor malignancies similarly impose a heavy burden on patients in the U.S., with the National Cancer Institute estimating that over 300,000 patients will have died from lung, colon and rectum, pancreas, breast, prostate, liver and bile duct, and melanoma of the skin cancers in 2023.

KB707

KB707is a redosable, immunotherapy designed to deliver genes encoding both human interleukin-2 (“IL-2”) and interleukin-12 (“IL-12”) to the tumor microenvironment and promote systemic immune-mediated tumor clearance. Two formulations of KB707 are in development, a solution formulation for transcutaneous injection and an inhaled (nebulized) formulation for lung delivery. IL-2 and IL-12 are secreted cytokines with complementary functions promoting cell-mediated immunity in humans. Both IL-2 and IL-12 have been shown to elicit anti-tumor immune responses in preclinical or clinical models and have been extensively studied for their potential in cancer immunotherapy. Despite promising signs of efficacy, it has proven difficult to effectively harness IL-2 and IL-12 for therapeutic benefit, as systemic administration is often poorly tolerated, and the inherently short half-lives of these cytokines necessitate high dose levels and extremely frequent dose intervals. KB707 leverages the Company’s HSV-1 vector platform – and its ability to efficiently deliver a durable DNA payload without active replication and minimal cytotoxicity – to drive local and sustained cytokine expression within the tumor microenvironment and maximize the therapeutic window and benefit of IL-2 and IL-12.

In preclinical studies, KB707 has been shown to efficiently transduce mammalian cells *in vitro* leading to the secretion of bioactive IL-2 and IL-12 and drive localized, durable cytokine expression in mouse skin after intradermal injection. Furthermore, in stringent, checkpoint inhibitor refractory ‘cold’ syngeneic mouse models, HSV-1 vector based delivery of murine equivalent *IL2* and *IL12* elicited robust antitumor responses and survival benefits, including via intratumoral injection in single and dual flank B16F10 melanoma models, as well as via intratracheal delivery in a metastatic K7M2 osteosarcoma model, with evidence of protection from tumor rechallenge in both models suggestive of prolonged adaptive immunity.

In July 2023, the FDA granted intratumoral KB707 Fast Track Designation for the treatment of anti-programmed cell death protein-1 (“PD-1”) relapsed/refractory locally advanced or metastatic melanoma. In February 2024, the FDA also granted inhaled KB707 Fast Track Designation for the treatment of patients with solid tumors with pulmonary metastases that are relapsed or refractory to standard of care therapy.

Clinical Development of KB707

In July 2023, we announced that the FDA had accepted our IND application to evaluate intratumoral KB707 in a clinical trial to treat patients with locally advanced or metastatic solid tumors. The study, OPAL-1, is an open-label, multi-center, monotherapy, dose escalation and expansion Phase 1 study, enrolling patients with locally advanced or metastatic solid tumors, who relapsed or are refractory to standard of care, with at least one measurable and injectable tumor accessible by transcutaneous route. The primary objective of the study is to evaluate safety and tolerability of KB707. Efficacy will also be assessed by multiple measures including overall response rate, progression free survival, and overall survival, and the immune effects of KB707 monotherapy will be assessed in tumor tissue, lymph nodes, and blood. The first patient in OPAL-1 was dosed in October 2023 and enrollment is ongoing. Details of the OPAL-1 study can be found at www.clinicaltrials.gov under NCT identifier NCT05970497. Nothing included on this website shall be deemed incorporated by reference into this Annual Report on Form 10-K.

In January 2024, the FDA accepted an amendment to our IND application to evaluate inhaled KB707 in a clinical trial to treat patients with locally advanced or metastatic solid tumors of the lung. We plan on initiating this open-label, multi-center, monotherapy, dose escalation and expansion Phase 1 study, KYANITE-1, in the first half of 2024. Details of the KYANITE-1

study can be found at www.clinicaltrials.gov under NCT identifier NCT06228326. Nothing included on this website shall be deemed incorporated by reference into this Annual Report on Form 10-K.

Dermatology

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 *TGM1* gene encoding the enzyme transglutaminase-1 ("TGM1"), 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. We estimate there are approximately 2,000 to 6,000 patients with of TGM1-deficient ARCI in the United States and Europe.

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 B-VEC, 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 ODD and Orphan Designation, respectively, 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 Society for Investigative Dermatology ("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 (TAs). Each treatment area was assigned to receive repeat doses of $4.0x10^9$ PFU (n=2 treatment areas) or $1.0x10^{10}$ 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 later in 2024.

KB104 for Netherton Syndrome

Disease Background

Netherton Syndrome is a debilitating monogenic autosomal recessive skin disorder. The disease arises due to mutations in the *SPINK5* gene, resulting in loss of activity of its encoded serine protease inhibitor Kazal-type 5 ("SPINK5"), also known as Lympho-Epithelial Kazal type-related Inhibitor. 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 are 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 with Netherton Syndrome 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 redosable off-the-shelf 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 application with the FDA and initiate a clinical trial of KB104 in Netherton Syndrome following initiation of the KB105 Phase 2 study.

Aesthetics

While our focus is on the development of gene therapies to treat patients with severe, life-threatening, or rare diseases with high unmet medical needs, we are also evaluating the potential of our platform to address more prevalent and/or non-genetic conditions. To that end, in April 2019, we incorporated Jeune Aesthetics, a wholly-owned subsidiary, for the purposes of undertaking preclinical and clinical studies for aesthetic skin conditions.

KB301 for Aesthetic Skin Conditions

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. The global aesthetic injectable market was valued at $8.5 billion in 2022 and is projected to grow to $13.8 billion by 2030. The United States remains the largest market but emerging markets' growth rates are significant. The growth drivers are expanded access to services at medical spas and beauty bars combined with growing consumer purchasing power, especially in emerging markets. Shifting consumer attitudes about wellness, beauty and healthy aging have increased awareness and acceptance of aesthetics, generating demand from new patient segments, including men and millennials.

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 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 in August 2020. The Phase 1 dose-ranging trial evaluated the safety, tolerability, and initial efficacy of intradermal injections of KB301 in adult

subjects aged 18-75. KB301 was well tolerated, and we were able to biopsy and demonstrate proof-of-mechanism. Complete results from Cohort 1 focused on safety were presented at the 2021 SID Annual Meeting.

In March 2022, we announced positive proof-of-concept efficacy and safety data from Cohort 2 of the PEARL-1 study of KB301 for the treatment of aesthetic skin indications. Cohort 2 was a randomized, double-blind, placebo-controlled clinical trial that evaluated the safety and efficacy of KB301 for the improvement of fine lines and skin texture in the lower and upper cheek and for improvement in skin thickness in the knee. Cohort 2 enrolled 27 subjects across two trial sites. Bilateral treatment areas included the neck behind the ear to assess initial safety and on the cheek below and above the zygomatic arch (lower and upper cheek), and around the knee. Subjects were randomized 2:1 to receive low dose KB301 or placebo in the upper cheek and knee as multiple micro depot injections over the selected treatment area with a 33 G needle. Subjects receiving KB301 in the lower check were randomized 2:1 to receive either low dose KB301, high dose KB301 or placebo. Four patients dropped out of the Cohort 2 study – one subject following the initial safety assessment behind the ear, two subjects for unspecified reasons, and one subject due to unevenness in face between active and placebo during the study.

A subset of subjects from the PEARL-1 Cohort 2 trial were enrolled into a durability trial to look for duration of effect, reduction of the unevenness in placebo treated sites, and for long term safety monitoring. Ten subjects were enrolled in the durability trial, an open-label extension study to assess duration of effect below the zygomatic arch (the lower cheek area). The durability trial enrolled subjects who had received the high dose regimen of KB301 during the PEARL-1 Cohort 2 trial in one or both of their lower cheeks. Subject Satisfaction Scores and Investigator Assessments were measured monthly for three consecutive visits that correspond to timepoints up to nine-months following administration of the last dose of KB301. In addition, subjects with placebo-treated lower cheeks were dosed with KB301 during the durability trial to normalize their appearance. In November 2022, we announced nine-month durability of effect in Cohort 2 of the PEARL-1 study of KB301.

In April 2023, we initiated and treated the first subject in the PEARL-1 Cohort 3 study. The PEARL-1 Cohort 3 study is an open label study to evaluate different doses of KB301 for the improvement of lateral canthal lines (“LCL”) at rest in up to 20 subjects. Jeune Aesthetics initiated and treated the first subject in the PEARL-1 Cohort 4 study in January 2024, an open label study to evaluate KB301 for the improvement of dynamic wrinkles of the décolleté in up to 20 subjects. The Cohort 3 and Cohort 4 studies are running simultaneously and Jeune Aesthetics expects to announce results for both cohorts in the first half of 2024. Following completion of these cohorts, Jeune Aesthetics plans to initiate a Phase 2 study of KB301. 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.

Future Opportunities

In addition to the programs specified herein, we are also conducting exploratory preclinical research and development to expand potential applications of proprietary HSV-1 based vector platform. Research focus areas include the development of new candidates for the treatment of additional monogenic rare diseases in the skin, lung, and eye, as well as exploration of new routes of administration to treat diseases in additional tissues. We also 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 for more common conditions that are not necessarily the result of an inherited genetic defect, such as KB707. As additional 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 these more common conditions, we intend to seek collaborative alliances towards the development and potential commercialization of these therapies.

Manufacturing

In-House 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 VYJUVEK for commercial sales. In December 2022, the FDA completed a successful audit of our ANCORIS facility.

Our second commercial scale CGMP facility, ASTRA, was completed and qualified in 2023. It is a state-of-the-art CGMP manufacturing facility that, in addition to adding significant capacity to support our growing pipeline, also allows for 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 in January 2020 and began operational production in the third quarter of 2023.

Our proprietary manufacturing process which was initially developed for B-VEC 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 VYJUVEK and 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. 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 VYJUVEK and 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 commercial and 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 VYJUVEK and our product candidates, as they ensure the reproducible production of multiple commercial and clinical batches in a short six-week cycle time frame and in a cost-effective manner.

We have made significant investments in developing the most comprehensive and optimized manufacturing process for VYJUVEK and 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.

VYJUVEK / B-VEC

Dystrophic Epidermolysis Bullosa

A number of companies are developing drug candidates for the treatment of DEB. VYJUVEK is the only corrective therapy for DEB approved worldwide. We believe our competitors fall into two broad categories:

- **Corrective Approaches:** We are aware of two companies, Abeona Therapeutics Inc. and Castle Creek Biosciences, Inc., which are developing autologous or grafting gene therapy approaches to treating DEB. We are also aware of a recombinant-protein based approach being developed by BridgeBio Pharma, Inc.'s affiliate company, Phoenix Tissue Repair.
- **Palliative Treatments:** We are aware of companies, such as Chiesi Farmaceutici S.p.A. and RHEACELL GmbH & Co., which are developing product candidates taking a palliative approach to treating the disease. Chiesi Farmaceutici S.p.A.'s palliative treatment Filsuvez® (birch triterpenes) was approved by the FDA in the United States in 2023 and was previously approved by the EMA for the EU.

Ophthalmology

Ocular Complications Secondary to Dystrophic Epidermolysis Bullosa

There are no approved therapies for ocular complications secondary to DEB at this time. We are aware of Eliksa Therapeutics' program evaluating amniotic fluid derived ELK-003 eye drops to treat corneal abrasions in individuals with epidermolysis bullosa.

Respiratory

Cystic Fibrosis

There are no approved therapies for CF patients ineligible or intolerant to modulator regiments. We are aware of several preclinical or early clinical stage nucleic-acid-based programs for treatment of this patient population including Vertex Pharmaceuticals Inc., ReCode Therapeutics, Inc., Spirovant Sciences, Inc., and 4D Molecular Therapeutics, Inc.

Alpha-1 Antitrypsin Deficiency

Currently approved treatments for AATD consist of IV administered alpha-1 antitrypsin augmentation therapy, administered weekly. We are aware of at least three companies marketing augmentation therapies globally: CSL Limited, Takeda Pharmaceutical Company Limited., and Grifols, S.A. We are also aware of several preclinical or clinical stage programs in development for the treatment of various clinical manifestations of AATD. These can be generally classified into four broad categories:

- **Gene Silencing Approaches:** We are aware of two companies, Takeda Pharmaceutical Company Limited (in partnership with Arrowhead Pharmaceutical Inc.) and Novo Nordisk A/S (in partnership with Alnylam Pharmaceuticals, Inc.), which are developing interfering RNA medicines to treat the liver manifestations of AATD.
- **Alternate Augmentation Approaches:** We are aware of companies, such as Kamada Ltd. and Sanofi S.A., which are developing new augmentation treatments with modified frequency or routes of administration to treat the lung manifestations of AATD.
- **Direct Protease Inhibition:** We are aware of companies, such as Peak Bio, Inc. and Mereo BioPharma Group plc, which are developing protease inhibitors to treat the lung manifestations of AATD.
- **Gene Editing Approaches:** We are aware of companies, such as Intellia Therapeutics, Inc., Wave Life Sciences Ltd., and Beam Therapeutics Inc., which are developing gene editing therapies inhibitors to treat both the lung and liver manifestations of AATD.

Oncology

Solid Tumors

A large number of companies are focused on the development and commercialization of new therapeutics for the treatment of locally advanced or metastatic tumors. We are aware of multiple programs across all stages of development as well as marketed products aiming to improve outcomes for patients with solid tumor malignancies. Some of the most established companies in the marketing and development of new cancer drugs include Merck & Co Inc., Bristol Myers Squibb Company, Johnson & Johnson, and Pfizer Inc.

Dermatology

Autosomal Recessive Congenital Ichthyosis

There are no approved therapies for ARCI at this time. We are aware of LEO Pharma A/S's clinical stage program evaluating topical isotretinoin for ARCI.

Netherton Syndrome

There are no approved therapies for Netherton Syndrome. We are aware of Quoin Pharmaceutical Ltd.'s clinical stage program evaluating QRX003 for the treatment of Netherton Syndrome and that Novartis Inc. had conducted clinical trials of a product for the treatment of Netherton Syndrome previously.

Aesthetics

Aesthetic Skin Conditions

There are multiple approved therapies for aesthetic skin conditions, including hyaluronic acid and botulinum toxin based products marketed by AbbVie Inc., Revance Therapeutics, Inc., Merz Pharma GmbH & Co., KGaA, Galderma S.A., and others. We are also aware of multiple preclinical and clinical stage programs for improvement in aesthetic skin conditions, including those underway at AbbVie Inc. and Galderma S.A.

Intellectual Property and Proprietary Rights

Our success depends in part upon our ability to obtain and maintain exclusivity for our approved product, product candidates and platform technology. We typically rely on a combination of patent protection and regulatory exclusivity to maintain exclusivity for our approved product and product candidates, whereas exclusivity for our platform technology is generally based on patent protection and trade secret protection. However, trade secrets can be difficult to protect. In addition to patent protection, regulatory exclusivity, and trade secret protection, we also protect our approved product, product candidates and platform technology with trademarks and contractual protections. Additionally, 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.

We actively seek patent protection for our product candidates and certain of our proprietary technologies by filing patent applications in the U.S. and other countries as appropriate. These patent applications are directed to various inventions. We do not have patents or patent applications in every jurisdiction where there is a potential commercial market for our approved product or our product candidates. For each of our programs, our decision to seek patent protection in specific foreign markets, in addition to the U.S., is based on many factors, including:

- our available resources;
- the number and types of patents already filed or pending;
- the likelihood of success of the product candidate;
- the size of the commercial market;
- the presence of a potential competitor in the market; and
- whether the legal authorities in the market effectively enforce patent rights.

We continually evaluate our patent portfolio and patent strategy and believe our patents and patent applications provide us with a competitive advantage; however, if markets where we do not have patents or patent applications become commercially important, our business may be adversely affected. A discussion of certain risks and uncertainties that may affect our freedom to operate, patent position, regulatory exclusivities, and other proprietary rights is set forth in Item 1A. Risk Factors included in this Annual Report on Form 10-K.

Certain of our product candidates are in therapeutic areas that have been the subject of many years of extensive research and development by academic organizations and third parties who may control patents or other intellectual property that they might assert against us, should one or more of our product candidates in these therapeutic areas succeed in obtaining regulatory approval and thereafter be commercialized. We continually evaluate the intellectual property rights of others in these areas in order to determine whether a claim of infringement may be made by others against us. Should we determine that a third party has intellectual property rights that could impact our ability to freely market a product candidate, we consider a number of factors in determining how best to prepare for the commercialization of any such product candidate. In making this determination we consider, among other things, the stage of development of our product candidate, the anticipated date of first

regulatory approval, whether we believe the intellectual property rights of others are valid, whether we believe we infringe the intellectual property rights of others, whether a license is available upon commercially reasonable terms, whether we will seek to challenge the intellectual property rights of others, the term of the rights, and the likelihood of and liability resulting from an adverse outcome should we be found to infringe the intellectual property rights of others.

Currently, U.S. patents, as well as most foreign patents, are generally effective for 20 years from the date the earliest regular application was filed. In some countries, the patent term may be extended to recapture a portion of the term lost during regulatory review of the product candidate. For example, in the U.S., under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly known as the Hatch-Waxman Act, a patent that covers an FDA-approved biologic may be eligible for patent term extension (for up to 5 years, but not beyond a total of 14 years from the date of product approval) as compensation for patent term lost during the FDA regulatory review process. The application for the extension must be submitted prior to the expiration of the patent and only one patent may be extended for any product based on FDA review delay. 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. In addition to patent term extension under the Hatch-Waxman Act, patents in the U.S. may be granted additional term due to delays at the USPTO during prosecution of a patent application. We actively strive to maximize the potential for patent protection for our product and product candidates in accordance with the law.

Patents

Our technology platform, VYJUVEK, and our product candidates are primarily protected by composition of matter and methods of use patents and patent applications. A summary of granted composition of matter and/or methods of use patents that we own, which cover our technology platform, VYJUVEK, and our product candidates in the U.S. and elsewhere, is provided below.

Our Technology Platform

Patent Number	Country / Region*	Patent Type	Expiration Date **	Owner
U.S. 10,441,614	United States	**Composition of Matter & Methods of Use** – Delivery platform for targeted therapeutics, as well as methods of its use for delivering any effector to the skin	12/28/2036	Krystal
U.S. 11,185,564	United States	**Methods of Use** – Methods of use of replication-defective HSV vectors for delivering any effector to skin-targeted therapeutics	12/28/2036	Krystal
U.S. 11,865,148	United States	**Methods of Use** – Methods of use of replication-defective HSV-1 for delivering any effector to the eye	12/28/2036	Krystal
AU 2019280069	Australia	**Composition of Matter & Methods of Use** – Delivery platform for targeted therapeutics, as well as methods of its use for delivering any effector to the skin	12/28/2036	Krystal

VYJUVEK / B-VEC

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

JP 6,970,086	Japan	C**omposition of Matter & Uses Thereof** – Pharmaceutical compositions comprising B-VEC, as well as uses thereof, including for providing prophylactic, palliative or therapeutic relief of a wound, disorder or disease of the skin	12/28/2036	Krystal
AU 2016401692	Australia	C**omposition of Matter & Uses Thereof** – Pharmaceutical compositions comprising B-VEC, as well as uses thereof, including for providing prophylactic, palliative or therapeutic relief of a wound, disorder or disease of the skin	12/28/2036	Krystal
MX 394867	Mexico	C**omposition of Matter & Uses Thereof** – Pharmaceutical compositions comprising B-VEC, as well as uses thereof, including for providing prophylactic, palliative or therapeutic relief of a wound, disorder or disease of the skin	12/28/2036	Krystal

Respiratory

KB407

Patent Number	Country / Region*	Patent Type	Expiration Date **	Owner
U.S. 10,829,529	United States	**Methods of Use** – Methods of using KB407 for the treatment of cystic fibrosis and other disease causing progressive lung destruction	2/7/2040	Krystal
ZA 2022/05420	South Africa	**Methods of Use** – Methods of using KB407 for the treatment of cystic fibrosis and other disease causing progressive lung destruction	2/7/2040	Krystal

Oncology

KB707

Patent Number	Country / Region*	Patent Type	Expiration Date **	Owner
U.S. 11,779,660	United States	**Composition of Matter** – Pharmaceutical compositions comprising HSV vectors encoding IL-2 and IL-12	4/14/2042	Krystal

Dermatology

KB105

Patent Number	Country / Region*	Patent Type	Expiration Date **	Owner
U.S. 10,525,090	United States	C**omposition of Matter & Methods of Use** – Pharmaceutical compositions comprising herpes virus vectors encoding TGM1, as well as methods of providing prophylactic, palliative, or therapeutic relief to TGM1-deficient ARCI subjects	4/11/2039	Krystal
U.S. 11,717,547	United States	C**omposition of Matter & Methods of Use** – Pharmaceutical compositions comprising replication-defective HSV-1 vectors encoding TGM, as well as methods of delivering TGM to cells	4/11/2039	Krystal
AU 2019252658	Australia	C**omposition of Matter & Methods of Use** – Pharmaceutical compositions comprising herpes virus vectors encoding TGM1, as well as methods of providing prophylactic, palliative, or therapeutic relief to TGM1-deficient ARCI subjects	4/11/2039	Krystal

KB104

Patent Number	Country / Region*	Patent Type	Expiration Date **	Owner
U.S. 11,642,384	United States	**Composition of Matter** – Pharmaceutical compositions comprising eplication-defective HSV vectors encoding SPINK5	9/24/2039	Krystal

Aesthetics

KB301

Patent Number	Country / Region*	Patent Type	Expiration Date **	Owner
U.S. 10,786,438	United States	C**omposition 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
AU 2019260757	Australia	C**omposition 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

* Granted patents in the U.S. and elsewhere are shown. Additional patent protection in the U.S., 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.

Regulatory Exclusivity

The various types of regulatory exclusivity or designations for which VYJUVEK and our product candidates have been granted, or which our current or future product candidates may be eligible to receive are generally discussed above or below, under "Government Regulation and Product Approval".

Trademarks

Our trademarks are important to us and are generally filed to protect our corporate brand, our approved product, our product candidates, and our platform technology. We typically file trademark applications and pursue their registration in the U.S., Europe and other markets in which we anticipate using such trademarks. We are the owner of several federal trademark registrations in the U.S. and have pending trademark applications and registrations in the U.S. and in major foreign markets. Trademark protection varies in accordance with local law and continues in some countries as long as the trademark is used and in other countries as long as the trademark is registered. Trademark registrations generally are for fixed but renewable terms.

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, importation, advertising and other promotional practices involving biologic products. IND 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. The FDA's authorization also must be obtained before marketing of biologic products. The process of obtaining regulatory approvals or licenses 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 Therapeutic Products ("OTP") and the FDA has established the Cellular, Tissue and Gene Therapies Advisory Committee 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 authorize the marketing of a product candidate for marketing 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 ("CGLP"), 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, if applicable, Institutional Biosafety Committee ("IBC"), before the clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials according to the FDA's Current Good Clinical Practice ("CGCP") 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 an application 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 Current Good Manufacturing Practice ("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 application; and
- payment of user fees and FDA review and marketing authorization.

Before testing any new 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 CGLPs.

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 biological product and finalize a process for manufacturing the biological product in commercial quantities in accordance with CGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the biological product candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final biological product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted, to demonstrate that the biological product 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 application. Some preclinical testing may continue even after the IND application is submitted. With gene therapy protocols, if

the FDA allows the IND application 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 application 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 application for our 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 application. An IND application 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 application 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 CGCP requirements, including the requirement that all research subjects provide informed consent. Further, each clinical trial must be reviewed and approved by an IRB and, if applicable, 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 at certain institutions 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 Biologics License Application ("BLA") or other submission requesting authorization 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. Under the Prescription Drug User Fee Act ("PDUFA"), each BLA (or New Drug Application ("NDA") for some biologics) 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 or NDAs 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 Strategy ("REMS") program 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 the IND application trial requirements and CGCP 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 or license 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 the submission 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") and Japan have similar, but not identical benefits.

Breakthrough Therapy

A breakthrough therapy is defined as a therapy that is intended, alone or in combination with one or more other therapies, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the therapy may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For therapies that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Therapies designated as breakthrough therapies by the FDA may also be eligible for priority review and accelerated approval.

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 PRIority MEdicines ("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.

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 promotion").

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 application, prior to the commencement of human clinical trials. In the EU, for example, a request for a Clinical Trial Authorization ("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 CGCPs 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 ("ACA") 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 ACA 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 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 Care Fraud statute imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- the Health Insurance Portability and Accountability Act of 1996, 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 federally sponsored 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. On August 16, 2022, the Inflation Reduction Act of 2022 (“IRA”) was signed into law. The IRA includes several provisions to lower prescription drug costs for people with Medicare and reduce drug spending by the federal government, including allowing Medicare to negotiate prices for certain prescription drugs, requiring drug manufacturers to pay a rebate to the federal government if prices for single-source drugs and biologicals covered under Medicare Part B and nearly all covered drugs under Part D increase faster than the rate of inflation (CPI-U), and limiting out of pocket spending for Medicare Part D enrollees. Additionally, on October 14, 2022, President Biden signed Executive Order 14087 on “Lowering Prescription Drug Costs for Americans.” The Executive Order specifically requests that the Center for Medicare and Medicaid Innovation consider “models that may lead to lower cost sharing for commonly used drugs and support value-based payment that supports high-quality care.”

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 19, 2024, we had 229 full-time employees, primarily engaged in research and development, manufacturing, administrative activities, and commercial activities for VYJUVEK. 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 in April 2016. In March 2017, we converted from a California limited liability company to a Delaware C-corporation, and changed our name from Krystal Biotech, LLC to Krystal Biotech, Inc. Our principal offices are located at 2100 Wharton Street, Suite 701, Pittsburgh, PA 15203, and our telephone number is 412-586-5830. In June 2018, the Company incorporated an Australian subsidiary, for the purpose of undertaking preclinical and clinical studies in Australia. In April 2019, the Company incorporated Jeune Aesthetics, Inc. in Delaware, a wholly-owned subsidiary, for the purpose of undertaking preclinical studies for aesthetic skin conditions. In January 2022, August 2022, December 2022, and August 2023, we incorporated subsidiaries in Switzerland, Netherlands, France, and Germany, respectively, for the purpose of establishing initial operations in Europe for the development and commercialization of Krystal's pipeline. 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.

Our business involves significant risks, some of which are described below. You should carefully consider the risks and uncertainties described below, together with all of the other information contained in this Annual Report on Form 10-K, including "Management's Discussion and Analysis of Financial Condition and Results of Operations" and the consolidated financial statements and the related notes. If any of the following risks actually occur, it could harm our business, prospects, operating results and financial condition and future prospects. In such event, the market price of our common stock could decline, and you could lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations. This Annual Report on Form 10-K also contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in the forward-looking statements as a result of factors that are described below and elsewhere in this Annual Report on Form 10-K.

Risks Related to Our Business and Industry

We are substantially dependent on the commercial success of VYJUVEK

To date, we have invested substantial efforts and financial resources in the research and development of our product candidates. Our near-term prospects, including our ability to develop our product candidates and generate revenue, and our future growth is substantially dependent on the commercial success of VYJUVEK.

Although we received approval from the FDA for VYJUVEK for the treatment of DEB on May 19, 2023, we can provide no assurances that we will obtain regulatory approval in any other jurisdiction, which would have an adverse impact on our results of operations. In addition, the successful commercialization of VYJUVEK will depend on a number of factors, including the risks identified in these "Risk Factors". One or more of these factors, many of which are beyond our control, could cause significant delays or an inability to successfully commercialize VYJUVEK.

We may not be successful in our efforts to identify, develop and commercialize additional product candidates, which may impair our ability to expand our business and achieve our strategic objectives, and we 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.

Although a substantial amount of our efforts focuses on the commercialization of VYJUVEK and the development and potential approval of our current product candidates, a key component our strategy is to identify, develop and potentially commercialize a portfolio of genetic medicines. Research programs to identify new product candidates require substantial technical, financial, and human resources and may not be successful in identifying potential product candidates. 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:

- competitors may develop alternatives that render our product candidates obsolete;
- product candidates we develop may 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.

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 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 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.

VYJUVEK and, if approved, our investigational product candidates regulated as biologics may face competition from biosimilars approved through an abbreviated regulatory pathway.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the ACA, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA, which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a Biologics License Application, or BLA, for the competing product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity, and potency of the other company's product. In addition, a competitor may choose to challenge our patent rights relating to the reference product by initiating litigation during the 12-year period of exclusivity. After the FDA approves the BLA for the competing product, the competitor may also bring a declaratory judgment action of non-infringement, invalidity, and/or unenforceability of our patent rights. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty.

We believe that any of our product candidates approved as a biological product under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider our investigational medicines to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. Moreover, the extent to which a biosimilar, once licensed, will be substituted for any one of our approved products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

If competitors are able to obtain marketing approval for biosimilars referencing any of our approved products, our approved products may become subject to competition from such biosimilars, which would impair our ability to successfully commercialize and generate revenue from sales of such products.

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 commercialize and market our product candidates.

We are aware of several companies and institutions that are currently developing alternative autologous or palliative gene therapy approaches for our targeted indications, including DEB 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 opportunities 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 VYJUVEK or 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 our product candidates, 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 of our product candidates uneconomical or obsolete, and we may not be successful in marketing VYJUVEK or any of our product candidates that obtain regulatory approval 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 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 VYJUVEK or any product candidate that we may develop and commercialize.

If any product liability lawsuits are successfully brought against us, we may incur substantial liabilities and may be required to limit commercialization of VYJUVEK or our product candidates.

We face an inherent risk of product liability lawsuits related to the sale of VYJUVEK, use of VYJUVEK and our product candidates, and testing of our product candidates. Product liability claims may be brought against us by participants enrolled in our clinical trials, patients, health care providers or others using, or administering VYJUVEK and our product

candidates. If we cannot successfully defend ourselves against any such claims, we may incur substantial liabilities. Regardless of their merit or eventual outcome, liability claims may result in:

- decreased demand for VYJUVEK;
- injury to our reputation;
- withdrawal of clinical trial participants;
- termination of clinical trial sites or entire trial programs;
- increased regulatory scrutiny;
- significant litigation costs;
- substantial monetary awards to or costly settlement with claimants;
- product recalls for any approved products or a change in the indications for which they may be used;
- loss of revenue;
- diversion of management and scientific resources from our business operations; and
- the inability to successfully commercialize VYJUVEK or our product candidates, if approved.

With respect to VYJUVEK and any of our product candidates that are approved for commercial sale in the future, we are, and will be, highly dependent upon physician and patient perceptions of us and the safety and quality of our products. We could be adversely affected if we are subject to negative publicity. We could also be adversely affected if any of our products or any similar products distributed by other companies prove to be, or are asserted to be, harmful to patients. Because of our dependence upon consumer perceptions, any adverse publicity could have a material adverse impact on our financial condition or results of operations.

Our product liability insurance coverage may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage now that VYJUVEK has been approved by the FDA and when we begin the commercialization of our product candidates, if approved. Insurance coverage is becoming increasingly expensive. As a result, we may be unable to maintain or obtain sufficient insurance at a reasonable cost to protect us against losses that could have a material adverse effect on our business. A successful product liability claim, or series of claims brought against us, particularly if judgments exceed any insurance coverage we may have, could decrease our cash resources and adversely affect our business, financial condition, and results of operations.

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. Ethical, social, and legal concerns about gene therapy could result in additional regulations restricting or prohibiting VYJUVEK or our product candidates. 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 VYJUVEK or our product candidates or demand for VYJUVEK or any product candidates 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 business operations may subject us to disputes, claims and lawsuits, which may be costly and time-consuming and could materially and adversely impact our financial position and results of operations.

From time to time, we may become involved in disputes, claims and lawsuits relating to our business operations. For example, we may, from time to time, face or initiate claims related to intellectual property matters, employment matters, or commercial matters. Any dispute, claim or lawsuit may divert management's attention away from our business, we may incur significant expenses in addressing or defending any dispute, claim or lawsuit, and we may be required to pay damage awards or settlements or become subject to equitable remedies that could adversely affect our operations and financial results. Litigation

related to these disputes may be costly and time-consuming and could materially and adversely impact our financial position and results of operations if resolved against us. In addition, the uncertainty associated with litigation could lead to increased volatility in our stock price.

The increasing use of social media platforms presents new risks and challenges.

Social media is increasingly being used by us, our employees, or others to communicate about our business, VYJUVEK, our clinical development programs, DEB, and the diseases our product candidates are being developed to treat. We use appropriate social media in connection with our commercialization efforts of VYJUVEK and intend to use it in connection with our commercialization efforts of our product candidates, if approved. Social media practices in the biotechnology and biopharmaceutical industries continue to evolve, and regulations and regulatory guidance relating to such use are evolving and not always clear. This evolution creates uncertainty and risk of noncompliance with regulations applicable to our business, resulting in potential regulatory actions against us, along with the potential for litigation and heightened scrutiny by the FDA, the Securities and Exchange Commission, or the SEC, and other regulators. For example, patients may use social media channels to comment on their experience in an ongoing clinical trial of our product candidates, or to report an alleged adverse event. If such disclosures occur, there is a risk that clinical trial enrollment may be adversely impacted, that we may fail to monitor and comply with applicable adverse event reporting obligations, or that we may not be able to defend our business or the public's legitimate interests in the face of the political and market pressures generated by social media due to restrictions on what we may say about our product candidates. There is also a risk of inappropriate disclosure of sensitive information, loss of trade secrets or other intellectual property, public exposure of personal information of our employees, patients who use VYJUVEK, clinical trial patients, and others, or negative or inaccurate posts or comments about us on any social networking website. In addition, we may encounter attacks on social media regarding our company, management, VYJUVEK, or our product candidates that seriously damage our reputation, brand image, and goodwill. If any of these events were to occur or we otherwise fail to comply with applicable regulations, we could incur liability, face regulatory actions, or incur other harm to our business that could have a material adverse effect on our business, prospects, operating results, and financial condition and could adversely affect the price of our common stock.

We have experienced significant growth in the number of employees and infrastructure and may experience difficulties in managing this growth. If we are unable to manage expected growth in the scale and complexity of our operations, our performance may suffer.

We have experienced a period of significant expansion in personnel and of our facilities, infrastructure and overhead as we developed our own manufacturing facilities, built our sales, marketing and distribution infrastructure that we believe is necessary to commercialize VYJUVEK, and increased our research and development efforts. The commercialization of VYJUVEK and our ongoing development of other product candidates will continue to impose significant 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 our growth effectively. 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. Our management, finance, development personnel, systems, and facilities currently in place may not be adequate to support this expected 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. 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.

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 European Union, or EU, and other jurisdictions, provide accurate information to the FDA, the European Medicines Agency ("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. 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 clinical 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 product 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 VYJUVEK and any product candidates for which we obtain marketing approval.

In the United States, there have been and continue to be a number of legislative efforts to contain healthcare costs. Any legislative 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. Any changes that reduce, or impede the ability to obtain, reimbursement for VYJUVEK or our product candidates that we intend to commercialize in the United States could adversely affect successful commercialization of VYJUVEK and our plans to introduce our product candidates in the United States. For example, the Bipartisan Budget Act of 2018, among other things, amended 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."

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, in August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2012 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 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. In August 2022, the Inflation Reduction Act of 2022 ("IRA") was signed into law. The IRA includes several provisions to lower prescription drug costs for people with Medicare and reduce drug spending by the federal government. In relevant part, the IRA allows Medicare to negotiate prices for certain prescription drugs, requires drug manufacturers to pay a rebate to the federal government if prices for single-source drugs and biologicals covered under Medicare Part B and nearly all covered drugs under Part D increase faster than the rate of inflation, caps out of pocket spending for Medicare Part D enrollees, and makes other benefit design changes to Medicare Part D intended to lower drug costs for enrollees and Medicare. Implementation of these changes began in 2023, and will continue to be implemented over the next several years. Multiple pharmaceutical manufacturers have challenged the law in court, largely on constitutional grounds. These suits will continue through 2024 and the ultimate effects of such legal challenges are unclear. At this time, we continue to

evaluate the effect of the IRA on our business operations and financial condition and results as the full impact of the IRA remains uncertain.

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. 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. In October 2022, President Biden signed Executive Order 14087 on "Lowering Prescription Drug Costs for Americans." The Executive Order specifically requests that the Center for Medicare and Medicaid Innovation consider "models that may lead to lower cost sharing for commonly used drugs and support value-based payment that supports high-quality care." The outcomes of the findings made under the Executive Order could lead to further drug pricing initiatives that could affect reimbursement for our product and product candidates.

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 and product candidates or additional pricing pressures and may adversely impact our ability to generate sufficient revenue, attain consistent profitability, or commercialize our product candidates, if approved.

We are 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.

With the FDA approval of VYJUVEK, our operations are 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 impact, among other things, our sales, marketing, access assistance, sponsored genetic patient testing, and educational programs. In addition, we are 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 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 ACA 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 ACA 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 ("FCA"). Cases against pharmaceutical manufacturers support the view that certain marketing practices, including off-label promotion, may implicate the FCA;
- the federal Health Care Fraud statute imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

- the Health Insurance Portability and Accountability Act of 1996 ("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 (the "Omnibus Rule" and together with HIPAA and HITECH, the HIPAA Rules), which impose certain requirements relating to the privacy, security and transmission of individually identifiable health information by certain entities subject to the HIPAA Rules, such as health plans, health care clearinghouses and health care providers that engage in certain covered transactions;
- federal transparency laws, including the federal Physician Payment Sunshine Act, that require certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare and Medicaid Services ("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 the HIPAA Rules, 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 FCA, health care providers will resolve allegations in a settlement without admitting liability. Any such settlement could materially affect our business, financial operations, and reputation.

Efforts to ensure that our business arrangements with third parties comply with applicable healthcare laws and regulations 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.

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 we 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. Moreover, certain environmental laws may impose liability without regard to fault or legality of the action at the time of its occurrence. 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 or hazardous 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.

We are subject to stringent and evolving U.S. and foreign laws, regulations and other obligations related to privacy and data security. Our actual or perceived failure to comply with such obligations could lead to regulatory inquiries or actions, litigation, fines and penalties, disruptions to our business operations, reputational harm, loss of revenue, and other adverse business consequences.

Privacy and data security have become significant areas of legal and regulatory focus in the United States, European Union and in many other jurisdictions where we conduct or may conduct our operations. In our ordinary course of business, we collect, receive, store, process, generate, use, transfer, disclose, make accessible, protect, secure, dispose of, transmit, and share (collectively, "process") personal information and other sensitive information, including, but not limited to, health information, individuals' financial information, as well as proprietary and confidential business data, including trade secrets, intellectual property, and sensitive third-party data (collectively, "sensitive data"). Our data processing activities may subject us to numerous privacy and data security obligations, including, but not limited to, domestic and international laws, regulations, guidance, industry standards, external and internal privacy and security policies, and contractual requirements.

In the United States, federal, state, and local governments have enacted numerous data privacy and security laws, including data breach notification laws, personal information privacy laws, consumer protection laws, and other similar laws. Notably, HIPAA, as amended by HITECH, imposes requirements on certain entities regarding the privacy, security, and transmission of individually identifiable health information and the California Consumer Privacy Act of 2018 ("CCPA") requires businesses to provide specific disclosures in their privacy notices and honor California residents' privacy rights. The CCPA provides for civil penalties of up to $7,500 per violation and allows private litigants affected by certain data breaches to recover significant statutory damages. Although the CCPA does not apply to certain data that we process in the context of clinical trials, efforts to comply with the CCPA may increase our annual compliance costs and subject us to potential liability with respect to other personal information we may maintain about California residents. In addition, the California Privacy Rights Act of 2020 ("CPRA"), which came into effect on January 1, 2023, expanded the CCPA's requirements, extending it to cover personal information of business representatives and employees and the CPRA established a new regulatory agency to implement and enforce the law. Other states, such as Virginia, Nevada, and Colorado, have also passed comprehensive privacy laws, and similar laws are being considered in several other states, as well as at the federal and local levels. While these states' laws, like the CCPA, also exempt some data processed in the context of clinical trials, these developments further complicate our compliance efforts and increase both legal risk and compliance costs for us and the third parties upon whom we rely.

Outside of the United States, there are an increasing number of laws, regulations, and industry standards regarding privacy and data security. For example, the EU General Data Protection Regulation ("GDPR") and UK GDPR impose strict requirements for processing personal information, and companies that violate the GDPR may face temporary or permanent bans on certain data processing activities and they may be subject to other penalties such as fines of up to 20 million Euros under the EU GDPR / 17.5 million pounds sterling under the UK GDPR or 4% of annual global revenue, whichever is greater; or private litigation related to processing of personal information brought by classes of data subjects or consumer protection organizations authorized to represent data subjects' interests.

In some circumstances, we may be unable to transfer personal information between certain jurisdictions due to data localization requirements or other limitations on cross-border data flows. Europe and other jurisdictions have enacted laws requiring data to be localized or limiting the transfer of personal information to other countries. In particular, the European Economic Area ("EEA") and the UK have significantly restricted the transfer of personal information to the United States and other countries whose privacy laws they consider inadequate. Although there are various mechanisms that may be used to transfer personal information from the EEA and UK to the United States in compliance with the law, such as the EEA and UK's standard contractual clauses, these mechanisms are subject to legal challenges, and we may be unable to rely on these measures to lawfully transfer personal information to the United States in all cases. If there is no lawful manner for us to transfer personal information from the EEA, the UK, or other jurisdictions to the United States, or if the requirements for a legally compliant transfer are too onerous, we could face significant adverse consequences, including increased exposure to regulatory actions, substantial fines and penalties, the inability to transfer data and work with partners, vendors and other third parties, and injunctions against our processing or transferring of personal information necessary to operate our business. Some European regulators have ordered certain companies to suspend or permanently cease certain transfers of personal information to recipients outside Europe for allegedly violating the EU GDPR's cross-border data transfer limitations. Additionally, companies

that transfer personal information to recipients outside of the EEA and/or UK to other jurisdictions, particularly to the United States, are subject to increased scrutiny from regulators, individual litigants, and activist groups.

In addition to any applicable privacy and data security laws and regulations, we may be subject to industry standards adopted by industry groups or bound by other contractual obligations related to privacy and data security. We may publish privacy policies, marketing materials, and other statements, such as compliance with certain certifications or self-regulatory principles, regarding data privacy and security. If these policies, materials, or statements are found to be deficient, lacking in transparency, deceptive, unfair, or misrepresentative of our practices, we may be subject to regulatory inquiries, regulatory enforcement actions and other adverse consequences.

Our obligations related to privacy and data security are quickly changing, becoming increasingly stringent, and creating regulatory uncertainty. Additionally, these obligations may be subject to differing applications and interpretations, which may be inconsistent between jurisdictions. Preparing for and complying with these obligations requires us to devote significant resources and may necessitate changes to our information technologies, systems, and practices and to those of any third parties that process personal information or other sensitive data on our behalf.

We may at times fail (or be perceived to have failed) in our efforts to comply with our privacy and data security obligations. Moreover, despite our efforts, our personnel or third parties on whom we rely on may fail to comply with such obligations, which could negatively impact our business operations. If we or the third parties that process personal information or other sensitive data our behalf fail, or are perceived to have failed, to address or comply with applicable privacy and data security obligations, we could face significant consequences, including but not limited to: government enforcement actions (e.g., investigations, fines, penalties, audits, and inspections); litigation (including class-action claims); additional reporting requirements and/or oversight; bans on processing personal information; and orders to destroy or not use personal information. Any of these events could have a material adverse effect on our reputation, business, or financial condition, including but not limited to loss of customers; significant reputational harm; an inability to process personal information or to operate in certain jurisdictions; limited ability to commercialize VYJUVEK or develop and commercialize our product candidates; expenditures of time and resources to defend ourselves against claims or inquiries; adverse publicity; or substantial changes to our business model or operations.

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 high inflation and interest rates and concerns of a recession in the United States or other major markets due to a number of factors. For example, inflation and rising interest rates have caused volatility and disruptions in the capital and credit markets, and it is unclear how long such volatility will continue. In addition, Russia's invasion of Ukraine and/or the Israel-Hamas conflict may lead to a prolonged, adverse impact on global economic, sociopolitical and market conditions. A severe or prolonged economic downturn could result in a variety of risks to our business, including our ability to raise additional capital when needed or on acceptable terms, if at all. A weak or declining economy, sanctions, trade restrictions and other global conditions could also strain our suppliers, possibly resulting in supply delays or disruptions. 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, financial condition, results of operations, and prospects.

Our internal computer systems, or those of our collaborators or other contractors or consultants, may fail or suffer a cyber-security incident, such as a data breach or computer virus, which could harm our business by damaging our reputation, exposing us to liability, or materially disrupting our operations, including production of VYJUVEK or our product development programs.

We receive, process, store, and transmit, often electronically, confidential data of others, including the participants in our clinical trials. Unauthorized access to our or our collaborators' computer systems or stored data could result in the theft or improper disclosure of personal or confidential information or other sensitive data, the deletion or modification of records, or could cause interruptions in our operations. Cybersecurity threats include, but are not limited to, ransomware attacks, phishing attempts, and the exploitation of software vulnerabilities to gain access to our information technology environment, and cyber-security risks increase when we transmit information from one location to another, including transmissions over the Internet or other electronic networks. Despite our robust security measures and our commitment to implementing and continually improving our cybersecurity posture to mitigate the risk of a cybersecurity incident, we cannot guarantee that such incidents will not occur. Any cybersecurity incident, even if promptly addressed, may harm our reputation, damage our brand, and erode trust. Our facilities and systems, and those of our third-party service providers, may also be vulnerable to acts of vandalism, software viruses, misplaced or lost data, programming and/or human errors, or other similar events which may disrupt our operations or expose personal and confidential information.

Moreover, in the event of a cybersecurity incident, we may face investigations, legal actions, including class action litigation, regulatory inquiries, and regulatory enforcement actions. We may also be subject to fines, consent orders, or mandated corrective actions that could have a material adverse impact on our operations and financial position. Furthermore,

cybersecurity incidents and their legal consequences may impact investor confidence, potentially leading to a decrease in our stock price or limitations on our access to capital markets. If such an event were to occur and cause material 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. 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.

Certain data breaches must be reported to affected individuals and various government and/or regulatory agencies, and in some cases to the media, under provisions of HIPAA, as amended by HITECH, other U.S. federal and state law, and requirements of non-U.S. jurisdictions, including the EU GDPR and relevant member state law in the European Union and other foreign laws, and financial penalties may also apply. Our insurance policies may not be adequate to compensate us for the potential losses arising from breaches, failures or disruptions of our infrastructure, catastrophic events and disasters or otherwise. In addition, such insurance may not be available to us in the future on economically reasonable terms, or at all. Further, our insurance may not cover all claims made against us and defending a suit, regardless of its merit, could be costly and divert management's attention. 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 third-party suppliers or service providers and have a material adverse effect on our business, financial condition, results of operations and prospects. The severity and frequency of weather-related natural disasters have been amplified, and are expected to continue to be amplified by, global climate change. Such natural disasters may cause damage to and/or disrupt our operations, which may result in a material adverse effect on our VYJUVEK sales, our other product candidates, business, and results of operations. Moreover, climate change may also result in various chronic physical changes, such as changes in temperature or precipitation patterns or sea-level rise, that may also have an adverse impact on our operations. Our suppliers, vendors and business partners also face similar risks, and any disruption to their operations could have an adverse effect on our supply and manufacturing chain. 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 our 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. A significant portion of our current supply of drug product for VYJUVEK and our product candidates is located at our manufacturing facilities in Pittsburgh, Pennsylvania. 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.

Increased attention to, and evolving expectations for, environmental, social, and governance ("ESG") initiatives could increase our costs, harm our reputation, or otherwise adversely impact our business.

Companies across industries are facing increasing scrutiny from a variety of stakeholders related to their ESG and sustainability practices. Expectations regarding voluntary ESG initiatives and disclosures may result in increased costs (including but not limited to increased costs related to compliance, stakeholder engagement, contracting and insurance), enhanced compliance or disclosure obligations, or other adverse impacts to our business, financial condition, or results of operations.

While we may at times engage in voluntary initiatives (such as voluntary disclosures, certifications, or goals, among others) to improve the ESG profile of our company and/or product and product candidates, such initiatives may be costly and may not have the desired effect. Moreover, we may not be able to successfully complete such initiatives due to factors that are within or outside of our control. Even if this is not the case, our actions may subsequently be determined to be insufficient by various stakeholders, and we may be subject to investor or regulator engagement on our ESG efforts, even if such initiatives are currently voluntary.

Certain market participants, including major institutional investors and capital providers, use third-party benchmarks and scores to assess companies' ESG profiles in making investment or voting decisions. Unfavorable ESG ratings could lead to increased negative investor sentiment towards us or our industry, which could negatively impact our share price as well as our access to and cost of capital. Furthermore, certain investors have been engaged in "anti-ESG" campaigns, and, to the extent we take actions that are seen as positive to some investors other investors may take issue with such actions. To the extent ESG matters negatively impact our reputation, it may also impede our ability to compete as effectively to attract and retain employees or customers, which may adversely impact our operations.

In addition, we expect there will likely be increasing levels of regulation, disclosure-related and otherwise, with respect to ESG matters. For example, the SEC has published proposed rules that would require companies to provide significantly expanded climate-related disclosures in their periodic reporting, which may require us to incur significant additional costs to comply, including the implementation of significant additional internal controls processes and procedures regarding matters that have not been subject to such controls in the past, and impose increased oversight obligations on our management and board of directors. These and other changes in stakeholder expectations will likely lead to increased costs as well as scrutiny that could heighten all of the risks identified in this risk factor. Additionally, our customers and suppliers may be subject to similar expectations, which may augment or create additional risks, including risks that may not be known to us.

Our international operations may expose us to business, regulatory, political, operational, financial, pricing and reimbursement and economic risks associated with doing business outside of the United States.

We currently have operations and employees located outside the United States and our business strategy incorporates potential additional international expansion to target patient populations outside the United States. Doing business internationally involves a number of risks, including, but not limited to:

- multiple, conflicting, and changing laws and regulations such as privacy regulations, tax laws, export and import restrictions, employment laws, regulatory requirements, and other governmental approvals, permits, and licenses;
- failure by us to obtain and maintain regulatory approvals for the use of our product candidates in various countries;
- additional potentially relevant third-party patent rights;
- complexities and difficulties in obtaining protection and enforcing our intellectual property;
- difficulties in staffing and managing foreign operations;
- complexities associated with managing multiple payor reimbursement regimes, government payors, or patient self-pay systems;
- limits in our ability to penetrate international markets;
- financial risks, such as longer payment cycles, difficulty collecting accounts receivable, the impact of local and regional financial crises on demand and payment for our products, and exposure to foreign currency exchange rate fluctuations;
- natural disasters, political and economic instability, including wars, terrorism, and political unrest, outbreak of disease, boycotts, curtailment of trade, and other business restrictions;
- certain expenses including, among others, expenses for travel, translation, and insurance; and
- regulatory and compliance risks that relate to maintaining accurate information and control over sales and activities that may fall within the purview of the U.S. Foreign Corrupt Practices Act, its books and records provisions, or its anti-bribery provisions.

Any of these factors could significantly harm our potential international expansion and operations and, consequently, our results of operations.

We are subject to U.S. and certain foreign export and import controls, anti-corruption laws and anti-money laundering laws and regulations. Compliance with these legal standards could impair our ability to compete in domestic and international markets. We can face criminal liability and other serious consequences for violations, which can harm our business.

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, and various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls, and anti-corruption and anti-money laundering laws and regulations, including the U.S. Foreign Corrupt Practices Act of 1977, as amended, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, contractors and other collaborators and partners from authorizing, promising, offering, providing, soliciting, or receiving, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector. We may engage third parties to sell VYJUVEK or our product candidates, if approved, abroad and/or to obtain necessary marketing authorizations, permits, licenses, patent registrations and other regulatory approvals. We may have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors and other collaborators and partners, even if we do not explicitly authorize or have actual knowledge of such activities. Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or

import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other adverse consequences.

Furthermore, U.S. export control laws and economic sanctions prohibit the provision of certain products and services to countries, governments, and persons targeted by U.S. sanctions.

The effect of pandemics, epidemics, outbreaks of infectious diseases, or similar public health crises on our operations and the operations of our customers, suppliers, third-party partners, and regulators could have an adverse impact our business.

Pandemics, epidemics, outbreaks of infectious diseases, or similar public health crises could adversely disrupt or impact our operations or those of our customers, suppliers, third-party partners, and regulators. In response to a pandemic or public health crisis, authorities may impose, and businesses and individuals may implement, numerous measures to try to contain the pandemic or public health crisis 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. In the event that such measures or similar measures or restrictions are implemented as a result of a pandemic or public health crisis, 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. In addition, the operations of our customers, suppliers, third-party partners, and regulators could be significantly limited or curtailed. Timely initiation and completion of clinical trials are essential to our business and clinical trials are dependent upon the availability of clinical trial sites, researchers and investigators, regulatory agency personnel, and materials, any of which may be adversely affected by public health crises, such as pandemics. The extent to which a health crisis may impact our business, results of operations and future growth prospects will depend on a variety of factors and future developments, which are highly uncertain and cannot be predicted with confidence, including the duration, scope, and severity of the public health crisis. A future public health crisis may have a material adverse effect on our business and results of operations.

Inadequate funding for the FDA and other government agencies, including from government shut downs, or other disruptions to these agencies' operations, could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which could adversely affect our business. For example, when the U.S. government has shut down in the past, certain regulatory agencies, such as the FDA and the United States Securities and Exchange Commission, or the SEC, have had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to review and process our regulatory submissions in a timely manner, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital. In addition, government funding of government agencies on which our operations may rely is subject to the political process, which is inherently fluid and unpredictable.

Risks Related to the Development, Regulatory Review and Approval of Our Product Candidates

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.

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 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 suppliers or manufacturers for clinical supply;
- commercial launch of our product candidates, if and when approved, whether alone or in collaboration with others; and

- 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 gene therapy platform is based on a novel technology, which makes it difficult to predict the time and cost of obtaining regulatory approvals for our product candidates.

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 the United States, the European Union, or elsewhere, or how long it will take to commercialize our product candidates. Approvals by the European Commission may not be indicative of what the 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. In 2016, the FDA established the Office of Tissues and Advanced Therapies ("OTAT") within its Center for Biologics Evaluation and Research to consolidate the review of gene therapy and related products, and has established the Cellular, Tissue and Gene Therapies Advisory Committee, among others, to advise this review. In September 2022, the FDA announced retitling of OTAT to the Office of Therapeutic Products ("OTP") and elevation of OTP to a "Super Office" to meet its growing cell and gene therapy workload. If we engage a National Institutes of Health funded institution to conduct a clinical trial, that institution's Institutional Biosafety Committee 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 our product candidates or lead to significant post-approval limitations or restrictions. These additional processes may result in a review and approval process that are 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.

Our product or product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial potential, or result in significant negative consequences before or 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 our product candidates, 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 and not by our product candidates, the FDA, the European Commission, the EMA, or other regulatory authorities could order us to cease further development of, or deny approval of, our product candidates 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 product candidates, the commercial prospects of such product candidates may be harmed and our ability to generate product revenue from the product candidates 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 a product candidate 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 or our product candidates, several potentially significant negative consequences could result, including:

- regulatory authorities may suspend or withdraw approvals of such product;
- regulatory authorities may require additional warnings on the label;
- we may be required to change the way VYJUVEK or 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 or our product candidates 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 product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidate for its intended indications. Obtaining marketing approval is an extensive, lengthy, expensive, and inherently uncertain process, and regulatory authorities may delay, limit, or deny approval of our product candidates for many reasons. 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 a sufficient number and diversity of 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 product 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 product candidate that are viewed to outweigh its potential benefits; or
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols.

The results of nonclinical and preclinical studies and early clinical trials may not be predictive of the results of later-stage clinical trials, and interim results of a clinical trial do not necessarily predict final results. In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. In addition, preclinical and clinical data are often susceptible to various interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy profile despite having progressed through nonclinical studies and initial clinical trials.

If we make manufacturing or formulation changes to our product or product candidates, we may need to conduct additional studies to bridge our modified product or 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 product 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;
- obtain approval without labeling claims that are necessary or desirable for the successful commercialization of our product candidates;
- be subject to additional and costly post-marketing testing requirements or clinical trials;
- be required to perform additional clinical trials to support approval;
- have regulatory authorities withdraw, or suspend, their approval of the product or impose restrictions on its distribution;
- be subject to the addition of labeling statements, such as warnings, precautions, or contraindications;
- be sued; or
- experience damage to our reputation.

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

Further, we, the FDA or an IRB, may suspend our clinical trials at any time if it appears that we or our collaborators are failing to conduct a trial in accordance with regulatory requirements, including the FDA's Current Good Clinical Practice, or CGCP, regulations, that we are exposing participants to unacceptable health risks, or if the FDA finds deficiencies in our Investigational New Drug, or 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 product candidates could be negatively impacted, and our ability to generate revenue from our product candidates may be eliminated or delayed.

We rely on third parties to conduct certain aspects of our preclinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or comply with regulatory requirements, we may not be able to obtain regulatory approval for, or commercialize, our product candidates.

We depend upon third parties to conduct certain aspects of our preclinical studies and depend on third parties, including independent principal investigators, to conduct our clinical trials under agreements with universities, medical institutions, and others. We negotiate budgets and contracts with such third parties, which may result in delays to our development timelines and increased costs.

We rely on third parties over the course of our clinical trials, and, as a result, may have limited control over the clinical principal investigators and limited visibility into their day-to-day activities, including with respect to their compliance with the approved clinical protocol. Nevertheless, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities. We and these third parties are required to comply with CGCP requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for product candidates in clinical development. Regulatory authorities enforce these CGCP requirements through periodic inspections of clinical trial sponsors, clinical investigators, and clinical trial sites. If we or any of these third parties fail to comply with applicable CGCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to suspend or terminate these clinical trials or perform additional preclinical studies or clinical trials before approving our marketing applications. We cannot be certain that, upon inspection, such regulatory authorities will determine that any of our clinical trials comply with CGCP requirements. In addition, our later-stage clinical trials must be conducted with product produced under CGMP requirements and may require a large number of patients.

Our failure or any failure by these third parties to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be adversely affected if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

Any third parties conducting aspects of our preclinical studies, or our clinical trials will not be our employees and, except for remedies that may be available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our preclinical studies and clinical programs. These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other product development activities, which could affect their performance on our behalf. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the preclinical or clinical data they obtain is compromised due to the failure to adhere to our protocols or regulatory requirements or for other reasons, our development timelines, including clinical development timelines, may be extended, delayed or terminated, and we may not be able to complete development of, obtain regulatory approval of, or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed or precluded entirely. Though we carefully manage our relationships with principal investigators and other third parties, there can be no assurance that we will not encounter challenges or delays or that these delays or challenges will not have a material adverse impact on our business, financial condition, and prospects.

Interim, "top-line," and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available or as additional analyses are conducted, and as the data are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publish interim, "top-line" or preliminary data from our clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data becomes available. Preliminary or "top-line" data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Material adverse changes between preliminary, "top-line" or interim data and final data could significantly harm our business, financial condition, results of operations and prospects.

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 our product candidates, if approved, 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 and the process for obtaining such approval may be lengthy and expensive. 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. Obtaining a Marketing Authorization Application ("MAA") 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 European Union 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.

VYJUVEK and our product candidates remain subject to regulatory oversight even after regulatory approval. 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 VYJUVEK or any of our product candidates that obtain regulatory approval to lose that approval.

VYJUVEK, our first FDA-approved product, and any other product candidates that obtain regulatory approval in the future, will remain 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 our product candidates 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 an approved product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured or a regulatory authority 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, 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 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 our approved product and 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 negatively impact the existing marketing approval for VYJUVEK and prevent, limit, or delay regulatory approval of our 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, which would materially and adversely affect our business, financial condition, results of operations and prospects.

While we have obtained orphan drug exclusivity for VYJUVEK and orphan drug designation for KB105, KB407, and KB408, it may not effectively protect us from competition, and we may be unable to obtain orphan drug designation for other product candidates. If our competitors are able to obtain orphan drug exclusivity before us, we may not be able to have competing products approved by the applicable regulatory authority for a significant period of time.

Regulatory authorities in some jurisdictions, including the United States, the European Union, and Japan may designate drugs for relatively small patient populations as orphan drugs.

Under the Orphan Drug Act of 1983, as amended, 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. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process, but it can lead to financial

incentives, such as opportunities for grant funding toward clinical trial costs, tax advantages and user-fee waivers. In addition, if a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the drug is entitled to orphan drug marketing exclusivity for a period of seven years. Orphan drug marketing exclusivity generally prevents the FDA from approving another application to market the same drug or biological product for the same disease or condition for seven years, except in limited circumstances, including if the FDA concludes that the later drug is safer, more effective or makes a major contribution to patient care. A designated orphan drug may not receive orphan drug marketing exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. Orphan drug marketing exclusivity rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

In the European Union, 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 European Union would be sufficient to justify the necessary investment in developing the drug or biologic product. In the European Union, orphan medicinal product designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process, but orphan drug designation may entitle an applicant to financial incentives such as reduction of fees or fee waivers, protocol assistance, and access to the centralized marketing authorization procedure. Upon grant of a marketing authorization, orphan products are entitled to ten years of market exclusivity for the approved therapeutic indication, which means that the EMA and European Commission cannot accept another marketing authorization application, grant a marketing authorization, or accept an application to extend a marketing authorization for a similar product for the same indication for a period of ten years. The period of market exclusivity is extended by two years for orphan medicinal products that have also complied with an agreed Pediatric Investigation Plan, or PIP. The ten-year market exclusivity in the European Union may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for which it received orphan designation, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity, or where the prevalence of the condition has increased above the threshold. Additionally granting of an authorization for another similar orphan medicinal product where another product has market exclusivity can happen at any time: (i) the second applicant can establish that its product, although similar, is safer, more effective, or otherwise clinically superior; (ii) the applicant cannot supply enough orphan medicinal product, or (iii) where the applicant consents to a second orphan medicinal product application.

The orphan drug designation system in Japan aims to support the development of drugs for diseases that affect fewer than 50,000 patients in Japan, for which significant unmet medical need exists. An investigational therapy is eligible to qualify for orphan drug designation in Japan if there is no approved alternative treatment option or if there is high efficacy or safety compared to existing treatment options expected. Specific measures to support the development of orphan drugs in Japan include subsidies for research and development expenditures, prioritized consultation regarding clinical development, reduced consultation fees, tax incentives, priority review of applications, reduced application fees, and extended registration validity period. Up to 10 years of orphan exclusivity, known as the re-examination period, is granted for the product after approval. The orphan drug exclusivity may be rescinded by the Japanese government in certain circumstances.

Even though we have obtained orphan drug exclusivity for VYJUVEK in the United States; orphan drug designation for VYJUVEK in the European Union and Japan; orphan drug designation for KB105 and KB407 in the United States and the European Union; and orphan drug designation for KB408 in the United States, we cannot assure you that we will be able to obtain or maintain orphan drug exclusivity and if we are able to maintain the orphan drug exclusivity, the exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition. Further, we cannot assure you that any of our other product candidates will be approved for any orphan-designated use in any jurisdiction, in a timely manner or at all, or that a competitor will not obtain orphan drug exclusivity that could block the regulatory approval of any of our drug candidates for several years. If we are unable to maintain or obtain orphan drug exclusivity, our ability to generate sufficient revenue may be negatively affected. If a competitor is able to obtain orphan drug exclusivity that would block our product candidates' regulatory approval, our ability to generate revenue could be significantly reduced, which would harm our business prospects, financial condition and results of operations. We do not know if, when, or how the FDA or other regulators may change the applicable orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes may be made to orphan drug regulations and policies, our business could be adversely impacted.

Accelerated approval by the FDA, even if granted for any of our product candidates, may not lead to a faster development or regulatory review or approval process and it does not increase the likelihood that our product candidates will receive marketing approval.

We may seek approval of our current or future product candidates using the FDA's accelerated approval pathway. This pathway may not lead to a faster development, regulatory review or approval process and does not increase the likelihood that our product candidates will receive marketing approval. A product may be eligible for accelerated approval if it treats a serious or life-threatening condition, generally provides a meaningful advantage over available therapies, and demonstrates an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. As a condition of approval, the FDA may require that a sponsor of a product receiving accelerated approval perform adequate and well-controlled post-marketing confirmatory clinical trials. These confirmatory trials must be completed with due diligence. Under the Food and Drug Omnibus Reform Act of 2022, or FDORA, the FDA is permitted to require, as appropriate, that a post-approval confirmatory trial or trials be underway prior to approval or within a specified time after the date accelerated approval was granted. FDORA also requires sponsors to send updates to the FDA every 180 days on the status of such studies, including progress toward enrollment targets, and the FDA must promptly post this information publicly. Furthermore, under FDORA, the FDA is empowered to take action, such as issuing fines, against companies that fail to conduct with due diligence any post-approval confirmatory trial or submit timely reports to the agency on their progress. In addition, for products under consideration for accelerated approval, the FDA currently requires, unless otherwise requested by the agency, pre-approval of promotional materials intended for dissemination or publication within 120 days of marketing approval be submitted to the agency for review during the review period, which could adversely impact the timing of the commercial launch of the product. There can be no assurance that the FDA would allow any of our product candidates to proceed on an accelerated approval pathway, and even if the FDA did allow such pathway, there can be no assurance that any expedited development, review, or approval will be granted on a timely basis, or at all.

Breakthrough Therapy Designation, Fast Track Designation, Regenerative Medicine Advanced Therapy Designation or Priority Review by the FDA, or PRIME Scheme by the EMA, even if granted for any of our product candidates, may not lead to a faster development, regulatory review or approval process, and such designations may not increase the likelihood that any of our product candidates will receive marketing approval.

We may seek a Breakthrough Therapy Designation for some of our product candidates. A breakthrough therapy is defined as a therapy that is intended, alone or in combination with one or more other therapies, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the therapy may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For therapies that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Therapies designated as breakthrough therapies by the FDA may also be eligible for priority review and accelerated approval. Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a Breakthrough Therapy Designation for a product candidate may not result in a faster development process, review or approval compared to therapies considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that such product candidates no longer meet the conditions for qualification or decide that the time for FDA review or approval will not be shortened.

We have obtained and may seek Fast Track Designation for some of our product candidates. For instance, VYJUVEK, KB105, and KB707 were granted Fast Track Designation by the FDA. If a therapy is intended for the treatment of a serious or life-threatening condition and the therapy demonstrates the potential to address unmet medical needs for this condition, the sponsor may apply for Fast Track Designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive Fast Track Designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. For products that receive Fast Track Designation, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of the marketing application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a Fast Track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing an application does not begin until the last section of the application is submitted. The FDA may withdraw Fast Track Designation if it believes that the designation is no longer supported by data from clinical programs. Many biologics that have received Fast Track Designation have failed to obtain marketing approval. Fast Track Designation alone does not guarantee qualification for the FDA's priority review procedures.

We have obtained and may seek Regenerative Medicine Advanced Therapy, or RMAT, designation for some of our product candidates. For instance, VYJUVEK was granted RMAT designation by the FDA. In 2017, the FDA established the RMAT designation as part of its implementation of the 21st Century Cures Act to expedite review of any drug that meets the following criteria: it qualifies as a RMAT, which is defined as a cell therapy, therapeutic tissue engineering product, human cell

and tissue product, or any combination product using such therapies or products, with limited exceptions; it is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition; and preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such a disease or condition. Like Breakthrough Therapy Designation, RMAT designation provides potential benefits that include more frequent meetings with the FDA to discuss the development plan for the product candidate, and eligibility for rolling review and priority review. Products granted RMAT designation may also be eligible for accelerated approval on the basis of a surrogate or intermediate endpoint reasonably likely to predict long-term clinical benefit, or reliance upon data obtained from a meaningful number of sites, including through expansion to additional sites. RMAT-designated products that receive accelerated approval may, as appropriate, fulfill their post-approval requirements through the submission of clinical evidence, clinical trials, patient registries, or other sources of real-world evidence, such as electronic health records; through the collection of larger confirmatory data sets; or via post-approval monitoring of all patients treated with such therapy prior to approval of the therapy. There is no assurance that we will be able to obtain RMAT designation for our product candidates. RMAT designation does not change the FDA's standards for product approval, and there is no assurance that such designation will result in expedited review or approval or that the approved indication will not be narrower than the indication covered by the designation. Additionally, RMAT designation can be revoked if the criteria for eligibility cease to be met as clinical data emerges.

If the FDA determines that a product candidate offers a treatment for a serious condition and, if approved, the product would provide a significant improvement in safety or effectiveness, the FDA may designate the product candidate for priority review. A priority review designation means that the goal for the FDA to review an application is six months, rather than the standard review period of ten months. The FDA has broad discretion with respect to whether or not to grant priority review status to a product candidate, so even if we believe a particular product candidate is eligible for such designation or status, the FDA may decide not to grant it. Moreover, a priority review designation does not necessarily result in an expedited regulatory review or approval process or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. Receiving priority review from the FDA does not guarantee approval within the six-month review cycle, or at all.

We have obtained and may seek to qualify our product candidates under the PRIority MEdicines ("PRIME") scheme from the EMA. For instance, VYJUVEK was granted PRIME designation. The PRIME scheme is open to medicines under development and for which the applicant intends to apply for an initial MAA through the centralized procedure. Eligible products must target conditions for which where is an unmet medical need (there is no satisfactory method of diagnosis, prevention or treatment in the European Union or, if there is, the new medicine will bring a major therapeutic advantage) and they must demonstrate the potential to address the unmet medical need by introducing new methods or therapy or improving existing ones. There is no assurance that we will be able to obtain PRIME qualification for our product candidates. PRIME does not change the standards for product approval, and there is no assurance that such qualification will result in expedited review or approval. Moreover, where, during the course of development, a product no longer meets the eligibility criteria, support under the PRIME scheme may be withdrawn.

We have obtained a rare pediatric disease designation for certain of our product candidates; however, there is no guarantee that FDA approval will result in issuance of a priority review voucher.

In 2012, Congress authorized the FDA to award priority review vouchers to sponsors of certain rare pediatric disease product applications. This program is designed to encourage development of new drug and biological products for prevention and treatment of certain rare pediatric diseases. Specifically, under this program, a sponsor that receives an approval for a drug or biologic for a "rare pediatric disease" that meets certain criteria may qualify for a voucher that can be redeemed to receive a priority review of a subsequent marketing application for a different product. The sponsor of a rare pediatric disease drug product receiving a priority review voucher may transfer (including by sale) the voucher to another sponsor. The voucher may be further transferred any number of times before the voucher is used, as long as the sponsor making the transfer has not yet submitted the application. The FDA may also revoke any priority review voucher if the rare pediatric disease drug for which the voucher was awarded is not marketed in the United States within one year following the date of approval. We received rare pediatric disease designation for VYJUVEK and were awarded a priority review voucher following FDA approval of VYJUVEK in May 2023. The priority review voucher was sold in August 2023. We have also obtained a rare pediatric disease designation for KB105, KB104, and for KB407. However, there is no guarantee that we will be able to obtain a priority review voucher if these product candidates are approved by the FDA. Congress included a sunset provision in the statute authorizing the rare pediatric disease priority review voucher program. Under the current statutory sunset provisions, after September 30, 2024, the FDA may only award a voucher for an approved rare pediatric disease product application if the sponsor has rare pediatric disease designation for the product candidate, and that designation was granted by September 30, 2024. After September 30, 2026, the FDA may not award any rare pediatric disease priority review vouchers.

We may seek designation for our platform technology as a designated platform technology, but we might not receive such designation, and even if we do, such designation may not lead to a faster development or regulatory review or approval process.

We may seek designation for our platform technology as a designated platform technology. Under the Food and Drug Omnibus Reform Act of 2022, or FDORA, a platform technology incorporated within or utilized by a drug or biologic is eligible for designation as a designated platform technology if (1) the platform technology is incorporated in, or utilized by, a product approved under a New Drug Application, or NDA, or BLA; (2) preliminary evidence submitted by the sponsor of the approved product, or a sponsor that has been granted a right of reference to data submitted in the application for such product, demonstrates that the platform technology has the potential to be incorporated in, or utilized by, more than one product without an adverse effect on quality, manufacturing, or safety; and (3) data or information submitted by the sponsor indicates that incorporation or utilization of the platform technology has a reasonable likelihood to bring significant efficiencies to the product development or manufacturing process and to the review process. A sponsor may request the FDA to designate a platform technology as a designated platform technology concurrently with, or at any time after, submission of an IND application for a product that incorporates or utilizes the platform technology that is the subject of the request. If so designated, the FDA may expedite the development and review of any subsequent NDA or BLA for a product that uses or incorporates the platform technology. Even if we believe our platform technology meets the criteria for such designation, the FDA may disagree and instead determine not to grant such designation. In addition, the receipt of such designation for a platform technology does not ensure that our applicable product candidates will be developed more quickly or receive a faster FDA review process or ultimate FDA approval. Moreover, the FDA may revoke a designation if the FDA determines that a designated platform technology no longer meets the criteria for such designation.

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 disrupt our production of VYJUVEK or delay or disrupt our development and commercialization efforts with respect to our product candidates.

Before we can begin to commercially manufacture our product candidates, we must pass a pre-approval inspection of our manufacturing facilities by the FDA. 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 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, contract laboratories, or suppliers. The CGMP requirements govern quality control of the manufacturing process and documentation policies and procedures. In complying with CGMP, we are 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 will be subject to possible regulatory action and may not be permitted to sell any approved product that we may develop.

In addition, the manufacturing process used to produce VYJUVEK and our product candidates is complex and novel. The production of VYJUVEK and our product candidates require processing steps that are more complex than those required for most chemical pharmaceuticals. Moreover, unlike chemical pharmaceuticals, the physical and chemical properties of a biologic such as 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 VYJUVEK and 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 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 facilities for VYJUVEK and our product candidates, we may also utilize third parties to conduct our product manufacturing or components thereof. Therefore, we are subject to the risk that these third parties may not perform satisfactorily.

We may maintain third-party manufacturing capabilities in order to provide multiple sources of supply of VYJUVEK or a product candidate that is approved for sale. In addition, we may utilize third parties to manufacture components of our products. For example, we use a third-party to manufacture the sterile gel that is mixed with our in-house produced vector for VYJUVEK. Our ability to commercially supply VYJUVEK depends, in part, on the ability of third parties to supply and manufacture the raw materials and other important components related to our manufacture of VYJUVEK. If we fail to develop and maintain supply relationships with these third parties, we may be unable to successfully commercialize VYJUVEK or any approved product candidate. Any of our existing suppliers may:

- fail to supply us on a timely basis or in the requested amount due to unexpected damage to or destruction of facilities or equipment or otherwise;

- fail to increase manufacturing capacity and at higher yields in a timely or cost-effective manner, or at all, to sufficiently meet our commercial needs;
- be unable to meet our production demands due to issues related to their reliance on sole-source suppliers and manufacturers;
- supply us with materials that fail to meet regulatory requirements;
- become unavailable through business interruption or financial insolvency;
- lose regulatory status as an approved supply source;
- be unable or unwilling to (i) honor current supply agreements or (ii) renew current supply agreements when such agreements expire on a timely basis, on acceptable terms or at all; or
- discontinue production or manufacturing of materials that we acquire through such third-party supplier.

In the event of any of the foregoing, if we do not have an alternative supplier or manufacturer in place, we may not be able to manufacture our products for commercial, regulatory, or clinical purposes and would be required to expend substantial management time and expense to identify, qualify and transfer to alternative suppliers or manufacturers. There can be no assurance that replacements would be available to us on a timely basis, on acceptable terms, or at all. Any need to find and qualify new suppliers or manufacturers could significantly delay production of VYJUVEK or any product candidate, if approved, adversely impact our ability to market VYJUVEK or any product candidate, if approved, and have a material adverse effect on our business, financial condition, results of operations and prospects.

If we or a third-party supplier or 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 ability to produce VYJUVEK for commercial supply or any product candidate for clinical development.

Given the nature of biologics manufacturing, there is a risk of contamination. Any contamination could materially adversely affect our ability to produce VYJUVEK or 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 VYJUVEK or 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.

Our failure to maintain or continuously improve our quality management program could have an adverse effect upon our business, subject us to regulatory actions and cause patients to lose confidence in us or our products, among other negative consequences.

Quality management plays an essential role in the manufacturing of drugs or drug products, conducting clinical trials, preventing defects, improving our product candidates, and assuring the safety and efficacy of our product and product candidates. We seek to maintain a robust quality management program which includes the following broad pillars of quality:

- monitoring and assuring regulatory compliance for clinical trials, manufacturing, and testing of good applicable practice (“GxP”) (e.g., CGCP and CGMP regulated) products;
- monitoring and providing oversight of all GxP suppliers;
- establishing and maintaining an integrated, robust quality management system for clinical, manufacturing, supply chain and distribution operations; and
- cultivating a proactive, preventative quality culture and employee and supplier training to ensure quality.

Our success depends on our ability to maintain and continuously improve our quality management program. A quality or safety issue may result in adverse inspection reports, warning letters, monetary sanctions, injunctions to halt manufacture and distribution of our products, civil or criminal sanctions, costly litigation, refusal of a government to grant approvals and licenses, restrictions on operations, or withdrawal, suspension or variation of existing approvals and licenses. An inability to address a quality or safety issue in an effective and timely manner may also cause negative publicity, or a loss of patient

confidence in us or our product or product candidates, which may result in difficulty in successfully launching products and the loss of potential future sales, which could have an adverse effect on our business, financial condition, and results of operations.

Risks Related to Commercialization of VYJUVEK and Our Product Candidates

We have limited experience as a commercial company and the sales, marketing, and distribution of VYJUVEK or any future approved products may be unsuccessful or less successful than anticipated.

We received FDA approval of VYJUVEK in May 2023 and initiated a commercial launch of VYJUVEK in the United States in the second quarter of 2023. As a company, we have no prior experience commercializing a biologic. The success of our commercialization efforts is difficult to predict and subject to the effective execution of our business plan, including, among other things, the continued development of our internal sales, marketing, and distribution capabilities and our ability to navigate the significant expenses and risks involved with the development and management of such capabilities. For example, our commercial launch of VYJUVEK may not develop as planned or anticipated, which may require us to, among others, adjust or amend our business plan and incur significant expenses. Further, given our lack of experience commercializing products, we do not have a track record of successfully executing a commercial launch. If we are unsuccessful in accomplishing our objectives and executing on our business plan, or if our commercialization efforts do not develop as planned, we may not be able to successfully commercialize VYJUVEK and any future approved products, we may require significant additional capital and financial resources, we may not become profitable on a consistent basis, and we may not be able to compete against more established companies in our industry.

If we are unable to maintain our agreements with third parties to distribute VYJUVEK to patients in the United States, our results of operations and business could be adversely affected.

We rely on a small number of third parties to commercially distribute VYJUVEK to patients in the United States. We have contracted with a third-party packaging company to package VYJUVEK, a third-party logistics company to warehouse, process, and ship VYJUVEK to a limited number of specialty pharmacies that mix the medication and administer it to patients in the patient's home by a healthcare professional and a specialty distributor that distributes VYJUVEK to hospitals and outpatient clinics where patients are administered the medication at a healthcare professional's office. This distribution network requires significant coordination with our sales and marketing and finance organizations. In addition, failure to coordinate financial systems could negatively impact our ability to accurately report product revenue from VYJUVEK. If we are unable to effectively manage the distribution process, the sales of VYJUVEK could be compromised and our results of operations may be harmed.

If the third parties involved in the commercial distribution of VYJUVEK in the United States do not fulfill their contractual obligations to us or refuse or fail to adequately or to properly distribute VYJUVEK and serve patients, or the agreements with them are terminated without adequate notice, shipments of VYJUVEK, and associated revenue, could be adversely affected. In addition, if we were required to replace such third-parties, it could take time to locate an appropriate replacement third-party on acceptable terms, which could cause delays in our distribution network and increased expenses, and thereby adversely impact our commercial sales of VYJUVEK in the United States and result in a material adverse effect on our business, financial condition, results of operations, and prospects.

We plan on using local distributors to market and sell VYJUVEK in certain jurisdictions outside of the U.S., the U.K., certain EU countries, and Japan, which subjects us to certain risks.

We plan on using local distributors to market and sell VYJUVEK outside of the U.S., the U.K., certain EU countries, and Japan. We may be unable to enter into appropriate supply, marketing, and distribution arrangements on favorable terms, if at all. Our use of distributors in these market to market and sell VYJUVEK involves certain risks, including, but not limited to, risks that these organizations will not comply with applicable laws and regulations, not effectively sell or support VYJUVEK or reduce or discontinue their efforts to sell or support VYJUVEK, not devote the resources necessary to market and sell VYJUVEK in the volumes and within the time frame we expect, not be able to satisfy financial obligations to us or others, not provide us with accurate or timely information regarding their inventories of VYJUVEK or the number of patients who are using VYJUVEK, or not provide us with accurate or timely information regarding serious adverse events and/or product complaints. Any such events may result in regulatory actions that may include suspension or termination of the distribution and sale of our products in a certain country, loss of revenue, and/or reputational damage, which could harm our results of operations and business.

In connection with the commercial launch of VYJUVEK in the United States, we recruited a sales force and established marketing, market access and medical affairs teams and distribution capabilities and if the commercial launch of VYJUVEK is not successful for any reason, we could incur substantial costs and our investment would be lost if we cannot retain or reposition our sales, marketing, market access and medical affairs personnel.

To achieve commercial success for VYJUVEK, we have devoted and anticipate that we will continue to devote significant resources to support our sales force, marketing, market access, and medical affairs teams and distribution

capabilities. There are risks involved with establishing our own sales, marketing, distribution, training, and support capabilities. For example, recruiting and training sales and marketing personnel is expensive and time-consuming and could delay our ability to focus on other priorities. If the commercial launch of VYJUVEK in the United States is not successful for any reason, this would be costly, and our investment would be lost if we cannot retain or reposition our sales, marketing, market access and medical affairs personnel or terminate on favorable terms any agreements entered into with third parties to support our commercialization efforts.

Factors that may inhibit our efforts to commercialize VYJUVEK or any other product candidates, if approved, on our own in the United States or elsewhere include:

- our inability to train and retain adequate numbers of effective sales, marketing, training, and support personnel;
- the inability of sales personnel to obtain access to physicians, including key opinion leaders, or to educate an adequate number of physicians of the benefits of VYJUVEK or any approved product candidate;
- the lack of complementary products to be offered by our sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive or integrated product offerings; and
- unforeseen costs and expenses associated with establishing and maintaining an independent sales, marketing, training, and support organization.

If our salesforce, marketing, market access, and medical affairs teams and distribution capabilities fail, or are otherwise unsuccessful, it would materially adversely impact the commercial launch of VYJUVEK, impact our ability to generate revenue and harm our business.

If we are unable to expand our medical affairs, marketing, market access, sales, and distribution capabilities or collaborate with third parties to market and sell our product candidates for which we obtain marketing approval, we may be unable to generate sufficient product revenue.

To successfully commercialize any products for which we obtain marketing approvals, we will need to expand our salesforce, marketing, market access, and medical affairs teams and distribution capabilities, either on our own or in collaboration with others. The development of a salesforce, marketing, market access, and medical affairs teams and distribution capabilities effort is expensive and time-consuming, and our expenses associated with maintaining our sales force may be disproportional compared to the revenue we may be able to generate on sales of VYJUVEK and future products. We cannot be certain that we will be able to internally develop this capability successfully. We may enter into collaborations regarding VYJUVEK or any future approved product candidates with other entities to utilize their established marketing and distribution capabilities. However, we may be unable to enter into such agreements on favorable terms, if at all.

We compete with many companies that currently have extensive, experienced, and well-funded medical affairs, marketing, market access, distribution, and sales operations to recruit, hire, train and retain personnel, and we may not be able to hire or retain such talent on commercially reasonable terms, if at all. We also face competition in our search for third parties to assist us with the sales and marketing efforts. If any future collaborators do not commit sufficient resources to commercialize our product candidates, if approved, 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.

Our efforts to educate the medical community and third-party payors on the benefits of VYJUVEK or our product candidates, if approved, 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 VYJUVEK or any of our product candidates that are approved fails to achieve market acceptance among physicians, patients, or third-party payors, we will not be able to generate significant revenue from such product, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

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

We focus our research and product development on genetic medicines for patients with debilitating diseases. We base our market opportunity estimates on a variety of factors, including our estimates of the number of people who have these diseases, the potential scope of our approved product labels, the subset of people with these diseases who have the potential to benefit from treatment with VYJUVEK or our product candidates, various pricing scenarios, and our understanding of reimbursement policies in particular countries. These estimates are based on many assumptions and may prove incorrect, and new studies may reduce the estimated incidence or prevalence of these diseases. Estimating market opportunities can be particularly challenging for rare indications, such as the ones we currently address, as epidemiological data is often more limited than for more prevalent indications and can require additional assumptions to assess potential patient populations. For example, as we commercialize VYJUVEK in the United States and learn more about market dynamics and engage with regulators on additional potential marketing approvals, our view of VYJUVEK's initial potential market opportunity will

become more refined. The addressable patient population in the United States and internationally may turn out to be lower than expected, patients may not be otherwise amenable to treatment with VYJUVEK or our product candidates, if approved, or may become increasingly difficult to identify and access, all of which would adversely affect our business, financial condition, results of operations and prospects. If we are unable to successfully commercialize VYJUVEK or any future product candidates with attractive market opportunities, our future product revenue may be smaller than anticipated, and our business may suffer.

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 VYJUVEK and our product candidates will depend upon their degree of market acceptance by physicians, patients, third-party payors, and others in the medical community.

Even with the requisite approvals from the FDA in the United States, potential approvals of VYJUVEK from the EMA in the European Union and other regulatory authorities internationally (and potential approvals of any of our product candidates by regulatory authorities), the commercial success of VYJUVEK and our product candidates will depend, in part, on the acceptance of physicians, patients and health care payors of gene therapy products in general, and VYJUVEK and our product candidates, in particular, as medically necessary, cost-effective, and safe. VYJUVEK and any product candidate 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 VYJUVEK and our product candidates, if approved for commercial sale, will depend on several factors, including:

- the efficacy and safety of VYJUVEK and our product candidates as demonstrated in clinical trials;
- the potential and perceived advantages of VYJUVEK and our product candidates over alternative treatments, if available;
- the cost of VYJUVEK and our product candidates relative to alternative treatments if any are available;
- the clinical indications for which VYJUVEK and our product candidates are approved by the FDA and other regulatory authorities;
- 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 VYJUVEK and our product candidates or competing products and treatments;
- any restrictions on the use of VYJUVEK and our products together with other medications; and
- favorable third-party payor coverage and adequate reimbursement.

Even if a product candidate 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 VYJUVEK and 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 United States 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 United States 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 United States. 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 VYJUVEK or our product candidates, if approved, not commercially viable or may adversely affect our anticipated future revenue 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 drugs or biologics generally could restrict the amount that we are able to charge for VYJUVEK or our product candidates, if approved, 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 VYJUVEK or our product candidates, 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 approved products. Accordingly, sales of VYJUVEK and our product candidates, if approved, will depend substantially, both domestically and abroad, on the extent to which the costs of our product or 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, if approved. Even if coverage is provided, the coverage may be more limited than the purposes for which the product is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for coverage and reimbursement does not imply that a product will be paid for in all cases or at a rate that covers our costs, including research, development, intellectual property, manufacture, sale, and distribution expenses, and therefore, 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 drug 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. 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 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 approved products may be reduced compared with the United States and may be insufficient to generate commercially reasonable product revenue.

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 product candidates 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, additional legislative changes, statements by elected officials, 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.

Prior to receiving VYJUVEK, patients are required to undergo genetic testing, and we anticipate that prior to receiving certain of our other product candidates, if approved, 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 VYJUVEK and our product candidates, if approved.

Increasing demand for compassionate use or expanded access of our unapproved therapies could negatively affect our reputation and harm our business.

We are developing our product candidates for illnesses for which there are currently limited to no available therapeutic options. At least one other company has been the target of disruptive social media campaigns related to a request for access to unapproved drugs for patients with significant unmet medical need. If we experience a similar social media campaign regarding our decision to provide or not provide our product candidates under an expanded access corporate policy, our reputation may be negatively affected, and our business may be harmed. Recent media attention to individual patients' expanded access requests has resulted in the introduction of legislation at the local and national level referred to as "Right to Try" laws, such as the Right to Try Act, which are intended to give patients access to unapproved therapies. New and emerging legislation regarding expanded access to unapproved drugs for life-threatening illnesses could negatively impact our business in the future.

A possible consequence of both activism and legislation in this area is the need for us to initiate an unanticipated expanded access program or to make our product candidates more widely available sooner than anticipated. We are a small company with limited resources and unanticipated trials or access programs could result in diversion of resources from our primary goals.

In addition, some patients who receive access to unapproved drugs through compassionate use or expanded access programs have life-threatening illnesses and have exhausted all other available therapies. The risk for serious adverse events in this patient population is high which could have a negative impact on the safety profile of our product candidates if we were to provide them to these patients in accordance with our expanded access corporate policy, which could cause significant delays or an inability to successfully commercialize our product candidates, which could materially harm our business. If we were to provide patients with our product candidates under our expanded access corporate policy, we may in the future need to restructure or pause ongoing compassionate use and/or expanded access programs in order to perform the controlled clinical trials required for regulatory approval and successful commercialization of our product candidates, which could prompt adverse publicity or other disruptions related to current or potential participants in such programs.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain adequate United States and foreign patent protection for VYJUVEK, our current product candidates, 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 VYJUVEK, 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 our approved product, current product candidates, additional product candidates in our pipeline and current and future innovations related to our vector platform. 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.

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. 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 our intended 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 earliest priority date or, in some cases, not at all until patents are issued. 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 VYJUVEK, each and every one of our product candidates, and current and future innovations related to our vector platform, 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 VYJUVEK and our product candidates that are approved, 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, 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 market and sell VYJUVEK and to develop, manufacture, market and sell our product candidates, and to freely use our proprietary technologies without infringing the rights and intellectual property of others. Many companies and institutions have filed, and continue to file, patent applications related to various aspects of gene therapy. 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 VYJUVEK or any of our product candidates, if approved. The biotechnology and pharmaceutical industries are

characterized by extensive and complex litigation regarding patents and other intellectual property rights. We may become party to, or be threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to VYJUVEK or our product candidates or related technologies, including, for example, interference proceedings, post grant review challenges, and *inter partes* review before The United States Patent and Trademark Office. Our competitors or other third parties may assert infringement claims against us, alleging that our products, 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 VYJUVEK or any of our product candidates, if approved. 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, 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 approved product, product candidates and 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 product or technologies. 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 products and technologies 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 and adversely impact our financial results 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 have been subject to claims asserting that we, our employees or our advisors have wrongfully used or disclosed alleged trade secrets of other parties, and we may face such claims in the future or claims asserting ownership of what we regard as our own intellectual property.

Certain of our employees or advisors are currently, or were previously, employed at universities or other biotechnology or pharmaceutical companies, including potential competitors, and we have and may in the future enter into agreements providing us with rights to intellectual property of third parties for limited purposes. Although we endeavor 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 in Note 7 of the Notes to the Consolidated Financial Statements included in Part II, Item 8 of this Annual Report on Form 10-K, in April of 2022, we entered into a settlement agreement with PeriphaGen, Inc., which had alleged breach of contract and misappropriation of trade secrets. If we fail to successfully defend 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 VYJUVEK or our product candidates, which could 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 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 VYJUVEK or 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, in September 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 United States Patent and Trademark Office ("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 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.

Although we have registered certain of our trademarks and trade names, 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 approved product or any of 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 Our Financial Position and Need for Additional Capital

We have incurred net losses in the past and may not sustain profitability.

Although we generated net income for the year ended December 31, 2023, we have otherwise incurred recurring losses and negative cash flows from operations since inception. Our transition to operating profitability depends on our ability to (i) successfully commercialize VYJUVEK in the U.S. and obtain the necessary regulatory approvals to commercialize VYJUVEK outside of the U.S. and then successfully commercialize VYJUVEK outside the U.S., and (ii) complete the development of, and obtain the regulatory approvals necessary to successfully commercialize our product candidates with significant market potential. We have devoted substantially all our efforts to date to (i) research and development of our gene therapy platform, product candidates and our manufacturing infrastructure, and, more recently, (ii) commercializing VYJUVEK in the U.S. We expect to continue to incur significant expenses for the foreseeable future and our operating results may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially if, and as, we:

- manufacture, market and sell our lead product, VYJUVEK, in the U.S. and prepare for regulatory approvals outside of the U.S. and if such approvals are received, commercialize VYJUVEK in those geographies;
- continue our research, preclinical studies, and the clinical development of our current product candidates, including our current clinical trials and planned clinical trials;
- initiate preclinical studies and clinical trials for any additional product candidates that we may pursue in the future;
- prepare for regulatory approvals for our product candidates in the United States, EU and in other key geographies;
- continue to operate our in-house commercial-scale current good manufacturing practice, or CGMP, manufacturing facilities, ANCORIS and ASTRA;
- manufacture material for commercial sales of VYJUVEK and clinical trials or potential commercial sales of our product candidates;
- further develop our gene therapy platform;

- further establish our sales, marketing and distribution infrastructure to commercialize VYJUVEK and product candidates for which we may obtain marketing approval;
- develop, maintain, expand and protect our intellectual property portfolio; and
- acquire or in-license other product candidates and technologies.

To remain profitable, we must be successful in a range of challenging activities, including designing, initiating, and completing clinical trials for our product candidates, developing, validating, and maintaining commercial scale manufacturing processes, obtaining marketing approvals, manufacturing, marketing, and selling VYJUVEK and any 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 VYJUVEK does not receive regulatory approvals outside the U.S., or any of our product candidates do not receive regulatory approvals, or if VYJUVEK or any of our product candidates, if approved, fails to achieve sufficient market acceptance for any indication, our ability to remain profitable, our business prospects and financial condition could be materially adversely affected. Moreover, if we decide to leverage any success with VYJUVEK or any of our current product candidates to develop other product opportunities, we may not be successful in such efforts. In any such event, our business may be materially adversely affected.

We currently have one product, VYJUVEK, approved by the FDA and several product candidates in the clinical trials stages. However, we may never develop, acquire or in-license additional product candidates. We may never generate revenue from any of our product candidates. We may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to 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 stockholders to lose all or part of their 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. 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 our product candidates, our expenses could increase and potential revenue from product candidates in development could be delayed.

We may need to raise additional funding to maintain and expand our commercialization capabilities for VYJUVEK and to complete the development of, and obtain the regulatory approvals necessary to, commercialize 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.

To complete the process of obtaining regulatory approval for our product candidates and to continue building the manufacturing, sales, marketing, and distribution infrastructure that we believe is or will be necessary to successfully commercialize VYJUVEK and commercialize our product candidates, if approved, we may require substantial additional funding. We expect to continue to incur significant expenses related to sales, medical affairs, marketing, manufacturing, and distribution of VYJUVEK. In addition, if we obtain marketing approval for our product candidates, we expect to incur significant additional expenses related to product sales, medical affairs, marketing, manufacturing and distribution. 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 ability of VYJUVEK to generate sufficient revenue;
- the costs of product sales, medical affairs, marketing, manufacturing, and distribution for VYJUVEK;
- the outcome, timing and costs of seeking regulatory approvals for VYJUVEK outside the U.S.;
- the progress, timing, results, and costs of any clinical trials required for VYJUVEK outside the U.S.;
- the progress, timing, results, and costs of our current and planned clinical trials of B-VEC (in Japan), KB105, KB301, KB407, KB707, and KB408;
- the continued development and the filing of IND applications for KB104 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 product candidates that we may pursue in the future;
- the costs of maintaining our own commercial-scale CGMP manufacturing facilities;
- the outcome, timing, and costs of seeking regulatory approvals for any of our product candidates;
- the costs associated with the manufacturing process development and evaluation of third-party suppliers or 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;
- 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 current or future collaborations, distribution, licensing, consulting, or other arrangements;
- 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;
- the terms of our license agreements, if any, 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 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 for our product candidates in development or future product candidates. Revenue will be derived from VYJUVEK until we have another product candidate receive marketing approval. Accordingly, we may 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. 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 approved product, VYJUVEK, and product candidates, our growth potential, and the market price per share of our common stock. See "Raising additional capital could cause the price of our common stock to decline and cause dilution to our stockholders, restrict our operations or require us to relinquish rights."

Changes in tax law may adversely affect our business and financial condition

We are subject to evolving and complex tax laws in the U.S. and the foreign jurisdictions in which we operate. New income, sales, use or other tax laws, statutes, rules, regulations, or ordinances could be enacted at any time, or interpreted, changed, modified, or applied adversely to us, any of which could adversely affect our business operations and financial performance. Changes to tax laws (which could apply retroactively) could adversely affect us and our stockholders. In recent years, such changes have been made and changes are likely to occur in the future, which could have a material adverse effect on our business, cash flow, financial condition, and results of operations.

Our ability to use our net operating loss carryforwards and certain tax credit carryforwards may be subject to limitation.

We have U.S. federal and state net operating loss carryforwards, which are available to reduce future taxable income. Federal net operating loss carryforwards generated in tax years beginning after December 31, 2017 may be carried forward indefinitely but are limited to offset 80% of taxable income in any tax year. Our other federal net operating loss carryforwards and our state net operating loss carryforwards expire beginning in 2037. We also have federal research and development tax credits which may be used to offset future tax liabilities and expire beginning in 2039. We also have federal orphan drug tax credits which may be used to offset future tax liabilities, which expire beginning in 2039.

Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, changes in our ownership may limit the amount of our net operating loss carryforwards and tax credit carryforwards that could be utilized annually to offset our future taxable income. This limitation would generally apply in the event of a cumulative change in ownership of our company of more than 50% within a three-year period. Any such limitation may significantly reduce our ability to utilize our net operating loss carryforwards and tax credit carryforwards before they expire. Private placements and other transactions that have occurred since our inception, as well as our initial public offering, may trigger such an ownership change pursuant to Sections 382 and 383. Any such limitation, whether as the result of the initial public offering, prior private placements, sales of

our common stock by our existing stockholders or additional sales of our common stock by us, could have a material adverse effect on our results of operations in future years.

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 commenced operations in 2016. Our efforts to date have been primarily related to organizing and staffing our company, business planning, raising capital, developing our vector platform and related technologies, identifying potential gene therapy product candidates, undertaking preclinical studies and clinical trials, scaling our manufacturing capabilities, obtaining FDA approval for VYJUVEK, and commercializing VYJUVEK. 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 and commercializing 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 are transitioning from a company with a research and development focus to a company undertaking commercial activities. We may encounter unforeseen expenses, difficulties, complications and delays and may not be successful in such a transition. Accordingly, you should not rely upon the results of any particular quarterly or annual period as indications of future operating performance.

Risks Related to Ownership of Our Common Stock

Our Chief Executive Officer and Chairman of the Board of Directors and our Founder, President, Research & Development and Director will have the ability to substantially influence all matters submitted to stockholders for approval.

As of December 31, 2023, Krish S. Krishnan and Suma M. Krishnan, our Chief Executive Officer and Chairman of the Board and our Founder, President, Research & Development and Director, respectively, in the aggregate, beneficially owned shares representing approximately 14% of our outstanding common 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.

Raising additional capital could cause the price of our common stock to decline and cause dilution to our stockholders, restrict our operations or require us to relinquish rights.

Until such time, if ever, as we can generate substantial and consistent product revenue, we expect to finance our cash needs through a combination of private and public equity offerings, debt financings, collaborations, strategic alliances, and licensing arrangements. We may issue additional common stock or restricted securities as part of such financing activities and any such issuances may have a dilutive effect on our then-existing stockholders. 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 incurrence of indebtedness would result in 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.

If we are unable to raise additional funds through equity or debt financings when needed, and instead raise additional capital through marketing and distribution agreements or other collaborations, strategic alliances, or licensing arrangements with third parties, we may have to relinquish certain valuable rights to our current and future product candidates, technologies, future revenue streams or discovery programs or grant licenses on terms that may not be favorable to us.

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

The price of our common stock 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, a stockholder may not be able to sell

their common stock at or above the price that they paid for it. The market price of our common stock may be influenced by many factors, including:

- our ability to successfully commercialize VYJUVEK;
- our ability to successfully proceed to and conduct clinical trials;
- results of clinical trials of our product candidates or those of our competitors;
- our ability to obtain regulatory approval for our product candidates and our ability to successfully commercialize any of our approved product candidates;
- the success of competitive products or technologies;
- commencement or termination of collaborations;
- regulatory or legal developments in the United States and other countries;
- the recruitment or departure of key personnel;
- the level of expenses related to VYJUVEK or 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 manufacture adequate product supply for VYJUVEK and any other approved product or inability to do so at acceptable prices;
- disputes or other developments relating to proprietary rights, including patent applications, and issued patents;
- our ability to obtain patent protection for our product candidates and 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.

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 market 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 stockholders might otherwise receive a premium for their 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 common stock in the foreseeable future, capital appreciation, if any, will be stockholders' sole source of gain.

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

Issuing additional shares of our common stock could cause the price of our common stock to decline and cause dilution to our stockholders.

To the extent we raise additional capital by issuing additional shares of our common stock, or securities convertible into or exchangeable or exercisable for common stock, our existing stockholders may experience substantial dilution. Additionally, if we issue additional shares of our common stock or instruments convertible into our common stock, the trading price of our common stock could decline. We cannot predict whether we will raise additional capital by issuing shares of our common stock, or securities convertible into or exchangeable or exercisable for common stock, the size of any future issuances, or the effect, if any, that they may have on the market price for our common stock. We also have stock options, restricted common stock, restricted stock units, and performance stock units outstanding, and we expect to issue additional equity awards to directors and employees. The issuance of restricted common stock, common stock upon exercise of outstanding options, common stock upon vesting of restricted stock units, or common stock upon vesting of performance stock units would be dilutive and may cause the market price for our common stock to decline. If we issue preferred stock in the future, the holders of that preferred stock could gain rights superior to our existing stockholders, such as liquidation and other preferences, or the market price of our common stock could be adversely affected.

Item 1B. Unresolved Staff Comments.

None.

Item 1C. Cybersecurity.

Cybersecurity represents a critical component of our overall approach to risk management. Our cybersecurity policies, standards, and practices are integrated into our enterprise risk management approach, and cybersecurity risks are among the core enterprise risks that are subject to oversight by our Board of Directors (the "Board"). We generally approach cybersecurity threats through a cross-functional, multilayered approach, with specific goals of: (i) identifying, preventing and mitigating cybersecurity threats to the Company; (ii) preserving the confidentiality, security and availability of the information that we collect and store; (iii) protecting the Company's intellectual property; (iv) maintaining the confidence of our customers, suppliers and other third parties; and (v) providing appropriate public disclosure of cybersecurity risks and incidents when required.

Cyber Security Risk Management and Strategy

Our cybersecurity program focuses on the following areas:

- Vigilance: Our cybersecurity threat operations function 24/7 with the specific goal of identifying, preventing and mitigating cybersecurity threats and responding to cybersecurity incidents in accordance with our established incident response and recovery plans.
- Systems Safeguards: We deploy systems safeguards that are designed to protect the Company's information systems from cybersecurity threats, including firewalls, intrusion prevention and detection systems, anti-malware functionality and access controls, which are evaluated and improved through ongoing vulnerability assessments and cybersecurity threat intelligence.
- Third-Party Risk Management: We maintain a comprehensive, risk-based approach to identifying and overseeing cybersecurity risks presented by third parties, including vendors, service providers and other external users of the Company's systems, as well as the systems of third parties that could adversely impact our business in the event of a cybersecurity incident affecting those third-party systems.
- Training: We provide periodic mandatory training for personnel regarding cybersecurity threats, which reinforces the Company's information security policies, standards and practices.
- Incident Response and Recovery Planning: We have established and maintain incident response and recovery plans that address the Company's response to a cybersecurity incident and the recovery from a cybersecurity incident, and such plans are tested and evaluated on an regular basis.
- Communication, Coordination and Disclosure: We utilize a cross-functional approach to address the risk from cybersecurity threats, involving management personnel from the Company's technology, operations, legal, financial, and other key business functions, as well as the members of the Board in an ongoing dialogue regarding cybersecurity threats and incidents, while also implementing controls and procedures so that decisions regarding the disclosure and reporting of such incidents can be made by management in a timely manner.

A part of our strategy for managing risks from cybersecurity threats is assessment and testing of the effectiveness of our cybersecurity measures. We engage third parties to perform assessments on our cybersecurity measures, and we adjust our cybersecurity measures as necessary based on the information provided by the assessments.

Governance

The Board oversees the management of risks from cybersecurity threats. The Board receives regular presentations and reports on cybersecurity, which address a wide range of topics and also receives prompt and timely information regarding any cybersecurity incident that is or may become material, as well as ongoing updates regarding such incident until it has been addressed. At least once each year, the Board discusses the Company's approach to cybersecurity risk management with the Company's Vice President of Information Technology, who is the member of management that is principally responsible for overseeing cybersecurity at the Company, in partnership with other business leaders across the Company, including our Chief Executive Officer, Chief Accounting Officer, General Counsel, and Human Resources leader. Our Vice President of Information Technology has served in various roles in information technology and information security for over 28 years, including serving as Chief Information Security Officer of several public companies. He holds undergraduate and graduate degrees in electrical engineering and computer science and has attained numerous professional certifications in Information Security throughout his career.

Cybersecurity threats, including as a result of any previous cybersecurity incidents, have not materially affected or are reasonably likely to affect the Company, including its business strategy, results of operations, or financial condition.

Item 2. Properties.

As of December 31, 2023, we leased approximately 54,000 square feet of combined laboratory and office space in Pittsburgh, Pennsylvania that we use for our research, development and manufacturing efforts. The lease for approximately 7,000 square feet of office space expires in September 2024, and the lease covering the remaining combined laboratory and office space expires in October 2031.

As of December 31, 2023, we also leased additional U.S. office space in Boston, Massachusetts and European office space in Zug, Switzerland, and Amsterdam, Netherlands.

In December 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. In January 2021, we entered into a Purchase and Sale Agreement ("PSA") with Northfield I, LLC, an Ohio limited liability company to acquire ASTRA, and the related purchase closed in March 2021. In June 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 constructed and managed the construction of ASTRA. The facility was completed and validated in 2023. Refer to Note 8 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 7 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 trades on the NASDAQ Global Select Market under the symbol KRYS.

Holders of Record

As of February 19, 2024, there were two stockholders of record of our common stock. The actual number of stockholders is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

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 three months ended December 31, 2023.

Sales of Unregistered Securities

There have been no sales of unregistered securities by us during the past three years except as previously disclosed on prior Quarterly Reports on Form 10-Q and Current Reports on Form 8-K.

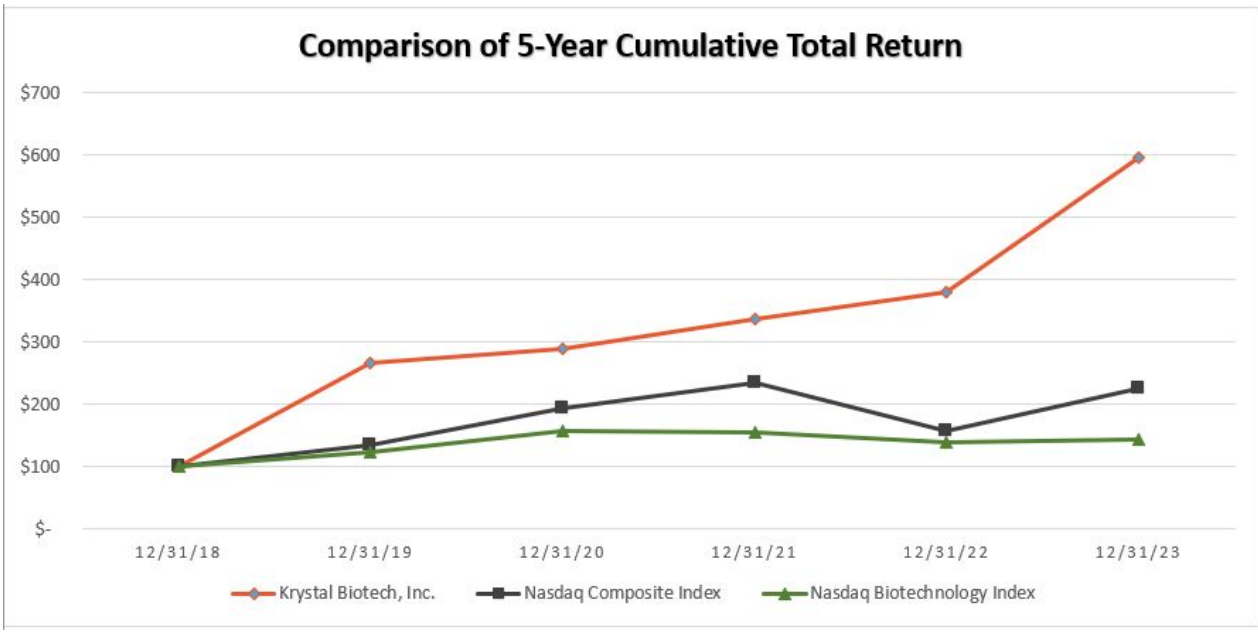
Stock Performance Graph

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 December 31, 2018 and continuing through December 31, 2023. The graph assumes our closing sale price on December 31, 2018 of $20.78

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 U.S. Securities and Exchange Commission, or 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 2023, 2022 and 2021 items and year-to-year comparisons between 2023 and 2022, and 2022 and 2021 of the Company's results of operations and cash flows.

Overview

We are a fully integrated, commercial-stage biotechnology company focused on the discovery, development, and commercialization of genetic medicines to treat diseases with high unmet medical needs. Using our patented gene therapy technology 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 healthcare professional's office or 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 and serious diseases. Our innovative technology platform is supported by an in-house, FDA-inspected, commercial scale Current Good Manufacturing Practice ("CGMP") manufacturing facility and a second, completed and qualified, commercial scale CGMP facility to support future expansion. Refer to *Part I, Item 1 - Business* for more information about our United States Food and Drug Administration ("FDA") approved product, VYJUVEK®, clinical development pipeline and research programs, and the status of our product candidates.

Highlights and Recent Developments

VYJUVEK (beremagene geperpavec-svdt or B-VEC; referred to as B-VEC outside the U.S.)

In May 2023, the FDA approved B-VEC for the treatment of patients, six months of age or older, suffering from dystrophic epidermolysis bullosa ("DEB"). FDA approval was based, in part, on our pivotal Phase 3 clinical trial, a randomized, double-blind, intra-patient placebo-controlled multi-center study, that demonstrated that B-VEC was both well-tolerated and significantly improved wound closure in DEB patients. Clinical data from our registrational Phase 3 B-VEC trial were published in the *New England Journal of Medicine* in December 2022. B-VEC is marketed as VYJUVEK in the United States and is the first and only corrective medicine approved by the FDA for the treatment of DEB, both recessive and dominant. VYJUVEK can be administered by a healthcare professional in either a healthcare professional or home setting.

We launched VYJUVEK in the United States in the second quarter of 2023. Net product revenue for VYJUVEK for the year ended December 31, 2023 was $50.7 million.

We have made steady progress securing access and reimbursement for VYJUVEK since launch and have secured positive policies or coverage decisions from plans covering over 93% of commercial and Medicaid lives in the United States. In January 2024, we announced that the United States Centers for Medicare & Medicaid Services, or CMS, had assigned a permanent and product-specific J-code (J3401) for VYJUVEK, effective on January 1, 2024.

We seek to make the patient experience of starting and continuing on VYJUVEK treatment as seamless as possible. Since launch, the infrastructure has been in place for patients to be treated in their home by a healthcare provider, or HCP, reducing the need for regular visits to a clinic or hospital. Krystal Connect™, our U.S. in-house patient services call center, has been active since FDA approval and assists patients, care givers and HCPs interested in accessing VYJUVEK. We also continue to offer no-cost genetic testing through our DecodeDEB program. Through the end of 2023, patient compliance with once weekly VYJUVEK treatment has been 96%.

We continue to pursue development and commercialization activities to maximize access to B-VEC in the United States and globally. Recent highlights subsequent to FDA approval are summarized below:

- In December 2023, B-VEC was granted orphan drug designation, or ODD, status for the treatment of DEB by the Japan Ministry of Health, Labour and Welfare, a designation which confers specific benefits for orphan drug development including priority review of applications, extended registration validity, and reduced development costs. We anticipate filing our Japan New Drug Application with Japan's Pharmaceuticals and Medical Devices Agency ("PMDA") in the second half of 2024 enabling a potential authorization in 2025
- In October 2023, we submitted a Marketing Authorization Application ("MAA") to the European Medicines Agency ("EMA") for B-VEC for the treatment of DEB in patients from birth. In November 2023, we were notified that the MAA had been validated and was now under Committee for Medicinal Products for Human Use review. We expect an EMA decision on our MAA in the second half of 2024.
- In July 2023, the PMDA in Japan officially accepted the open label extension ("OLE") study of B-VEC. Following that acceptance, we initiated the Japan OLE study and completed study enrollment. A total of 5 Japanese DEB patients have been enrolled. Details of the study can be found at jrct.niph.go.jp under JRCT ID jRCT2053230075. Nothing included on this website shall be deemed incorporated by reference into this Annual Report on Form 10-K.
- In April 2023, we announced clinical data on the compassionate use of B-VEC, administered as an eye drop, to treat a patient suffering from ocular complications of DEB. Data were first presented at the Association for Research in Vision and Ophthalmology 2023 Annual Meeting in April 2023, and subsequently published in the *New England Journal of Medicine* in February 2024. Regular application of B-VEC to the eye was well tolerated and associated with full corneal healing at 3 months and visual acuity improvement from hand motion to 20/25 by 8 months. Based on this early clinical evidence of safety and potential benefit under compassionate use, we started discussions with the FDA in the first quarter of 2024 to align on a potential clinical development path for ophthalmic B-VEC.
- In January 2024, the United States Patent and Trademark Office, or USPTO, issued U.S. Patent No. 11,865,148, covering methods of delivering human transgenes to the eye using replication-incompetent HSV-1. This patent covers the administration of B-VEC to the eye, as well as novel applications of our HSV-1 based platform to deliver genetic material to the eye via multiple routes of administration for the potential treatment of genetic eye diseases. The patent expires in 2037. Refer to Part I, Item 1 - Business for more information about our intellectual property and issued patents.
- In February 2024, the FDA agreed with our proposed single arm, open label study in approximately 10 patients to enable approval of B-VEC eyedrops to treat ocular complications which are thought to affect over 25% of DEB patients. We plan to initiate this study in the second half of 2024.

Pipeline

- KB407 is an inhaled (nebulized) formulation of our novel vector designed to deliver two copies of the full-length cystic fibrosis transmembrane conductance regulator, or CFTR, transgene for the treatment of cystic fibrosis ("CF"), a serious rare lung disease caused by missing or mutated CFTR protein. In August 2022, we announced that the FDA had accepted our investigational new drug ("IND") application to evaluate KB407 in a clinical trial to treat patients with cystic fibrosis. In July 2023, we dosed the first patient in our Phase 1 CORAL-1 study evaluating KB407, delivered via a nebulizer, for the treatment of patients with CF. The CORAL-1 study is a multi-center, dose-escalation trial of KB407 in patients with CF, regardless of their underlying genotype. In the fourth quarter of 2023, we completed the first cohort of the CORAL-1 study with no severe or serious adverse events and, in January 2024, we initiated dosing in the second of three cohorts. Details of the Phase 1 study can be found at www.clinicaltrials.gov under NCT identifier NCT05504837. Nothing included on this website shall be deemed incorporated by reference into this Annual Report on Form 10-K. In January 2023, the European Commission granted Orphan Designation for KB407 for the treatment of CF.
- 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, or AATD. In September 2023, the FDA accepted our IND application to evaluate KB408, delivered via a nebulizer, in a clinical trial to treat patients with AATD. In February 2024, the Company dosed the first patient in the KB408 Phase 1 SERPENTINE-1 study for the treatment of Alpha-1 Antitrypsin Deficiency. SERPENTINE-1 is a Phase 1 open-label, single dose escalation study in adult patients with AATD with a PI*ZZ genotype. Three planned dose levels of KB408 will be evaluated in up to 12 patients to evaluate the safety, tolerability, and proof-of-mechanism of KB408. Cohorts 1 and 2 will focus predominantly on safety with dose escalation and pharmacodynamic activity in the lung will be assessed at the highest dose by bronchoscopy in Cohort 3. We are working closely with the Alpha-1 Foundation and their Therapeutic Development Network on SERPENTINE-1 study and intend to announce interim data from the study in the second half of 2024. The FDA granted ODD to KB408 for the treatment of AATD in September 2023. We presented preclinical pharmacology data for KB408 at the European Society of Gene & Cell Therapy Congress that was held in October 2023.

- KB707 is a redosable, immunotherapy designed to deliver genes encoding both human IL-2 and IL-12 to the tumor microenvironment and promote systemic immune-mediated tumor clearance. Two formulations of KB707 are in development, a solution formulation for transcutaneous injection and an inhaled (nebulized) formulation for lung delivery. In July 2023, the FDA granted intratumoral KB707 Fast Track Designation for the treatment of anti-PD-1 relapsed/refractory locally advanced or metastatic melanoma and accepted our IND application to evaluate intratumoral KB707 in a clinical trial to treat patients with locally advanced or metastatic solid tumors. The study, OPAL-1, is an open-label, multi-center, monotherapy, dose escalation and expansion Phase 1 study, enrolling patients with locally advanced or metastatic solid tumors, who relapsed or are refractory to standard of care, with at least one measurable and injectable tumor accessible by transcutaneous route. We dosed the first patient in the OPAL-1 study in October 2023 and enrollment is ongoing. Details of the Phase 1 study can be found at www.clinicaltrials.gov under NCT identifier NCT05970497. Nothing included on this website shall be deemed incorporated by reference into this Annual Report on Form 10-K. We presented preclinical efficacy data generated in syngeneic mouse models using murine equivalents to KB707 at the Society for Immunotherapy in Cancer Annual Meeting that was held in November 2023.
- In January 2024, the FDA accepted an amendment to our IND application to evaluate inhaled KB707 in a clinical trial to treat patients with locally advanced or metastatic solid tumors of the lung. We plan on initiating this open-label, multi-center, monotherapy, dose escalation and expansion Phase 1 study, KYANITE-1, in the first half of 2024. Details of the Phase 1 study can be found at www.clinicaltrials.gov under NCT identifier NCT06228326. Nothing included on this website shall be deemed incorporated by reference into this Annual Report on Form 10-K. Inhaled KB707 also received Fast Track Designation from the FDA in February 2024, for the treatment of patients with solid tumors with pulmonary metastases that are relapsed or refractory to standard of care therapy.
- In October 2023, the USPTO issued U.S. Patent No. 11,779,660, covering compositions of matter containing engineered HSV constructs encoding IL-2 and IL-12, including KB707. The patent expires in 2042. Refer to Part I, Item 1 - Business for more information about our intellectual property and issued patents.
- KB105 is a topical gel containing our novel vector designed to deliver two copies of the *TGM1* transgene encoding the human enzyme transglutaminase-1 ("TGM1"*)* for the treatment of TGM1-deficient autosomal recessive congenital ichthyosis, 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 complete data from the Phase 1 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. We plan to resume enrollment in the Phase 2 portion of this trial later in 2024. In August 2023, the USPTO issued U.S. Patent No. 11,717,547, the second composition of matter and method of use patent related to KB105. The patent expires in 2039. Refer to Part I, Item 1 - Business for more information about our intellectual property and issued patents.
- KB104 is a topical gel formulation of our novel vector designed to deliver two copies of the *SPINK5* transgene encoding serine protease inhibitor Kazal-type 5 ("SPINK5") for the treatment of Netherton Syndrome, a debilitating autosomal recessive skin disorder caused by missing or mutated SPINK5 protein. The FDA has granted KB104 Rare Pediatric Designation for the treatment of Netherton Syndrome. We plan to file an IND application and initiate a clinical trial of KB104 to treat patients with Netherton Syndrome following initiation of the KB105 Phase 2 study. In May 2023, the USPTO issued U.S. Patent No. 11,642,384, covering compositions of matter containing replication-defective HSV constructs encoding *SPINK5*, including KB104. The patent expires in 2039. Refer to Part I, Item 1 – Business for more information about our intellectual property and issued patents.
- 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. In April 2023, Jeune Aesthetics, Inc. ("Jeune Aesthetics"), our wholly-owned subsidiary, initiated and treated the first subject in the PEARL-1 Cohort 3 clinical study. The PEARL-1 Cohort 3 study is an open label study to evaluate different doses of KB301 for the improvement of lateral canthal lines, or LCL, at rest in up to 20 subjects. In January 2024, Jeune Aesthetics initiated the PEARL-1 Cohort 4 clinical study, an open label study to evaluate KB301 for the improvement of dynamic wrinkles of the décolleté in up to 20 subjects. These studies are running simultaneously, and Jeune Aesthetics expects to announce results for both cohorts in the first half of 2024. Following completion of this study, Jeune Aesthetics plans to initiate a Phase 2 study of KB301. 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 Aesthetics has several other aesthetic medicine product candidates in various stages of preclinical development.

2023 Business Highlights

- In August 2023, we sold our Rare Pediatric Disease Priority Review Voucher, or PRV, for $100.0 million. The PRV was awarded in connection with the FDA's accelerated approval of VYJUVEK for the treatment of DEB for patients 6 months of age and older.
- In August 2023, we began research and development operations in our second commercial scale CGMP biologics manufacturing facility, ASTRA, a 155,000 sq. ft. state-of-the-art CGMP facility with comprehensive end-to-end capabilities.
- In May 2023, shortly after we received FDA approval of VYJUVEK, we issued and sold 1,729,729 shares of common stock at a price of $92.50 per share in a private placement (the "PIPE") to certain accredited investors. Net proceeds from the PIPE were approximately $160.0 million. We filed a registration statement with the SEC in July 2023 registering the resale of the shares of common stock issued in the PIPE.
- On March 6, 2023, we announced the appointment of Catherine Mazzacco to our Board of Directors.

Financial Overview

Product Revenue

After FDA approval of VYJUVEK in May 2023, we began commercial marketing and sales of the product throughout the United States and began recognizing revenue in 3Q 2023. Our future revenue will fluctuate from quarter to quarter for many reasons, including the uncertain timing and amount of any such sales.

We have contracted to sell VYJUVEK to a limited number of specialty pharmacy providers ("SPs") that mix the medication and administer it to patients in the patient's home by a healthcare professional and through a specialty distributor ("SD") to hospitals and outpatient clinics where patients are administered the medication at a healthcare professional's office. The transaction price that we recognize as revenue for VYJUVEK sales includes an estimate of variable consideration, which includes discounts, returns, copay assistance, and rebates that are offered within our contracts. Refer to Note 2 of our consolidated financial statements for additional information.

Cost of Goods Sold

We recognize cost of goods sold for direct and indirect costs related to the manufacturing of VYJUVEK. These costs consist of manufacturing costs, personnel costs, including stock-based compensation, facility costs, and other indirect overhead costs. Cost of goods sold may also include period costs related to certain manufacturing services and inventory adjustment charges.

Prior to receiving FDA approval in May 2023, costs associated with the manufacturing of VYJUVEK were expensed as research and development expense. As such, a portion of the cost of inventory sold during 2023 was expensed prior to FDA approval.

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 ("CMOs"), 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 Japan OLE study for B-VEC, continue our Phase 1 trials for KB407, KB408, and intratumoral KB707, initiate our Phase 1 trials for inhaled KB707, resume dosing with KB105 Phase 1/2 clinical trial, complete Phase 1 Cohorts 3 and 4 and initiate a Phase 2 trial for KB301, begin our open label study with ophthalmic B-VEC, 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.

Selling, General and Administrative Expenses

Selling, general and administrative expenses consist principally of salaries and other related costs, including stock-based compensation for personnel in our executive, commercial, business development and other administrative functions. Selling, general and administrative expenses also include professional fees associated with corporate and intellectual property-related legal expenses, consulting and accounting services, facility-related costs and expenses associated with obtaining and maintaining patents. Other selling, general, and administrative costs include travel expenses, patient access program fees, management service fees, and other selling expenses which include transportation, shipping and handling fees.

We anticipate that our selling, general and administrative expenses will increase in the future to support the continued research and development of our product candidates. 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 continue to increase our salary and personnel costs and other expenses to support B-VEC commercialization globally.

ASTRA Capital Expenditures

In March 2021, we closed on the purchase of the building that was constructed to house our second CGMP facility, ASTRA. We received the permanent occupancy permit for ASTRA in March 2023, which permitted utilization of certain parts of the building, and subsequently placed a portion of ASTRA into service. Qualification of the facility was completed later in 2023, and we began research and development operations. We incurred significant capital expenditures related to the construction of ASTRA in 2023 and expect to continue to incur capital expenditures related to ASTRA throughout the operational life of the facility.

Gains from Sale of Priority Review Voucher

Gain from sale of priority review voucher relates to proceeds from sale of the rare pediatric PRV we received in connection with the FDA's approval of VYJUVEK.

Interest and Other Income

Interest and other 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, variable consideration associated with revenue recognition, stock-based compensation expense, accrued expenses, the fair value of financial instruments, and the valuation allowance included in the deferred income tax calculation 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.

Revenue Recognition

After FDA approval of VYJUVEK in May 2023, we began commercial marketing and made our first product sales in 3Q 2023. *ASC 606 Revenue from Contracts with Customers* requires us to make estimates of variable consideration, included in our contracts, to be included in the transaction price.

Product revenue, net is recorded at the net sales price, or transaction price, upon delivery and transfer of control to the customer, and includes an estimate of variable consideration, which results from discounts, rebates, copay assistance, and returns that are offered within contracts between the Company and its customers.

- *Prompt Pay Discounts:* As an incentive for prompt payment, we offer a cash discount to our counterparty. We estimate accrued prompt pay discounts using the most likely amount method. We expect that all eligible counterparties will comply with the contractual terms to earn the discount. We record the discount as an allowance against accounts receivable, net and a reduction of revenue.
- *Government Rebates:* We participate in certain government rebate programs including Medicaid, Medicare and Tricare. We estimate accrued government rebates using the expected value method. We accrue estimated rebates based on estimated percentages of VYJUVEK that will be prescribed to qualified patients, estimated rebate percentages and estimated levels of inventory in the distribution channel that will be prescribed to qualified patients and record the rebates as a reduction of revenue. Accrued government rebates are included in other accrued liabilities on the consolidated balance sheets. For Medicare, the Company also estimates the accrued liability based on the number of patients in the prescription drug coverage gap under the Medicare Part D program.
- *Commercial Rebates:* We participate in certain commercial rebate programs. Under these rebate programs, we pay a rebate to the commercial entity or third-party administrator of the program. Accrued commercial rebates are estimated using the expected value method. We accrue estimated rebates based on contract prices, estimated percentages of VYJUVEK that will be prescribed to qualified patients and estimated levels of inventory in the distribution channel and record the rebate as a reduction of revenue. Accrued commercial rebates are included in other accrued liabilities on the consolidated balance sheets.
- *Copay Assistance:* The Company provides copay assistance to qualified patients with commercial insurance in states that allow copay assistance, helping them meet copay obligations to their insurance provider. The Company reimburses pharmacies for this discount through third-party vendors. The Company estimates copay assistance costs using the expected value method. The estimate is based on contract prices, estimated percentages of VYJUVEK that will be prescribed to qualified patients, average assistance paid based on reporting from third-party vendors and estimated levels of inventory in the distribution channel. Copay assistance costs are recorded as reductions to revenue and are accrued in other accrued liabilities on the consolidated balance sheets.
- *Product Returns:* We offer SPs and SDs limited return rights relating only to product damage or defects identified upon receipt, and therefore we expect minimal returns. Returns are estimated taking into consideration several factors including these limited product return rights, historical return activity, and other relevant factors.. There were no returns for the year ended December 31, 2023.

Variable consideration is estimated and reduces the transaction price to reflect our best estimate of the amount of consideration to which we are entitled based on the terms of the contracts and are recorded in the same period the related product revenue is recognized. The amount of variable consideration that is included in the transaction price may be constrained and is included in the net sales price only to the extent that it is considered probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. Actual amounts of consideration ultimately received may differ from our estimates. If actual results in the future vary from our estimates, we will adjust these estimates in the period these variances become known.

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 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 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 record our expenses related to clinical manufacturing based 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 actual results in the future vary from our estimates, we will adjust these estimates in the period these variances become known.

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 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 our own sufficient historical volatility data was obtained, we eliminated the use of a representative peer group and as of Q4 2021 we use only our own historical volatility data in its estimate of expected volatility given that there is now sufficient amount of historical information regarding the volatility of our 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 Payments* 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.

Results of Operations

Years Ended December 31, 2023, 2022 and 2021

	Years Ended December 31,			Change	
(in thousands)	**2023**	**2022**	**2021**	**2023 vs. 2022**	**2022 vs. 2021**
Product revenue, net	$ 50,699	$ —	$ —	$ 50,699	$ —
Expenses					
Cost of goods sold	3,094	—	—	3,094	—
Research and development	46,431	42,461	27,884	3,970	14,577
Selling, general and administrative	98,401	77,735	40,391	20,666	37,344
Litigation settlement	12,500	25,000	—	(12,500)	25,000
Total operating expenses	160,426	145,196	68,275	15,230	76,921
Loss from operations	(109,727)	(145,196)	(68,275)	35,469	(76,921)
Other income (expense)					
Gain from sale of priority review voucher	100,000	—	—	100,000	—
Interest and other income, net	22,624	5,221	197	17,403	5,024
Interest expense	—	—	(1,492)	—	1,492
Income (loss) before income taxes	12,897	(139,975)	(69,570)	152,872	(70,405)
Income tax expense	(1,965)	—	—	(1,965)	—
Net income (loss)	$ 10,932	$ (139,975)	$ (69,570)	$ 150,907	$ (70,405)

Product Revenue, net

Product revenue, net was $50.7 million for the year ended December 31, 2023 as compared to zero for the years ended December 31, 2022 and 2021 due to initial sales of VYJUVEK after FDA approval was obtained on May 19, 2023. To date, all of our product revenue has been generated in the United States.

Cost of Goods Sold

Cost of goods sold was $3.1 million for the year ended December 31, 2023 as compared to zero for the years ended December 31, 2022 and 2021 due to initial sales of VYJUVEK after FDA approval was obtained on May 19, 2023. Prior to

receiving FDA approval for VYJUVEK in May 2023, costs associated with the manufacturing of VYJUVEK were expensed as research and development expense. As such, a portion of the cost of inventory sold during 2023 was expensed prior to FDA approval.

Research and Development Expenses

Research and development expenses increased approximately $4.0 million for the year ended December 31, 2023 compared to the year ended December 31, 2022. Higher research and development expenses were due to increases in payroll related expenses of $5.8 million which was primarily driven by an increase in personnel to support overall growth and includes a $2.2 million increase in stock-based compensation, an increase in depreciation of $2.2 million, and an increase in other research and development expenses of approximately $428 thousand, primarily due to increases in facilities expenses. These increases were partially offset by decreases of $2.0 million in preclinical, clinical and pre-commercial manufacturing due to the costs related to the manufacturing of VYJUVEK following FDA approval being recorded as inventory and due to fewer receipts of raw materials and lab supplies period over period that were purchased for planned manufacturing runs of our products, a decrease from overhead allocations to inventory of $1.3 million, and a decrease from outsourced research and development costs of $1.2 million.

Research and development expenses increased $14.6 million for the year ended December 31, 2022 compared to the year ended December 31, 2021. Higher research and development expenses were due to increases in payroll related expenses of $8.9 million which was primarily driven by an increase in personnel to support overall growth and includes a $4.5 million increase in stock-based compensation, an increase in outsourced research and development activities of $2.3 million, an increase in preclinical, clinical and pre-commercial manufacturing activities of $1.0 million, and an increase in other research and development expenses of $2.4 million, primarily due to increases in depreciation and licensing fees.

The following table summarizes our research and development expenses by product candidate or program, and for unallocated expenses, by type, for the years ended December 31, 2023, 2022 and 2021:

(in thousands)	Years Ended December 31,			Change	
	2023	2022	2021	2023 vs. 2022	2022 vs. 2021
KB103[1]	$ 9,039	$ 8,096	$ 6,204	$ 943	$ 1,892
KB105	282	276	74	6	202
KB407	1,668	1,895	987	(227)	908
KB301	460	1,312	1,217	(852)	95
KB707	3,828	400	—	3,428	400
Other dermatology programs	2	500	789	(498)	(289)
Other respiratory programs	1,043	972	280	71	692
Other aesthetics programs	91	114	16	(23)	98
Other research programs	638	876	799	(238)	77
Other development programs	939	645	708	294	(63)
Stock-based compensation	10,051	7,897	3,435	2,154	4,462
Other unallocated manufacturing expenses[2]	12,550	15,036	9,207	(2,486)	5,829
Other unallocated expenses[3]	5,840	4,442	4,168	1,398	274
Research and development expense	$ 46,431	$ 42,461	$ 27,884	$ 3,970	$ 14,577

(1) For the year ended December 31, 2023, KB103 expenses consist of pre-approval activity costs, post marketing study costs and overseas preclinical and clinical trial costs, licensing and regulatory costs.

(2) Unallocated manufacturing expenses consist of shared pre-commercial manufacturing costs, primarily relating to raw materials, contract manufacturing, contract testing, process development, quality control and quality assurance activities and other manufacturing costs which support the development of multiple product candidates in our preclinical and clinical development programs.

(3) Other unallocated expenses include rental, storage, depreciation, and other facility related costs that we do not allocate to our individual product candidates.

As noted above, research and development expenses increased approximately $4.0 million in the year ended December 31, 2023 compared to the year ended December 31, 2022. Expenses for KB103 increased $943 thousand due to increased payroll related expenses to support VYJUVEK's pre-approval activities, clinical trial costs, license and regulatory costs, costs associated with overseas clinical trials and regulatory agency filings, and increased allocated research and

development expenses. KB707 spending increased $3.4 million due to increased payroll related costs and increased contract research costs in preparation for the Phase 1 clinical trial. Stock-based compensation increased $2.2 million due to an increase in internal resources to support overall research and development growth. Additionally, other unallocated expenses increased by $1.4 million primarily due to increases in depreciation expense offset by a decrease from rent expense allocated to inventory. These increases were partially offset by a decrease in other unallocated manufacturing expenses of $2.5 million due to the costs related to the manufacturing of VYJUVEK following FDA approval being recorded as inventory and due to fewer receipts of raw materials period over period that were purchased for planned manufacturing runs of our products and product candidates, a decrease in KB301 expenses of $852 thousand due to the timing of clinical research costs, and a decrease in spending on other dermatology programs of $498 thousand due to a reduction in contract manufacturing expenses.

Research and development expenses increased $14.6 million in the year ended December 31, 2022 compared to the year ended December 31, 2021. Expenses for KB103 increased $1.9 million primarily due to increased payroll expenses and clinical trial costs related to OLE studies. Expenses for KB407 increased $908 thousand due to increased payroll expenses and pre-clinical costs. Other respiratory expenses increased $692 thousand due to increased contract research costs. Expenses for KB707 increased $400 thousand primarily related to payroll supporting initial research activities. Stock-based compensation increased due to an increase of $4.5 million in internal resources to support overall research and development growth. Unallocated manufacturing expenses increased by $5.8 million primarily due to receipts of raw materials purchased for planned manufacturing runs our products.

Selling, General and Administrative Expenses

Selling, general and administrative expenses increased $20.7 million for the year ended December 31, 2023 compared to the year ended December 31, 2022. Higher selling, general and administrative spending was due largely to increased payroll related expenses of approximately $15.1 million which is primarily driven by an increase in personnel to support overall growth and includes an approximate $4.5 million increase in stock-based compensation, increased selling expenses related to the launch of VYJUVEK of $1.7 million, increased information technology infrastructure costs of $2.1 million, increased software-related costs of $1.3 million, increased travel costs of $1.1 million, an increase in sponsorships of $425 thousand, an increase in net legal costs of $381 thousand, which consists of a decrease in litigation proceeds of $570 thousand, offset by a decrease in legal and professional fees of $189 thousand and an increase of other selling, general and administrative expense of $676 thousand, primarily due to increases in depreciation and rent expense. These increases were partially offset by a decrease of $1.2 million of commercial preparedness expenses, a decrease in medical affairs costs of $466 thousand, and a decrease in business development costs of $428 thousand.

General and administrative expenses increased $37.3 million for the year ended December 31, 2022 compared to the year ended December 31, 2021. Higher general and administrative spending was due largely to increased payroll related expenses of approximately $28.8 million which is primarily driven by an increase in personnel to support overall growth and includes an approximate $13.4 million increase in stock-based compensation, increased commercial preparedness expenses of approximately $5.7 million, increased medical affairs costs of $581 thousand, increased travel costs of $536 thousand, and an increase in other administrative expenses of $2.9 million, primarily due to increases in utilities, information technology costs, and conference fees. These increases were partially offset by a decrease in net legal costs of $1.2 million, which consists of a decrease in legal and professional fees of $2.8 million offset by a decrease in litigation proceeds of approximately $1.6 million, due primarily to the settlement of the PeriphaGen litigation.

Litigation Settlement

Litigation settlement for the years ended December 31, 2023 and 2022 was $12.5 million and $25.0 million, respectively, and consisted of amounts related to the settlement of litigation with PeriphaGen. See "Legal Proceedings" in Note 7 of the notes to consolidated financial statements included in this Form 10-K for more information.

Gain from sale of Priority Review Voucher

Gain from sale of priority review voucher for the year ended December 31, 2023 was $100.0 million related to the sale of our rare pediatric PRV, which was awarded to the Company in connection with the FDA’s approval of VYJUVEK.

Other Income (Expense)

Interest and other income for the years ended December 31, 2023, 2022, and 2021 was $22.6 million, $5.2 million and $197 thousand, respectively, and consisted of realized gains from maturities of our investments, interest income earned from our cash, cash equivalents and investments.

Interest expense for the years ended December 31, 2023, 2022 and 2021 was zero, zero, and $1.5 million, respectively. The 2021 interest expense related to accretion of the financial obligation for the build to suit lease liability during the year ended December 31, 2021.

Income Tax Expense

Income tax expense for the years ended December 31, 2023, 2022, and 2021 was $2.0 million, zero, and zero, respectively. In 2023, income tax expense related to U.S. state and federal taxes related to the PRV sale and our initial commercial activities in those jurisdictions. See Note 11 of the notes to consolidated financial statements included in this Form 10-K for more information.

Liquidity and Capital Resources

Overview

On December 31, 2023, our cash, cash equivalents and short-term investments balance was approximately $532.2 million. Since operations began, we have incurred operating losses. Net income was $10.9 million for the year ended December 31, 2023, and our net losses were $140.0 million and $69.6 million for the years ended December 31, 2022, and 2021, respectively. At December 31, 2023, we had an accumulated deficit of $269.8 million. With the net proceeds raised from our previous public and private offerings and sale of the PRV, we believe that our 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.

Our transition to operating profitability is dependent upon the continued successful commercialization of VYJUVEK and the successful development, approval and commercialization of our product candidates and the achievement of a level of revenue adequate to support our cost structure. Furthermore, we expect to incur increasing costs associated with satisfying regulatory and quality standards, maintaining product and clinical trials, and furthering our efforts around our current and future product candidates. We intend to fund future operations through on hand cash and cash equivalents, revenue generated from the sale of VYJUVEK, the sale of equity, debt financings, and we may also seek additional capital through arrangements with strategic partners or other sources.

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 KB105, KB407, KB301, KB707 or our planned clinical and preclinical studies for our other product candidates, or our operations. Further, we expect future revenue to fluctuate between periods for many reasons, including the uncertain timing and amount of any product sales. 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 some of our clinical development activities. As we seek to obtain regulatory approval for our product candidates, we expect to continue to incur significant manufacturing and commercialization expenses as we prepare for product sales, marketing, commercial manufacturing, packaging, labeling and distribution. Furthermore, pursuant to our settlement agreement with PeriphaGen, we will be required to pay three $12.5 million contingent milestone payments upon reaching $100.0 million in total cumulative sales, $200.0 million in total cumulative sales and $300.0 million in total cumulative sales. Our funds may not be sufficient to enable us to conduct pivotal clinical trials for, seek marketing approval for or commercial launch of KB104, KB105, KB407, KB408, KB301, KB707 or any other product candidate. Accordingly, to obtain marketing approval for and to commercialize these 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, regulatory expenses, third-party clinical trial research and development services, laboratory and related supplies, selling expenses, costs to manufacture our commercial product, legal expenses, payments of settlement amounts to PeriphaGen 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 costs needed to commercialize and market our lead product, VYJUVEK;
- the progress, timing and costs of clinical trials of our current product candidates;

- the progress, timing and costs of manufacturing of VYJUVEK and revenue received from commercial sale of VYJUVEK;
- the continued development and the filing of an IND application for current and future product candidates;
- the initiation, scope, progress, timing, costs and results of drug discovery, laboratory testing, manufacturing, preclinical studies and clinical trials for any 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 extent to which the costs of VYJUVEK and 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;
- 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 may 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 our commitments for future minimum rent made under non-cancelable leases for our corporate headquarters in Pittsburgh, Pennsylvania, office location in Boston, Massachusetts, office locations in Switzerland and Netherlands, 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, 2023 are $16.2 million, of which $1.5 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 8 to our consolidated financial statements included in this Annual Report on Form 10-K.

Clinical Supply and Product Manufacturing Agreements

We enter into various agreements in the normal course of business with CROs, CMOs and other third parties for preclinical research studies, clinical trials and testing and manufacturing services. We are obligated to make milestone payments under certain of these agreements. The estimated remaining commitment as of December 31, 2023 under these agreements is approximately $1.7 million, all of which is expected to be due in the next twelve months.

ASTRA Contractual Obligations

We have contracted with various third parties to complete and qualify our second CGMP facility, ASTRA. 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, 2023 is $8.2 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,		
	2023	2022	2021
Net cash used in operating activities	$ (88,804)	$ (100,569)	$ (47,938)
Net cash provided by (used in) investing activities	82,638	(114,083)	(226,770)
Net cash provided by financing activities	202,750	35,347	347,685
Effect of exchange rate changes on cash and cash equivalents	(156)	(41)	—
Net change in cash	$ 196,428	$ (179,346)	$ 72,977

Operating Activities

Net cash used in operating activities for the year December 31, 2023 was $88.8 million and consisted primarily of net income of $10.9 million adjusted for non-cash items of $61.9 million primarily comprised of a gain on sale of the rare pediatric PRV of $100.0 million, stock-based compensation expense of $39.9 million, realized gain on investments of $5.1 million, depreciation and amortization of $3.7 million, other non-cash items of $451 thousand, and cash used by increases in net working capital of approximately $37.9 million.

Net cash used in operating activities for the year December 31, 2022 was $100.6 million and consisted primarily of a net loss of $140.0 million adjusted for non-cash items of $36.6 million primarily made up of stock-based compensation expense of $33.2 million and depreciation and amortization of $4.1 million, and cash provided by decreases in net working capital of approximately $2.8 million.

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 $19.1 million primarily made up of stock-based compensation expense of $15.3 million, depreciation and amortization of $2.8 million and build to suit interest expense of $1.5 million, and cash provided by decreases in net working capital of approximately $2.5 million.

Investing Activities

Net cash provided by investing activities for the year ended December 31, 2023 was approximately $82.6 million and consisted primarily of proceeds of $100.0 million from the sale of the rare pediatric PRV, proceeds from maturities of investments of $503.2 million, offset by purchases of available-for-sale investment securities of $508.8 million, and expenditures of $11.8 million on the build-out of our ASTRA facility, leasehold improvement of new office space, and purchases of computer and laboratory equipment.

Net cash used in investing activities for the year ended December 31, 2022 was approximately $114.1 million and consisted primarily of purchases of $318.8 million of available-for-sale investment securities, and expenditures of $53.0 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 $257.7 million from maturities of investments.

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.

Financing Activities

Net cash provided by financing activities for the year ended December 31, 2023 was $202.8 million and consisted primarily of proceeds of $160.0 million received from a private placement equity offering and proceeds of $43.5 million primarily from exercises of stock options, partially offset by $749 thousand used for the employee tax withholding payment for settlement of vested restricted stock awards.

Net cash provided by financing activities for the year ended December 31, 2022 was $35.3 million and was primarily from proceeds from public offerings of 434,782 shares of our common stock at a weighted average price of $69.00 per share through our at-the-market equity offering program ("ATM") Program. Our net proceeds from the offerings were $29.1 million after deducting underwriting discounts and commissions of approximately $900 thousand. Additionally, we received $7.0 million of proceeds related to the exercise and settlement of employee stock options and restricted stock awards, offset by $649 thousand of taxes paid for the settlement of restricted stock awards.

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 our common stock, including 288,461 shares purchased by the underwriters, at $65.00 per share and 2,866,667 shares of our common stock, including 200,000 shares purchased by the underwriters, at $75.00 per share. Our net proceeds from the offerings were $336.8 million after deducting underwriting discounts and commissions of approximately $21.5 million, and other offering expenses payable of $425 thousand.

Recent Accounting Pronouncements

See note 2 to our consolidated financial statements.

Item 7A. Qualitative and Quantitative Disclosures About Market Risk

We had cash, cash equivalents and short-term investments of approximately $532.2 million as of December 31, 2023, which consist primarily of money market funds, 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.

As of December 31, 2023, we have established operations in Europe and Australia and hold cash in Swiss Francs, Euros, and Australian Dollars. We are subject to foreign exchange rate risk arising from transactions conducted in the aforementioned foreign currencies, however our foreign operations are not currently material to our business. We do not believe that our results of operations or our financial position would be materially affected by an immediate change of 10% in foreign currency exchange 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 have 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 Stockholders and Board of Directors
Krystal Biotech, Inc.:

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Krystal Biotech, Inc. and subsidiaries (the Company) as of December 31, 2023 and 2022, the related consolidated statements of operations and comprehensive income (loss), stockholders' equity, and cash flows for each of the years in the two-year period ended December 31, 2023, and the related notes (collectively, the consolidated financial statements). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2023 and 2022, and the results of its operations and its cash flows for each of the years in the two-year period ended December 31, 2023, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2023, based on criteria established in Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission, and our report dated February 26, 2024 expressed an unqualified opinion on the effectiveness of the Company's internal control over financial reporting.

Basis for Opinion

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

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated 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 consolidated 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 consolidated 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 consolidated 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 consolidated 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 consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. We determined that there are no critical audit matters.

/s/ KPMG LLP

We have served as the Company's auditor since 2022.

Pittsburgh, Pennsylvania
February 26, 2024

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 statements of operations and comprehensive loss, stockholders' equity and cash flows of Krystal Biotech, Inc. (the "Company") for the year 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 results of the Company's operations and their cash flows for the year ended December 31, 2021, in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audit. 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 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 the financial statements are free of material misstatement, whether due to error or fraud. Our audit 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 audit 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 audit provides a reasonable basis for our opinion.

We have served as the Company's auditor since 2017, which ended in 2022.

/s/ Mayer Hoffman McCann P.C.
San Diego, California
February 28, 2022

Krystal Biotech, Inc.
Consolidated Balance Sheets

(In thousands, except shares and par value data)	December 31, 2023	December 31, 2022
Assets		
Current assets		
Cash and cash equivalents	$ 358,328	$ 161,900
Short-term investments	173,850	217,271
Accounts receivable, net	42,040	—
Inventory	6,985	—
Prepaid expenses and other current assets	6,706	4,608
Total current assets	587,909	383,779
Property and equipment, net	161,202	161,684
Long-term investments	61,954	4,621
Right-of-use assets	7,027	8,042
Other non-current assets	263	324
Total assets	$ 818,355	$ 558,450
Liabilities and Stockholders' Equity		
Current liabilities		
Accounts payable	$ 4,132	$ 3,981
Current portion of lease liability	1,474	1,561
Accrued expenses and other current liabilities	27,488	23,305
Total current liabilities	33,094	28,847
Lease liability	6,620	7,372
Total liabilities	39,714	36,219
Commitments and contingencies (Note 7)		
Stockholders' equity		
Common stock; $0.00001 par value; 80,000,000 shares authorized at December 31, 2023 and 2022; 28,236,673 and 25,763,743 shares issued and outstanding at December 31, 2023 and 2022, respectively	—	—
Additional paid-in capital	1,047,830	803,718
Accumulated other comprehensive gain (loss)	638	(728)
Accumulated deficit	(269,827)	(280,759)
Total stockholders' equity	778,641	522,231
Total liabilities and stockholders' equity	$ 818,355	$ 558,450

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

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

(In thousands, except share and per share data)	Year Ended December 31, 2023	2022	2021
Product revenue, net	$ 50,699	$ —	$ —
Expenses			
Cost of goods sold	3,094	—	—
Research and development	46,431	42,461	27,884
Selling, general and administrative	98,401	77,735	40,391
Litigation settlement	12,500	25,000	—
Total operating expenses	160,426	145,196	68,275
Loss from operations	(109,727)	(145,196)	(68,275)
Other income (expense)			
Gain from sale of priority review voucher	100,000	—	—
Interest and other income, net	22,624	5,221	197
Interest expense	—	—	(1,492)
Income (loss) before income taxes	12,897	(139,975)	(69,570)
Income tax expense	(1,965)	—	—
Net income (loss)	10,932	(139,975)	(69,570)
Unrealized income (loss) on available-for-sale securities and other	1,366	(565)	(169)
Comprehensive income (loss)	$ 12,298	$ (140,540)	$ (69,739)
Net income (loss) per common share:			
Basic	$ 0.40	$ (5.49)	$ (3.13)
Diluted	$ 0.39	$ (5.49)	$ (3.13)
Weighted-average common shares outstanding:			
Basic	27,154,190	25,491,721	22,196,846
Diluted	27,751,809	25,491,721	22,196,846

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 (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balances at January 1, 2021	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 (1)	—	—	—	(169)	—	(169)
Net loss	—	—	—	—	(69,570)	(69,570)
Balances at December 31, 2021	25,207,985	$ —	$ 734,523	$ (163)	$ (140,784)	$ 593,576
Issuance of common stock, net	573,637	—	36,063	—	—	36,063
Shares surrendered for taxes and forfeitures	(17,879)	—	(649)	—	—	(649)
Stock-based compensation expense	—	—	33,781	—	—	33,781
Unrealized loss on investments and other (1)	—	—	—	(565)	—	(565)
Net loss	—	—	—	—	(139,975)	(139,975)
Balances at December 31, 2022	25,763,743	$ —	$ 803,718	$ (728)	$ (280,759)	$ 522,231
Issuance of common stock, net	2,482,481	—	203,682	—	—	203,682
Shares surrendered for taxes	(9,551)	—	(749)	—	—	(749)
Stock-based compensation expense	—	—	41,179	—	—	41,179
Unrealized gain on investments and other (1)	—	—	—	1,366	—	1,366
Net income	—	—	—	—	10,932	10,932
Balances at December 31, 2023	28,236,673	$ —	$ 1,047,830	$ 638	$ (269,827)	$ 778,641

(1) Includes foreign currency translation losses of $66 thousand and $78 thousand, and a gain of $7 thousand for the years ended December 31, 2023, 2022, and 2021, respectively.

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

Krystal Biotech, Inc.
Consolidated Statements of Cash Flows

(In thousands)	Years Ended December 31, 2023	2022	2021
Operating Activities			
Net income (loss)	$ 10,932	$ (139,975)	$ (69,570)
Adjustments to reconcile net income (loss) to net cash used in operating activities			
Gain from sale of priority review voucher	(100,000)	—	—
Depreciation	5,007	2,643	1,849
(Accretion) amortization	(1,278)	1,412	920
Stock-based compensation expense	39,933	33,230	15,319
Loss on disposal of fixed assets	27	72	—
Non-cash interest expense	—	—	1,492
Realized gain on investments	(5,092)	(570)	—
Other, net	(451)	(192)	(454)
Changes in operating assets and liabilities			
Accounts receivable	(42,040)	—	—
Inventory	(4,475)	—	—
Prepaid expenses and other current assets	(908)	(311)	(691)
Other non-current assets	(64)	(150)	65
Lease liability	(829)	(647)	(285)
Accounts payable	(101)	(1,254)	712
Accrued rebates	5,977	—	—
Accrued expenses and other current liabilities	4,558	5,173	2,705
Net cash used in operating activities	(88,804)	(100,569)	(47,938)
Investing Activities			
Proceeds from sale of priority review voucher	100,000	—	—
Purchases of property and equipment	(11,799)	(52,979)	(68,336)
Purchases of investments	(508,776)	(318,781)	(190,462)
Maturities of investments	503,213	257,677	32,028
Net cash provided by (used in) investing activities	82,638	(114,083)	(226,770)
Financing Activities			
Issuance of common stock, net of issuance costs	203,499	35,996	355,645
Taxes paid related to settlement of restricted stock awards	(749)	(649)	—
Repayment of ASTRA build-to-suit liability	—	—	(7,960)
Net cash provided by financing activities	202,750	35,347	347,685
Effect of exchange rate changes on cash and cash equivalents	(156)	(41)	—
Net change in cash and cash equivalents	196,428	(179,346)	72,977
Cash and cash equivalents at beginning of year	161,900	341,246	268,269
Cash and cash equivalents at end of year	$ 358,328	$ 161,900	$ 341,246
Supplemental Disclosures of Non-Cash Investing and Financing Activities			
Unpaid purchases of property and equipment	$ 8,602	$ 14,927	$ 15,363
Initial recognition of right-of-use assets	$ —	$ 1,556	$ 4,396

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 in April 2016. In March 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. In June 2018, the Company incorporated a wholly-owned subsidiary in Australia for the purpose of undertaking preclinical and clinical studies in Australia. In April 2019, the Company incorporated Jeune Aesthetics, Inc ("Jeune Aesthetics"), in Delaware, a wholly-owned subsidiary, for the purpose of undertaking preclinical and clinical studies for aesthetic skin conditions. In January 2022, August 2022, December 2022, and August 2023, the Company incorporated wholly-owned subsidiaries in Switzerland, Netherlands, France, and Germany respectively, for the purpose of establishing initial operations in Europe for the commercialization of the Company's product pipeline.

We are a fully integrated, commercial-stage biotechnology company focused on the discovery, development, and commercialization of genetic medicines to treat diseases with high unmet medical needs. Our first commercial product, VYJUVEK®, was approved by the FDA on May 19, 2023 for the treatment of DEB, and we subsequently initiated our U.S. commercial launch. VYJUVEK is the first medicine approved by the FDA for the treatment of DEB.

Using our patented gene therapy technology 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 healthcare professional's office or 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 and serious diseases. Our innovative technology platform is supported by an in-house, FDA-inspected commercial scale Current Good Manufacturing Practice ("CGMP") manufacturing facility and a second, completed and qualified, commercial scale CGMP facility to support future expansion.

Liquidity

As of December 31, 2023, the Company had an accumulated deficit of $269.8 million. Our transition to operating profitability is dependent upon the continued successful commercialization of VYJUVEK as well as successful development, approval, and commercialization of our other product candidates and the achievement of a level of revenue adequate to support the Company's cost structure. Management intends to fund future operations through its on hand cash and cash equivalents, revenue generated from the sale of VYJUVEK, the sale of equity, 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. The Company expects to incur significant costs to further its pipeline and to expand its commercialization capabilities in advance of the potential global regulatory approvals of VYJUVEK. The Company believes that its cash, cash equivalents and short-term investments of approximately $532.2 million as of December 31, 2023 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.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying consolidated financial statements have been prepared in conformity with generally accepted accounting principles in the United States of America ("GAAP"). 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 operations.

Use of Estimates

The preparation of consolidated financial statements in conformity with 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 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. If actual results in the future vary from the Company's estimates, the Company will adjust these estimates in the period these variances become known. Estimates are used in the following areas, among others: variable consideration associated with revenue recognition, stock-based compensation expense, accrued expenses, the fair value of financial instruments, 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 pharmaceutical products.

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 less than one year are classified as short-term investments on the consolidated balance sheets and consist of commercial paper, corporate bonds, and U.S. 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 U.S. 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 gain (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 statements of operations and comprehensive income (loss).

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, accounts receivable, net, prepaid expenses and other current assets, accounts payable, accrued expenses and other current liabilities included in the Company's consolidated financial statements, are reasonable estimates of fair value, primarily due to their short maturities.

Our available-for-sale, short-term and long-term investments, which consist of commercial paper, corporate bonds, and U.S. government agency securities are considered to be Level 2 financial instruments. 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.

Revenue Recognition

The Company has contracted to sell VYJUVEK to a limited number of specialty pharmacy providers ("SPs") that mix the medication and administer it to patients in the patient's home by a healthcare professional and through a single specialty distributor ("SD") to hospitals and outpatient clinics where patients are administered the medication at a healthcare professional's office. The Company entered into a third-party logistics distribution agreement to engage a logistics agent (the "3PL Agent") to distribute the Company's products to its customers. The 3PL Agent provides services to the Company that include storage, shipping and distribution, processing product returns, as well as customer service, order to cash, and logistics support. The Company and an affiliate of the 3PL Agent (the Title Company) entered into a Title Model Amendment (the Title Amendment) to the 3PL Agreement so that the Title Company may purchase and take title to the product and sell the product to the SPs who have contracted to purchase the product from the Company or SD who has contracted to deliver the product to our customers. Although, under the Title Amendment the Title Company takes title to the product, the economic substance of the transaction provides that the Title Company does not possess the risk of loss or participate in the significant risks and rewards of ownership of the product. The Title Company also lacks the ability to control, direct the use of, and obtain substantially all of the remaining benefits from the product. Accordingly, the Company does not recognize revenue on the transfer of the goods until the goods are sold from the Title Company to the SPs or delivered by the SD. Revenue is recognized upon transfer of control of the product to the customer.

The Company recognizes product revenue under ASC Topic 606, *Revenue from Contracts with Customers ("Topic 606").* Under Topic 606, the Company is required to complete the following five steps:

(i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price, including variable consideration, if any; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation.

The Company recognizes revenue when the customer obtains control of the product, which occurs at a point in time, upon delivery to the customer. Sales and other taxes collected concurrent with revenue-producing activities are excluded from revenue. Revenue is measured as the amount of consideration the Company expects to receive in exchange for transferring VYJUVEK and is generally based upon a list or fixed price less allowances for returns, copay assistance, rebates and discounts. The Company's payment terms are generally 80 days from the invoice date.

Variable Consideration

Product revenue, net is recorded at the net sales price, or transaction price, upon delivery and transfer of control to the customer, and includes an estimate of variable consideration, which results from discounts, rebates, and returns that are offered within our contracts.

- *Prompt Pay Discounts:* As an incentive for prompt payment, the Company offers cash discounts to its counterparties. The Company estimates accrued prompt pay discounts using the most likely amount method. The Company expects that all eligible counterparties will comply with the contractual terms to earn the discount. The Company records the discount as an allowance against accounts receivable, net and a reduction of revenue.
- *Government Rebates:* The Company participates in certain government rebate programs including Medicaid, Medicare and Tricare. The Company estimates accrued government rebates using the expected value method. The Company accrues estimated rebates based on estimated percentages of VYJUVEK that will be prescribed to qualified patients, estimated rebate percentages and estimated levels of inventory in the distribution channel that will be prescribed to qualified patients and records the rebates as a reduction of revenue. Accrued government rebates are recorded as a reduction of revenue and are included in other accrued liabilities on the consolidated balance sheets. For Medicare, the Company also estimates the accrued liability based on the number of patients in the prescription drug coverage gap under the Medicare Part D program.
- *Commercial Rebates:* The Company participates in certain commercial rebate programs. Under these rebate programs, the Company pays a rebate to the commercial entity or third-party administrator of the program. Accrued commercial rebates are estimated using the expected value method. The Company accrues estimated rebates based on contract prices, estimated percentages of VYJUVEK that will be prescribed to qualified patients and estimated levels of inventory in the distribution channel. Accrued commercial rebates are recorded as a reduction of revenue and are included in other accrued liabilities on the consolidated balance sheets.

- *Copay Assistance:* The Company provides copay assistance to qualified patients with commercial insurance in states that allow copay assistance, helping them meet copay obligations to their insurance provider. The Company reimburses pharmacies for this discount through third-party vendors. The Company estimates copay assistance costs using the expected value method. The estimate is based on contract prices, estimated percentages of VYJUVEK that will be prescribed to qualified patients, average assistance paid based on reporting from third-party vendors and estimated levels of inventory in the distribution channel. Copay assistance costs are recorded as reductions to revenue and are accrued in other accrued liabilities on the consolidated balance sheets.
- *Product Returns:* The Company offers SPs and SDs limited return rights relating only to product damage or defects identified upon receipt, and therefore the Company expects minimal returns. Returns are estimated taking into consideration several factors including these limited product return rights, historical return activity, and other relevant factors.. There were no returns for the year ended December 31, 2023.

Variable consideration is estimated and reduces the transaction price to reflect the Company's best estimate of the amount of consideration to which the Company is entitled based on the terms of the contracts and are recorded in the same period the related product revenue is recognized. The amount of variable consideration that is included in the transaction price may be constrained and is included in the net sales price only to the extent that it is considered probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. Actual amounts of consideration ultimately received may differ from the Company's estimates. If actual results in the future vary from the Company's estimates, the Company will adjust these estimates in the period these variances become known.

Cost of Goods Sold

Cost of goods sold includes direct and indirect costs related to the manufacturing of VYJUVEK. These costs consist of manufacturing costs, personnel costs including stock-based compensation, facility costs, and other indirect overhead costs. Cost of goods sold may also include period costs related to certain manufacturing services and inventory adjustment charges.

Accounts Receivable

Accounts receivable is recorded net of allowances for prompt payment discounts, returns, and credit losses. The Company estimates an allowance for credit losses by considering factors such as credit quality, the age of the accounts receivable balances, and current economic conditions that may affect a customer's ability to pay. As of December 31, 2023, the credit profile for the Company's counterparty was deemed to be in good standing, and as such an allowance for credit losses was not recorded.

Concentration of Credit Risk and Off-Balance Sheet Risk

Financial instruments that subject the Company to credit risk primarily consist of cash and cash equivalents, short-term investments, long-term investments, and accounts receivable, net. The Company maintains its cash and cash equivalent balances with high-quality financial institutions and, consequently, the Company believes that such funds are subject to minimal credit risk. The Company is exposed to credit risk in the event of default by the financial institutions to the extent amounts recorded on the consolidated 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's accounts receivable, net and marketable securities, which primarily consist of U.S. government agency securities and treasuries, corporate bonds and commercial paper, potentially subject the Company to concentrations of credit risk. The Company had one customer for the year ended December 31, 2023 and no product revenue for the years ended December 31, 2022 and 2021. The Company has no financial instruments with off-balance sheet risk of loss.

Inventories

The Company capitalizes inventory costs associated with products when future economic benefit is expected to be realized. These costs consist of raw materials, manufacturing-related costs, personnel costs including stock-based compensation, facility costs, and other indirect overhead costs. Prior to receiving FDA approval for VYJUVEK in May 2023, the Company expensed costs related to inventory for clinical and pre-commercial purposes directly to research and development expense. Following the FDA's approval of VYJUVEK, the Company began capitalizing inventory related to commercialized products held for sale, in-process of production for sale, and raw materials to be used in the manufacturing of inventory.

The Company values its inventories at the lower-of-cost and net realizable value, on a first-in, first-out ("FIFO") basis. The Company adjusts the net realizable value of any excess, obsolete or unsalable inventories in the period in which they are identified. For the years ended December 31, 2023, 2022, and 2021, there were no inventory write-downs. See Note 6.

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:

Buildings and building improvements	7 - 47 years
Computer equipment and software	3 - 7 years
Manufacturing equipment	3 - 20 years
Laboratory equipment	3 - 15 years
Furniture and fixtures	3 - 7 years
Leasehold improvements	lesser of remaining useful life or remaining life of lease

The Company reviews the estimated useful lives of its property and equipment on a continuing basis. In evaluating the useful lives, the Company considers how long assets will remain functionally effective, whether the technology continues to be relevant and considers other competitive and economic factors. If the assessment indicates that the assets will be used for a shorter or longer period than previously anticipated, the useful life of the assets is adjusted, resulting in a change in estimate. Changes in estimates are accounted for on a prospective basis by depreciating the current carrying values of the assets over their revised remaining useful lives.

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. We review the recoverability of the net book value of long-lived assets whenever events and circumstances indicate ("triggering events") that the net book value of an asset may not be recoverable from the estimated undiscounted future cash flows expected to result from its use and eventual disposition. In cases where a triggering event occurs and undiscounted expected future cash flows are less than the net book value, we recognize an impairment loss equal to an amount by which the net book value exceeds the fair value of the asset. Long-lived assets to be disposed of are reported at the lower of carrying amount or fair value less cost to sell. The Company has not experienced any triggering events or recognized any impairment losses for the years ended December 31, 2023, 2022, and 2021.

Leases

The Company accounts for its lease agreements in accordance with Financial Accounting Standards Board (“FASB”) Accounting Standards Codification (“ASC”) Topic 842, *Leases*. Right-of-use lease assets represent the right to use an underlying asset during the lease term and the lease liabilities represent the 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 existing lease agreements do not provide an implicit rate and as the Company does not have any external borrowings, the Company has 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 consolidated balance sheets and to account for lease and non-lease components of its operating leases as a single component.

Research and Development Expenses

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

The Company estimates contract research and manufacturing expenses based on the services performed pursuant to contracts with research organizations 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 FASB ASC Topic 718, *Compensation—Stock Compensation* ("ASC 718"), to account for stock-based compensation. Compensation costs related to stock options granted are 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 consolidated statements of operations and comprehensive income (loss) based on their grant-date fair values. Compensation expense for stock options, restricted stock awards, and restricted stock units 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. Compensation expense for performance-based restricted stock units is recognized for the awards that are probable of vesting over the service period of the award. On a quarterly basis, management estimates the probable number of performance-based restricted stock units that would vest until such time that the ultimate achievement of the performance criteria are known.

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 available in 2021, the Company eliminated the use of a representative peer group and began using only its own historical volatility data in its estimate of expected volatility.

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 years ended December 31, 2023, 2022, and 2021, 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, 2023 and 2022. 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, 2023 and 2022, 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, 2023 and 2022, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in the Company's consolidated statements of operations and comprehensive income (loss).

Comprehensive Income (Loss)

Comprehensive income (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 record reclassifications from other comprehensive gains or losses to interest and other income, net on the consolidated statements of operations and comprehensive income (loss) related to realized gains on sales of available-for-sale securities.

The Company reviews its securities quarterly to determine whether an other-than-temporary impairment has occurred. The Company determined that there were no other-than-temporary impairments during the years ended December 31, 2023, 2022, and 2021.

Recent Accounting Pronouncements

In December 2023, the FASB issued ASU 2023-09 *"Income Taxes (Topic 740): Improvements to Income Tax Disclosures"*. The purpose of this guidance is to enhance the transparency and usefulness of income tax disclosures and provide comprehensive income tax information, particularly in relation to rate reconciliation and income taxes paid in the U.S. and foreign jurisdictions. This new standard will be effective for fiscal years starting after December 15, 2024, with the option to apply it retrospectively. Early adoption is also allowed. Currently, the company is assessing the potential impact of this guidance on its consolidated financial statement disclosures.

In November 2023, the FASB issued Accounting Standard Update ("ASU") No. 2023-07: *Improvements to Reportable Segment Disclosures*. This new standard requires public entities to disclose significant segment expenses and additional segment items annually and in interim periods, and to provide all reported segment profit or loss information and assets currently required each year. The standard also requires disclosure of the Chief Operating Decision Maker's title and position. The standard does not change the manner in which public entities identify their operating segments, aggregate them, or apply the quantitative thresholds for determining their reportable segments. The new standard applies for fiscal years starting after December 15, 2023 and interim periods starting after December 15, 2024, with early adoption permitted. The Company has determined it operates as a single segment, therefore, we anticipate that this ASU will minimally impact our disclosed information and will not impact our consolidated balance sheets, consolidated statements of operations and comprehensive income (loss), consolidated statements of stockholders' equity, or consolidated statements of cash flows.

There were no recently adopted accounting pronouncements that had a material impact on the Company's consolidated financial statements, and no additional recently issued accounting pronouncements that are expected to have a material impact on the Company's consolidated financial statements.

3. Revenue Recognition

The Company began commercial marketing and sales of VYJUVEK throughout the United States and began recognizing revenue in 2023. For the years ended December 31, 2023, 2022, 2021, the Company recognized net product revenue of 50.7 million, zero, and zero, respectively. Accounts receivable, net balances were 42.0 million and zero as of December 31, 2023 and 2022, respectively.

The following table summarizes changes in allowances and discounts for the year ended December 31, 2023 (in thousands):

	Rebates	Prompt Pay	Other Accruals	Total
Balance as of December 31, 2022	$ —	$ —	$ —	$ —
Provision	5,990	1,164	323	7,477
Payments/Credits	(13)	(306)	(44)	(363)
Balance, as of December 31, 2023	$ 5,977	$ 858	$ 279	$ 7,114

4. Net Income (Loss) Per Share Attributable to Common Stockholders

Basic net income (loss) per share attributable to common stockholders is calculated by dividing net income (loss) attributable to common stockholders by the weighted average shares outstanding during the period, without consideration for common stock equivalents. Diluted net income (loss) per share attributable to common stockholders is computed by dividing the net income (loss) by the weighted-average number of shares of common stock and common stock equivalents outstanding for the period. Common stock equivalents consist of common stock issuable upon exercise of stock options and vesting of restricted stock awards, restricted stock units, and performance-based restricted stock units.

There were 896,745, 3,582,181, and 2,043,179 common stock equivalents outstanding in the form of stock options and zero, 66,600, and 98,800 unvested restricted stock awards as of December 31, 2023, 2022 and 2021, respectively, that have been excluded from the calculation of diluted net income (loss) per common share as their effect would be anti-dilutive.

(In thousands, except share and per share data)	Years Ended December 31, 2023	2022	2021
Numerator:			
Net income (loss)	$ 10,932	$ (139,975)	$ (69,570)
Denominator:			
Weighted-average basic common shares	27,154,190	25,491,721	22,196,846
Dilutive effect of stock options and unvested restricted stock	597,619	—	—
Weighted-average diluted common shares	27,751,809	25,491,721	22,196,846
Net income (loss) per common share — Basic	$ 0.40	$ (5.49)	$ (3.13)
Net income (loss) per common share — Diluted	$ 0.39	$ (5.49)	$ (3.13)

5. 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, 2023 and 2022, respectively (in thousands):

	December 31, 2023						
	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	$ 358,328	$ —	$ —	$ 358,328	$ 358,328	$ —	$ —
Subtotal	358,328	—	—	358,328	358,328	—	—
Level 2:							
Commercial paper	17,124	5	(1)	17,128	—	17,128	—
Corporate bonds	111,824	407	(27)	112,204	—	70,996	41,208
U.S government agency securities and treasuries	106,079	423	(30)	106,472	—	85,726	20,746
Subtotal	235,027	835	(58)	235,804	—	173,850	61,954
Total	$ 593,355	$ 835	$ (58)	$ 594,132	$ 358,328	$ 173,850	$ 61,954

	December 31, 2022						
	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	$ 161,900	$ —	$ —	$ 161,900	$ 161,900	$ —	$ —
Subtotal	161,900	—	—	161,900	161,900	—	—
Level 2:							
Commercial paper	63,624	5	(23)	63,606	—	63,606	—
Corporate bonds	82,241	13	(419)	81,835	—	77,214	4,621
U.S government agency securities and treasuries	76,683	161	(393)	76,451	—	76,451	—
Subtotal	222,548	179	(835)	221,892	—	217,271	4,621
Total	$ 384,448	$ 179	$ (835)	$ 383,792	$ 161,900	$ 217,271	$ 4,621

(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.

6. Balance Sheet Components

Inventory

Inventory consisted of the following as of December 31, 2023 and 2022, respectively (in thousands):

	December 31, 2023	December 31, 2022
Raw materials	$ 3,154	$ —
Work-in-process	3,204	—
Finished goods	627	—
Inventory	$ 6,985	$ —

Property and Equipment, Net

Property and equipment, net consisted of the following as of December 31, 2023 and 2022, respectively (in thousands):

	December 31, 2023	December 31, 2022
Building and building improvements	$ 111,180	$ —
Leasehold improvements	25,068	24,217
Manufacturing equipment	24,905	9,783
Construction-in-progress	7,291	131,331
Laboratory equipment	2,339	2,089
Furniture and fixtures	1,632	957
Computer equipment and software	1,614	100
Total property and equipment	174,029	168,477
Accumulated depreciation	(12,827)	(6,793)
Property and equipment, net	$ 161,202	$ 161,684

Depreciation expense was $5.0 million, $2.6 million and $1.8 million for the years ended December 31, 2023, 2022, and 2021, respectively.

On March 27, 2023, the Company received the permanent occupancy permit for its second commercial scale CGMP facility, ASTRA, which allowed the Company to begin utilizing certain portions of the building. As a result and as qualification of assets occurred throughout 2023, the majority of assets relating to ASTRA were reclassified from construction in progress to leasehold improvements, manufacturing equipment, buildings and building improvements, furniture and fixtures, or computer equipment and software as it was determined that assets were ready for their intended use. As certain pieces of equipment are not yet qualified, the Company will continue to hold the remaining assets within construction in progress until qualification has been completed and the assets are ready for their intended use.

Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following as of December 31, 2023 and 2022, respectively (in thousands):

	December 31, 2023	December 31, 2022
Accrued payroll and benefits	$ 8,778	$ 6,781
Accrued rebates	5,977	—
Accrued construction in progress	5,182	11,452
Accrued taxes	2,283	43
Other current liabilities	2,210	267
Accrued professional fees	1,810	3,397
Accrued preclinical and clinical expenses	1,248	1,365
Total	$ 27,488	$ 23,305

7. Commitments and Contingencies

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 primarily relate to the manufacturing of our cell and virus banks and for the manufacturing of our sterile gel that is mixed with in-house produced vectors as part of the final drug product for VYJUVEK. Agreements with third parties may also include research and development consulting activities, clinical-trial agreements, storage, packaging, labeling, and/or testing of our pre-commercial and clinical-stage products. The Company is obligated to make milestone payments under certain of these contracts. The Company may also be responsible for the payment of a monthly service fee for project management services for the duration of any agreements. The estimated remaining commitment as of December 31, 2023 under these agreements is approximately $1.7 million. The Company has incurred research and development expenses under these agreements of $5.2 million, $6.0 million and $5.0 million for the years ended December 31, 2023, 2022, and 2021, respectively.

ASTRA Contractual Obligations

The Company has contracted with various third parties to complete and qualify our second CGMP facility, ASTRA. The estimated remaining commitment as of December 31, 2023 is $8.2 million and primarily relates to building improvements and certain qualification activities of the facility that have been completed and placed into service as of December 31, 2023.

Legal Proceedings

In May 2020, a complaint was filed against the Company in the United States District Court for the Western District of Pennsylvania by PeriphaGen, Inc. ("PeriphaGen") alleging breach of contract and misappropriation of trade secrets. On April 27, 2022, the Company and PeriphaGen entered into a final settlement agreement, and the Company paid PeriphaGen an upfront payment of $25.0 million on April 28, 2022 for: (i) the release of all claims in the trade secret litigation with PeriphaGen; (ii) the acquisition of certain PeriphaGen assets, and (iii) the grant of a license by PeriphaGen for dermatological applications. In accordance with the settlement agreement, on June 15, 2023, the Company paid PeriphaGen an additional $12.5 million following the FDA's approval of VYJUVEK. The settlement agreement requires the Company to pay three additional $12.5 million contingent milestone payments upon reaching $100.0 million in total cumulative sales, $200.0 million in total cumulative sales and $300.0 million in total cumulative sales. As defined in the settlement agreement, cumulative sales shall include all revenue from sales of the Company products by the Company and its affiliates and licensees, as reported by the Company in its annual Form 10-K filings. If all milestones are achieved, the total consideration for settling the dispute, acquiring certain assets, and granting of a license from PeriphaGen will be $75.0 million, of which $37.5 million has been paid.

The Company recorded the settlement payments of $12.5 million, $25.0 million, and zero for the year ended December 31, 2023, 2022, and 2021, respectively, under litigation settlement expense on the consolidated statements of operations and comprehensive income (loss). The additional contingent milestone payments were not deemed probable due to uncertainty in the achievement of these milestones as of December 31, 2023, and therefore no additional accrual has been recorded.

The Company has received zero, $1.1 million, $1.6 million, of insurance proceeds during fiscal years ending December 31, 2023, 2022, and 2021 respectively. The reimbursements have been recorded as an offset to our legal fees included in selling, general and administrative expenses on the consolidated statements of operations and comprehensive income (loss) and within operating activities on the consolidated statements of cash flows.

8. Leases

Lease Agreements

In May 2016, the Company signed an operating lease for laboratory and office space in Pittsburgh, Pennsylvania that commenced in June 2016 and was scheduled to expire in October 2017 (the "2016 Lease"). The 2016 Lease has been amended several times to increase the area leased, which currently consists of approximately 54,000 square feet and includes the commercial scale CGMP-compliant manufacturing facility ("ANCORIS"). As a result of the lease amendments, the 2016 Lease expiration date was extended to October 2031. In September 2022, the Company amended the 2016 Lease ("Short-Term Amendment") to add a 12 month lease for additional office space that commenced in October 2022 and subsequently amended the lease again in September 2023, which commenced in October 2023 and extended the lease until September 2024. The Short-Term Amendment increased the area leased by approximately 7,000 square feet through September 2024. Due to the short-term nature of these amendments and the Company's lease accounting policy, the Company did not record a right-of-use asset or corresponding lease liability.

In December 2019, the Company entered into a lease agreement for a second commercial gene therapy facility, ("ASTRA"), in the Pittsburgh, Pennsylvania area ("ASTRA lease") with Northfield I, LLC (the "Landlord", "Northfield", or "Lessor") with an initial lease term that expired on October 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").

In October 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 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. The Company recorded a $10.0 million CIP asset and a corresponding build-to-suit lease liability related to the costs incurred by the Landlord, offset by the previous cash contributions of $2.4 million.

In January 2021, the Company entered into a Purchase and Sale Agreement ("PSA") for ASTRA with Northfield related to the purchase option exercised by the Company in October 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. In February 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. In March 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. 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. The building was placed into service as of December 31, 2023. For more information about the expected construction costs associated with ASTRA, see "ASTRA Contractual Obligations" above.

As part of the transaction, the Company also became the accounting owner of the Ground Lease, due to obtaining control over ASTRA. 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.

In December 2021, the Company entered into a 3 year lease agreement for the Boston, Massachusetts office that commenced in January 2022 and expires in January 2025.

In May 2022, the Company entered into a 16 month lease agreement for the Zug, Switzerland office that commenced in September 2022 and ended in December 2023. In September 2023, the Company entered into a 12 month lease that commenced January 2024 and expires in December 2024. Due to the short-term nature of the agreement and the Company's lease accounting policy, the Company did not record a right-of-use asset or corresponding lease liability.

As of December 31, 2023, future minimum commitments under the Company's operating leases were as follows (in thousands):

	Operating Leases
2024	$ 1,539
2025	1,277
2026	1,277
2027	1,300
2028	1,325
Thereafter	9,438
Future minimum operating lease payments	$ 16,156
Less: Interest	(8,062)
Present value of lease liability	$ 8,094

Supplemental balance sheet information related to leases is as follows:

	December 31, 2023	December 31, 2022
Operating leases:		
Right-of-use assets	$ 7,027	$ 8,042
Current portion of lease liability	1,474	1,561
Lease liability	6,620	7,372
Total lease liability	$ 8,094	$ 8,933
Weighted average remaining lease term, in years	12.3	12.5
Weighted average discount rate	9.5 %	9.4 %

The components of the Company's lease expense are as follows:

	Years Ended December 31,		
	2023	2022	2021
Lease cost:			
Operating lease expense	$ 1,596	$ 1,532	$ 1,275
Variable lease expense	203	226	160
Total lease expense	$ 1,799	$ 1,758	$ 1,435

9. Capitalization

Public Sale of Common Stock

In December 2021, the Company completed an underwritten public offering of 2,866,667 shares of its common stock, including 200,000 shares purchased by the underwriters pursuant to their option to purchase additional shares, 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.

In February 2021, the Company completed an underwritten public offering of 2,211,538 shares of its common stock, including 288,461 shares purchased by the underwriters pursuant to their option to purchase additional shares, 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.

ATM Program

On December 31, 2020, the Company entered into a sales agreement with Cowen and Company, LLC ("Cowen") with respect to an at-the-market equity offering program ("2020 ATM Program"), under which the Company issued and sold from time to time through Cowen, acting as agent and/or principal, shares of its common stock, par value $0.0001 per share, having an aggregate offering price up to $150.0 million ("Placement Shares"). The issuance and sale of the Placement Shares were made pursuant to the Company's effective "shelf" registration statement on Form S-3 that was filed with the Securities and Exchange Commission (the “SEC”) on May 4, 2020 (the “2020 Shelf Registration Statement”). During the year ended December 31, 2022, the Company issued and sold 434,782 Placement Shares at a weighted average price of $69.00 per share for net proceeds of $29.1 million after deducting selling commissions of approximately $900 thousand.

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,

The Company’s 2020 Shelf Registration Statement expired on May 4, 2023, and the Company put in place a new at-the-market equity offering program under substantially the same terms as the 2020 ATM Program (the “New ATM Program”). Accordingly, on May 8, 2023, the Company entered into a new sales agreement with Cowen to issue and sell shares of the Company’s common stock having an aggregate offering price of up to $150.0 million (the “New Placement Shares”) from time to time, under which Cowen will act as the Company’s agent and/or principal. The New Placement Shares will be offered and sold pursuant to the Company’s effective shelf registration statement on Form S-3 filed with the SEC on April 6, 2023, and a

prospectus supplement relating to the New Placement Shares that was filed with the SEC on May 8, 2023. During the year ended December 31, 2023, no shares of common stock were issued pursuant to the New ATM Program, resulting in $150.0 million available for issuance under the New ATM Program.

2023 Private Placement Offering

On May 22, 2023 and May 23, 2023, the Company sold 1,720,100 and 9,629 shares of common stock, respectively, in a private placement to certain institutional investors at a price of $92.50 per share for aggregate net proceeds of $160.0 million. In addition, the Company entered into a Registration Rights Agreement with the investors ("Registration Rights Agreement") that required the Company to file a registration statement with the SEC within 60 days of the date of the Registration Rights Agreement registering the resale of the shares of common stock issued in the private placement. On July 18, 2023, the Company filed the resale registration statement on Form S-3ASR with the SEC, which became effective upon filing.

10. Stock-Based Compensation

In 2017, the Company adopted the 2017 IPO Stock Plan (the "Plan"), which governs the issuance of equity awards to employees, certain non-employee consultants, and directors. Initially, the Company reserved 900 thousand shares for issuance under the Plan with an initial sublimit for incentive stock options of 900 thousand shares. On an annual basis, the amount of shares available for issuance under the Plan increases by an amount equal to four percent of the total outstanding shares as of the last day of the preceding calendar year. The sublimit of incentive stock options is not subject to the increase. The Company has historically granted stock options and restricted stock awards to its employees. In February 2023, the Company began issuing restricted stock units and performance-based restricted stock units to certain employees.

Stock Options

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

The Company granted 435,280 and 2,130,500 stock options to employees, non-employees, and directors during the years ended December 31, 2023 and 2022, 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, 2022	2,043,179	$ 57.00	9.0	$ 31,331
Granted	2,130,500	64.14		
Exercised	(138,855)	50.47		
Cancelled or forfeited	(438,892)	59.22		
Expired	(13,751)	78.80		
Balance at December 31, 2022	3,582,181	$ 61.50	8.7	$ 64,880
Granted	435,280	92.14		
Exercised	(752,752)	58.15		
Cancelled or forfeited	(658,117)	64.29		
Expired	—	—		
Balance at December 31, 2023	2,606,592	$ 66.39	7.9	$ 150,405
Exercisable at December 31, 2023	778,411	$ 57.20	6.9	$ 52,048

(1) Aggregate intrinsic value represents the difference between the closing stock price of our common stock on December 31, 2023 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 years ended December 31, 2023 and 2022 was $43.8 million and $2.9 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, 2023 and 2022 was $63.38 and $44.50, respectively.

There was $68.5 million of unrecognized stock-based compensation expense related to employees', non-employees', and directors' options that is expected to be recognized over a weighted-average period of 2.4 years as of December 31, 2023.

The Company has recorded aggregate stock-based compensation expense related to the issuance of stock option awards in the consolidated statements of operations and comprehensive income (loss) for the years ended December 31, 2023, 2022, and 2021 as follows (in thousands):

	Years Ended December 31,		
	2023	2022	2021
Research and development	$ 8,942	$ 7,897	$ 3,434
Selling, general and administrative	24,988	23,551	10,235
Total stock-based compensation	$ 33,930	$ 31,448	$ 13,669

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, 2023, 2022, and 2021:

	Years Ended December 31,		
	2023	2022	2021
Expected stock price volatility	73 %	78 %	72 %
Expected term of the award (years)	6.0	6.2	6.2
Risk-free interest rate	3.96 %	2.42 %	1.10 %
Weighted average exercise price	$ 92.14	$ 64.14	$ 66.88
Forfeiture Rate	— %	— %	— %
Dividend Yield	— %	— %	— %

Restricted Stock Awards

Restricted stock awards ("RSAs") granted to employees vest ratably over a four-year period. The Company granted no RSAs to employees of the Company for each of the years ended December 31, 2023 and 2022 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, 2021	98,800	$ 78.89
Granted	—	$ —
Vested	(14,321)	$ 78.89
Surrendered or forfeited	(17,879)	$ 78.89
Non-vested RSAs as of December 31, 2022	66,600	$ 78.89
Granted	—	$ —
Vested	(12,649)	$ 78.89
Surrendered or forfeited	(9,551)	$ 78.89
Non-vested RSAs as of December 31, 2023	44,400	$ 78.89

There was $2.0 million of unrecognized stock-based compensation expense related to employees' awards that is expected to be recognized over a weighted-average period of 1.2 years as of December 31, 2023.

The Company recorded the following stock-based compensation expense related to RSAs in the consolidated statements of operations and comprehensive income (loss) for the years ended December 31, 2023, 2022, and 2021 as follows (in thousands):

	Years Ended December 31,		
	2023	2022	2021
Selling, general and administrative	$ 1,747	$ 1,782	$ 1,650
Total stock-based compensation	$ 1,747	$ 1,782	$ 1,650

Restricted Stock Units

Restricted stock units ("RSUs") granted to employees vest ratably over a four-year period. The Company granted 186,900 and zero RSUs to employees of the Company during the years ended December 31, 2023 and 2022, respectively.

	Number of Shares	Weighted Average Grant Date Fair Value
Non-vested RSUs as of December 31, 2022	—	
Granted	186,900	$ 81.91
Vested	—	
Surrendered or forfeited	(26,000)	$ 81.91
Non-vested RSUs as of December 31, 2023	160,900	$ 81.91

There was $10.4 million of unrecognized stock-based compensation expense related to employees' RSU awards that is expected to be recognized over a weighted-average period of 3.2 years as of December 31, 2023.

The Company recorded stock-based compensation expense related to RSUs in the consolidated statements of operations and comprehensive income (loss) for the years ended December 31, 2023, 2022, and 2021 as follows (in thousands):

	Years Ended December 31,		
	2023	2022	2021
Research and development	$ 1,112	$ —	$ —
Selling, general and administrative	1,427	—	—
Total stock-based compensation	$ 2,539	$ —	$ —

Performance-Based Restricted Stock Units

Performance-based restricted stock units ("PSUs") granted to employees vest ratably over two years based upon continued service through the vesting date and the achievement of specific regulatory and commercial performance criteria as determined by the Compensation Committee of the Company's Board of Directors. The performance criteria are to be completed by the end of the year in which the PSU awards were granted. Each PSU represents the right to receive one share of the Company's common stock upon vesting. The Company recognizes stock-based compensation expense for the fair value of the PSU awards relating to the portion of the awards that are probable of vesting over the service period. On a quarterly basis, management estimates the probable number of PSU's that would vest until such time that the ultimate achievement of the performance criteria are known. As of December 31, 2023, the Company determined that 100% of the PSUs granted will be eligible to vest.

The Company granted 60,000 and zero PSUs to employees of the Company during the years ended December 31, 2023 and 2022.

	Number of Shares	Weighted Average Grant Date Fair Value
Non-vested PSUs as of December 31, 2022	—	
Granted	60,000	$ 81.91
Vested	—	
Surrendered or forfeited	(10,000)	$ 81.91
Non-vested PSUs as of December 31, 2023	50,000	$ 81.91

There was $2.4 million of unrecognized stock-based compensation expense related to employees' PSU awards that is expected to be recognized over a weighted-average period of 1.2 years as of December 31, 2023.

The Company recorded stock-based compensation expense related to PSUs in the consolidated statements of operations and comprehensive income (loss) for the years ended December 31, 2023, 2022, and 2021 as follows (in thousands):

	Years Ended December 31,		
	2023	**2022**	**2021**
Selling, general and administrative	$ 1,717	$ —	$ —
Total stock-based compensation	$ 1,717	$ —	$ —

Shares remaining available for grant under the Plan were 1,509,438, with a sublimit for incentive stock options of 22,786, at December 31, 2023.

After the FDA approval of VYJUVEK on May 19, 2023, the Company began capitalizing stock-based compensation associated with the allocation of labor costs related to work performed to manufacture VYJUVEK. For the years ended December 31, 2023, 2022 and 2021, the Company capitalized $1.1 million, zero, and zero, respectively, in inventory.

Historically, the Company also capitalized the portion of stock-based compensation related to work performed on the construction of our manufacturing facilities. For the years ended December 31, 2023, 2022 and 2021, the Company capitalized $162 thousand, $551 thousand, and $284 thousand, respectively, of stock-based compensation in property and equipment.

11. Income Taxes

Our income (loss) before income taxes by jurisdiction consisted of the following:

	Years Ended December 31,		
	2023	**2022**	**2021**
U.S.	$ 7,795	$ (135,691)	$ (69,570)
Foreign	5,102	(4,284)	—
Income (loss) before income taxes	$ 12,897	$ (139,975)	$ (69,570)

The provision (benefit) for income taxes consists of the following:

	Years Ended December 31,		
	2023	**2022**	**2021**
Federal	$ 125	$ —	$ —
State	1,702	$ —	$ —
Foreign	138	$ —	$ —
Total Tax Provision	$ 1,965	$ —	$ —

A reconciliation of income tax expense (benefit) computed at the statutory federal and state income tax rate for the year to income tax expense as reflected in our financial statements for years ended December 31, 2023, 2022 and 2021 are as follows (in thousands):

	Years Ended December 31,		
	2023	2022	2021
Federal income tax expense (benefit) at statutory rate	$ 2,708	$ (29,395)	$ (14,578)
Change in valuation allowance	(5,457)	39,781	20,689
State income tax expense (benefit) net of federal benefit	7,546	(10,438)	(5,436)
Credits	(4,458)	(3,167)	(1,259)
Stock Compensation	(1,715)	2,152	724
Section 162(m) limitation	2,674	620	—
GILTI	623	—	—
Other non-deductible expenses	136	30	(49)
Other	(92)	417	(91)
Total tax expense	$ 1,965	$ —	$ —

The significant components of the Company's deferred tax assets and liabilities as of December 31, 2023 and 2022 are as follows (in thousands):

	December 31, 2023	December 31, 2022
Deferred tax assets:		
Net operating loss carryforwards	$ 39,973	$ 52,569
Stock compensation	7,417	7,445
Lease liability	2,056	2,572
Accrued expenses	2,091	2,206
Section 174 R&D capitalization	20,006	5,782
Intangible assets	9,755	8,342
Credits	10,299	6,708
Unrealized loss on marketable securities	—	192
Total deferred tax assets	91,597	85,816
Valuation allowance	(76,995)	(82,513)
Deferred tax assets	$ 14,602	$ 3,303
Deferred tax liabilities:		
Depreciation	(11,537)	(137)
Right-of-use assets	(1,778)	(2,312)
Prepaid expenses	(1,090)	(854)
Unrealized gain on marketable securities	(197)	—
Total deferred tax liabilities	$ (14,602)	$ (3,303)
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 not more likely than not that the benefit of its deferred tax assets will be realized. Accordingly, the Company has provided a full valuation allowance for deferred tax assets as of December 31, 2023 and 2022.

As of December 31, 2023 and 2022, the Company had federal research and development credit carryforwards of approximately $4.8 million and $2.0 million, respectively. The federal tax credit carryforwards will begin to expire in 2039 if not utilized. As of December 31, 2023 and 2022, the Company also had orphan drug tax credit carryforwards of approximately $5.5 million and $4.4 million, respectively. The orphan drug tax credit carryforwards will begin to expire in 2039 if not utilized.

As of December 31, 2023, the Company fully utilized its state research and development credit carryforwards and as of December 31, 2022, the Company had $457 thousand of state research and development credit carryforwards.

As of December 31, 2023, the Company had cumulative U.S. federal NOL carryforwards of approximately $138.2 million. The federal NOL carryforwards are available indefinitely to offset future income tax liabilities with no expiration period.

As of December 31, 2023, the Company had cumulative U.S. state NOL carryforwards of approximately $186.0 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.

No deferred tax assets have been recognized on our consolidated balance sheets related to these NOLs, as they are fully offset by a valuation allowance. If we have previously had, or have in the future, one or more Section 382 “ownership changes,” including in connection with our initial public offering or another offering, or if we do not generate sufficient taxable income, we may not be able to utilize a material portion of our NOLs, even if we achieve profitability.

The Company files income tax returns in the United States at the federal and state level and in foreign jurisdictions in which the Company conducts business activities. The federal and state income tax returns are subject to tax examinations for the tax year ended December 31, 2022, 2021, 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. Additionally, the Company is subject to tax examinations by taxing authorities in foreign jurisdictions where it has business operations. At this time, the Company is not undergoing examination by the Internal Revenue Service or any state or foreign taxing authorities.

12. Gain on Sale of Priority Review Voucher

In August 2023, the Company entered into an agreement to sell the rare pediatric disease voucher (“PRV”), which was awarded to the Company in connection with the FDA’s approval of VYJUVEK. The transaction closed in August 2023 and was not subject to any commissions or closing costs. The proceeds of $100.0 million from the sale of the PRV were recorded as a gain from sale of priority review voucher on the Company’s consolidated statement of operations as it did not have a carrying value at the time of the sale, and as proceeds from sale of priority review voucher on the Company’s consolidated statement of cash flows.

13. 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. The Company concluded that no subsequent events have occurred that would require recognition or disclosure in the consolidated financial statements.

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) and 15d-15(e) of the Exchange Act) as of December 31, 2023. 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, 2023 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, 2023 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, 2023. The effectiveness of our internal control over financial reporting as of December 31, 2023 has been audited by KPMG, 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, 2023, the design of our disclosure controls and procedures, as defined in Rule 13a-15(e) under the Exchange Act, was effective, future events affecting our business may cause us to significantly modify our disclosure controls and procedures.

Changes in Internal Control over Financial Reporting

There was no change in our internal control over financial reporting identified in connection with the evaluation required by Rules 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the three months ended December 31, 2023 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 Stockholders and Board of Directors
Krystal Biotech, Inc.:

Opinion on Internal Control Over Financial Reporting

We have audited Krystal Biotech, Inc. and subsidiaries' (the Company) internal control over financial reporting as of December 31, 2023, based on criteria established in Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission. In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2023, based on criteria established in Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2023 and 2022, the related consolidated statements of operations and comprehensive income (loss), stockholders' equity, and cash flows for each of the years in the two-year period ended December 31, 2023, and the related notes (collectively, the consolidated financial statements), and our report dated February 26, 2024 expressed an unqualified opinion on those consolidated financial statements.

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

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

/s/ KPMG LLP

Pittsburgh, Pennsylvania
February 26, 2024

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 2024 Definitive Proxy Statement, which will be filed prior to April 30, 2024.

Item 11. Executive Compensation.

Information required by this Item is hereby incorporated by reference to our 2024 Definitive Proxy Statement, which will be filed prior to April 30, 2024.

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 2024 Definitive Proxy Statement, which will be filed prior to April 30, 2024.

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

Information required by this Item is hereby incorporated by reference to our 2024 Definitive Proxy Statement, which will be filed prior to April 30, 2024.

Item 14. Principal Accountant Fees and Services.

Information required by this Item is hereby incorporated by reference to our 2024 Definitive Proxy Statement, which will be filed prior to April 30, 2024.

PART IV

Item 15. Exhibits and 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 February 27, 2023)
10.1#	Form of 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, 2021 by and between Krystal Biotech, Inc. and Andy Orth (incorporated by reference to Exhibit 10.5 to the Company's Annual Report on Form 10-K, as filed with the SEC on February 28, 2022)
10.6#	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
10.7#	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)
10.8#	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)
10.9#	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)
10.10	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)
10.11	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)
10.12	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 the Company's Registration Statement on Form S-1 (Reg. No. 333-220085), as filed with the SEC on August 21, 2017)
10.13	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)
10.14	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)
10.15	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)
10.16	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. (incorporated by reference to Exhibit 10.17 to the Company's Annual Report on Form 10-K, as filed with the SEC on February 28, 2022)
10.17	Seventh amendment to Lease Agreement, dated as of May 11, 2021, by and between Wharton Lender Associates, L.P. and Krystal Biotech, Inc. (incorporated by reference to Exhibit 10.18 to the Company's Annual Report on Form 10-K, as filed with the SEC on February 28, 2022)
10.18	Eighth amendment to Lease Agreement, dated as of July 21, 2021, by and between Wharton Lender Associates, L.P. and Krystal Biotech, Inc. (incorporated by reference to Exhibit 10.19 to the Company's Annual Report on Form 10-K, as filed with the SEC on February 28, 2022)
10.19	Ninth amendment to Lease Agreement, dated as of January 4, 2022, by and between Wharton Lender Associates, L.P. and Krystal Biotech, Inc. (incorporated by reference to Exhibit 10.20 to the Company's Annual Report on Form 10-K, as filed with the SEC on February 28, 2022)
10.20	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)
10.21	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)

10.22	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)
10.23#	Form of Krystal Biotech, Inc. 2017 IPO Stock Incentive Plan Notice of Restricted Stock Award and Restricted Stock Award Agreement (incorporated by reference to Exhibit 10.23 to the Company's Annual Report on Form 10-K, as filed with the SEC on February 27, 2023)
10.24#	Form of Time-Based Restricted Stock Unit Award Agreement under the 2017 IPO Stock Incentive Plan (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q, as filed with the SEC on May 8, 2023)
10.25#	Form of Performance-Based Restricted Stock Unit Award Agreement under the 2017 IPO Stock Incentive Plan (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q, as filed with the SEC on May 8, 2023)
10.26	Securities Purchase Agreement, by and among Krystal Biotech, Inc. and the institutional investors listed on the signature pages thereto, dated as of May 21, 2023 (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K, as filed with the SEC on May 22, 2023)
10.27	Registration Rights Agreement, by and among Krystal Biotech, Inc. and the institutional investors listed on the signature pages thereto, dated as of May 21, 2023 (incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K, as filed with the SEC on May 22, 2023)
16.1	Letter to Securities and Exchange Commission from Mayer Hoffman McCann P.C. dated May 26, 2022 (incorporated by reference to Exhibit 16.1 to the Company's Current Report on Form 8-K, as filed with the SEC on May 26, 2022).
21.1*	Subsidiaries of Krystal Biotech, Inc.
23.1*	Consent of KPMG LLP
23.2*	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 and Chief Accounting Officer Pursuant to 18 U.S.C. Section 1350 as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
97.1*	Executive Incentive Compensation Recoupment Policy
101	(i) XBRL Instance Document, (ii) XBRL Taxonomy Extension Schema Document, (iii) XBRL Taxonomy Extension Calculation Linkbase Document, (iv) XBRL Taxonomy Extension Definition Linkbase Document, (v) XBRL Taxonomy Extension Label Linkbase Document, (vi) XBRL Taxonomy Extension Presentation Linkbase Document.
104	Cover Page Interactive Data File (formatted as inline XBRL and contained in Exhibit 101).

* 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, Commonwealth of Pennsylvania, on February 26, 2024.

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 26, 2024
/s/ Kathryn A. Romano Kathryn A. Romano	Chief Accounting Officer (Principal Financial Officer)	February 26, 2024
/s/ Suma M. Krishnan Suma M. Krishnan	President, R&D and Director	February 26, 2024
/s/ Daniel S. Janney Daniel S. Janney	Director	February 26, 2024
/s/ Dino A. Rossi Dino A. Rossi	Director	February 26, 2024
/s/ Kirti Ganorkar Kirti Ganorkar	Director	February 26, 2024
/s/ Julian Gangolli Julian Gangolli	Director	February 26, 2024
/s/ Chris Mason Chris Mason	Director	February 26, 2024
/s/ E. Rand Sutherland E. Rand Sutherland	Director	February 26, 2024
/s/ Catherine Mazzacco Catherine Mazzacco	Director	February 26, 2024

Exhibit 21.1

Subsidiaries of Krystal Biotech, Inc.

The following subsidiary constitutes a "significant subsidiary," as defined in Rule 1-02(w) of Regulation S-X.

– **Krystal Biotech Switzerland GmbH**

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the registration statements (Nos. 333-273303 and 333-271167) on Form S-3ASR and (Nos. 333-269539, 333-262825, 333-252351, and 333-220589) on Form S-8 of our reports dated February 26, 2024, with respect to the consolidated financial statements of Krystal Biotech, Inc. and the effectiveness of internal control over financial reporting.

/s/ KPMG LLP

Pittsburgh, Pennsylvania
February 26, 2024

Exhibit 23.2

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in Registration Statement on Form S-3-ASR (No. 333-271167, 333-273303) and Form S-8 (Nos. 333-269539, 333-220589, 333-252351, 333-262825) of our report dated February 28, 2022, with respect to the consolidated financial statements of Krystal Biotech, Inc. for the year ended December 31, 2021, included in this annual report on Form 10-K of Krystal Biotech, Inc. as of and for the year ended December 31, 2023.

/s/ Mayer Hoffman McCann P.C.

San Diego, California
February 26, 2024

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 26, 2024 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 26, 2024 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, 2023 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 26, 2024 By: /s/ Krish S. Krishnan

Krish S. Krishnan
President and Chief Executive Officer
(Principal Executive Officer)

Date: February 26, 2024 By: /s/ Kathryn A. Romano

Kathryn A. Romano
Chief Accounting Officer
(Principal Financial and Accounting Officer)

KRYSTAL BIOTECH, INC.

EXECUTIVE INCENTIVE COMPENSATION RECOUPMENT POLICY (Adopted August 4, 2023)

I. INTRODUCTION

The Board of Directors (the "Board") of Krystal Biotech, Inc. (the "Company") has determined that it is in the best interests of the Company to adopt a policy (the "Policy") providing for the Company's recoupment of "Erroneously Awarded Incentive-Based Compensation" (as defined below) received by Covered Officers (as defined below) of the Company.

This Policy is intended to comply with, shall be interpreted to comply with, and shall be deemed automatically amended to comply with, Rule 10D-1 adopted under the Securities Exchange Act of 1934, as amended (the "Exchange Act") and the Nasdaq Stock Market LLC ("Nasdaq") Listing Rule 5608, as such provisions may be amended from time to time, and any related rules, regulations or listing standards promulgated by the Securities and Exchange Commission (the "SEC") or Nasdaq, including any additional or new requirements that become effective after the last date that this Policy was adopted or amended. Any such amendment shall be effective at such time as is necessary to comply with the applicable listing standards of Nasdaq.

II. EFFECTIVE DATE

This Policy shall apply to all Incentive-Based Compensation (as defined below) paid or awarded to Covered Officers on or after October 2, 2023. This Policy shall survive and continue notwithstanding any separation of a Covered Officer's employment with the Company.

III. DEFINITIONS

For purposes of this Policy, the following terms shall have the meanings set forth below:

"Covered Officers" shall mean current or former "Executive Officers" as such term is defined in Rule 10D-1 adopted under the Exchange Act.

"Erroneously Awarded Incentive-Based Compensation" shall mean the amount of Incentive-Based Compensation received by a Covered Officer that exceeds the amount of Incentive-Based Compensation that otherwise would have been received had it been determined based on the information in a Restatement (as defined below) and must be computed without regard to any taxes paid. For Incentive-Based Compensation based on stock price or total shareholder return, where the amount is not subject to mathematical recalculation directly from the information in a Restatement, the amount must be based on a reasonable estimate of the effect of the Restatement on the stock price or total shareholder return, as applicable, upon which the Incentive-Based Compensation was received, and the Company must maintain documentation of that reasonable estimate and provide such documentation to Nasdaq. For the purposes of this Policy, Incentive-Based Compensation will be deemed to be received in the fiscal period during which the financial reporting measure specified in the applicable Incentive-Based Compensation award is attained, even if the payment or grant occurs after the end of that period.

"Incentive-Based Compensation" shall mean any compensation that is granted, earned, or vested based wholly or in part upon the attainment of a "financial reporting measure," which refers to measures that are determined and presented in accordance with Generally Accepted Accounting Principles which are used in preparing the Company's financial statements, and any measures that are derived wholly or in part from such measures. Stock price and total shareholder return are also financial reporting measures for this purpose. For avoidance of doubt, a financial reporting measure need not be presented within the Company's financial statements or included in a filing with the SEC.

"Restatement" shall mean any required accounting restatement of the Company's financial statements due to the material noncompliance of the Company with any financial reporting requirement under the securities laws, including any required accounting restatement to correct an error in previously issued financial statements that is

material to the previously issued financial statements (commonly referred to as "Big R" restatements), or to correct an error that is not material to previously issued financial statements but would result in a material misstatement if the error were corrected in the current period or left uncorrected in the current period (commonly referred to as "little r" restatements).

IV. RECOUPMENT OF ERRONEOUSLY AWARDED INCENTIVE-BASED COMPENSATION

In the event of a Restatement, the Company shall recover reasonably promptly from any Covered Officer the amount of any Erroneously Awarded Incentive-Based Compensation. Such recovery will be made without regard to any individual knowledge or responsibility of the Covered Officer with respect to the Restatement. The Company may, subject to applicable laws, seek recovery in the manner it chooses.

In determining the amount of Erroneously Awarded Incentive-Based Compensation to be recovered from a Covered Officer pursuant to the immediately preceding paragraph, this Policy shall apply to all Incentive-Based Compensation received by a Covered Officer: (i) after beginning service as a Covered Officer; (ii) who served as an Covered Officer at any time during the performance period for the Incentive-Based Compensation; (iii) while the Company has a class of securities listed on a national securities exchange or a national securities association; and (iv) during the three completed fiscal years immediately preceding the date that the Company is required to prepare a Restatement, including any applicable transition period that results from a change in the Company's fiscal year within or immediately following those three completed fiscal years. For this purpose, the Company is deemed to be required to prepare a Restatement on the earlier of: (i) the date the Board, or the Company's officers authorized to take such action if Board action is not required, concludes, or reasonably should have concluded, that the Company is required to prepare a Restatement; or (ii) the date a court, regulator, or other legally authorized body directs the Company to prepare a Restatement. The Company's obligation to recover Erroneously Awarded Incentive-Based Compensation is not dependent on if or when the restated financial statements are filed with the SEC.

The Company shall recover the Erroneously Awarded Incentive-Based Compensation from Covered Officers unless the Board determines that recovery is impracticable because: (i) the direct expense to a third party to assist in enforcing this Policy would exceed the amount of Erroneously Awarded Incentive-Based Compensation; provided that the Company must make a reasonable attempt to recover the Erroneously Awarded Incentive-Based Compensation before concluding that recovery is impracticable, document such reasonable attempt to recover the Erroneously Awarded Incentive-Based Compensation and provide such documentation to Nasdaq; or (ii) recovery would likely cause an otherwise tax-qualified retirement plan, under which benefits are broadly available to employees of the Company, to fail to meet the applicable requirements of 26 U.S.C. 401(a)(13) or 26 U.S.C. 411(a) and regulations thereunder.

V. BINDING EFFECT OF DETERMINATIONS BY BOARD; DELEGATION

The terms of this Policy shall be binding and enforceable against all persons subject to this Policy and their beneficiaries, heirs, executors, administrators or other legal representatives. The Board may delegate to the Compensation Committee of the Board (the "Committee") all determinations to be made and actions to be taken by the Board under this Policy. Any determination made by the Board or the Committee under this Policy shall be final, binding and conclusive on all parties.

VI. SEVERABILITY

If any provision of this Policy or the application of any such provision to any Covered Officer shall be adjudicated to be invalid, illegal or unenforceable in any respect, such invalidity, illegality or unenforceability shall not affect any other provisions of this Policy, and the invalid, illegal or unenforceable provisions shall be deemed amended to the minimum extent necessary to render any such provision or application enforceable.

VII. NO IMPAIRMENT OF OTHER REMEDIES

This Policy does not preclude the Company from taking any other action to enforce a Covered Officer's obligations to the Company, including termination of employment or institution of civil or criminal proceedings against such Covered Officer. This Policy is in addition to the requirements of Section 304 of the Sarbanes-Oxley

Act of 2002 that are applicable to the Company's Chief Executive Officer and Chief Financial Officer. Any amounts paid to the Company pursuant to Section 304 of the Sarbanes-Oxley Act of 2002 shall be considered in determining any amounts recovered under this Policy. Notwithstanding the terms of any other policy, program, agreement or arrangement, in no event will the Company indemnify or reimburse any Covered Officer for any amounts that are recovered under this Policy, and in no event will the Company pay premiums on any insurance policy that would cover a Covered Officer's potential obligations with respect to Erroneously Awarded Incentive-Based Compensation. If a Covered Officer fails to repay Erroneously Awarded Incentive-Based Compensation that is owed to the Company under this Policy, the Company shall take all appropriate action to recover such Erroneously Awarded Incentive-Based Compensation from the Covered Officer, and the Covered Officer shall be required to reimburse the Company for all expenses (including legal expenses) incurred by the Company in recovering such Erroneously Awarded Incentive-Based Compensation.

VIII. INTERPRETATION

This Policy shall be interpreted in a manner that is consistent with Rule 10D-1 under the Exchange Act, Rule 5608 of the Nasdaq listing rules and any related rules or regulations adopted by the Securities and Exchange Commission or Nasdaq (the "Applicable Rules") as well as any other applicable law. To the extent the Applicable Rules require recovery of incentive-based compensation in additional circumstances beyond those specified above, nothing in this Policy shall be deemed to limit or restrict the right or obligation of the Company to recover incentive-based compensation to the fullest extent required by the Applicable Rules.

IX. ACKNOWLEDGEMENT

Each Covered Officer shall sign and return to the Company, within 30 calendar days following the later of (i) the effective date of this Policy first set forth above or (ii) the date the individual becomes a Covered Officer, the Acknowledgement Form attached hereto as Exhibit A, pursuant to which the Covered Officer agrees to be bound by, and to comply with, the terms and conditions of this Policy.

EXHIBIT A

KRYSTAL BIOTECH, INC.

EXECUTIVE INCENTIVE COMPENSATION RECOUPMENT POLICY

ACKNOWLEDGEMENT FORM

By signing below, the undersigned acknowledges and confirms that the undersigned has received and reviewed a copy of the Krystal Biotech, Inc. (the "Company") Executive Incentive Compensation Recoupment Policy (the "Policy").

By signing this Acknowledgement Form, the undersigned acknowledges and agrees that the undersigned is and will continue to be subject to the Policy and that the Policy will apply both during and after the undersigned's employment with the Company. Further, by signing below, the undersigned agrees to abide by the terms of the Policy, including, without limitation, by returning any Erroneously Awarded Incentive-Based Compensation (as defined in the Policy) to the Company to the extent required by, and in a manner consistent with, the Policy.

COVERED OFFICER

Signature

Print Name

Date