Risk Factors Comparison 2025-02-19 to 2024-02-21 Form: 10-K

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Investing in our common stock involves a high degree of risk. You should carefully consider the following material risks, together with all the other information in this Annual Report, including our financial statements and notes thereto, before deciding to invest in our common stock. The risks and uncertainties described below are not the only ones we face **. Moreover, some of the factors, events and contingencies discussed below may have occurred in the past, but the disclosures below are not representations as to whether or not the factors, events or contingencies have occurred in the past, and instead reflect our beliefs and opinions as to the factors, events, or contingencies that could materially and adversely affect us in the future** . Additional risk and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. If any of the following risks actually materialize, our operating results, financial condition, and liquidity could be materially adversely affected. As a result, the trading price of our common stock could decline and you could lose part or all of your investment. Our company' s business, financial condition and operating results can be affected by a number of factors, whether currently known or unknown, including but not limited to those described below, any one or more of which could, directly or indirectly, cause our actual financial condition and operating results to vary materially from past, or from anticipated future, financial condition and operating results. Any of these factors, in whole or in part, could materially and adversely affect our business, prospects, financial condition, operating results and stock price. Because of the following factors, as well as other factors affecting our financial condition and operating results, past financial performance should not be considered to be a reliable indicator of future performance, and investors should not use historical trends to anticipate results or trends in future periods. Risk Factor Summary • We have a history of operating losses and **expect to** ~~anticipate that we will~~ continue to incur **operating** losses ~~for~~ **in** the ~~foreseeable future~~ **near term** . • We have limited experience in generating revenue from product sales. • We may need to raise additional capital to fund our activities. • Clinical drug development is a lengthy, complex, and expensive process with uncertain outcomes. • We may experience delays in commercialization of our products and other adverse effects if we do not achieve our projected development goals in the time frames we announce and expect. • We may experience difficulty in enrolling patients. • The regulatory approval processes of the FDA and comparable foreign authorities are lengthy and inherently unpredictable. • Fast Track Product, Breakthrough Therapy, Priority Review or RMAT designations by the FDA, and analogous designations by the EMA, for our product candidates may not lead to faster development or approval. • Our product candidates may cause undesirable or serious side effects. • We face a multitude of manufacturing risks, particularly with respect to our gene therapy ~~and mRNA~~ product candidates. • Our products remain subject to regulatory scrutiny even if we obtain regulatory approval. • Product liability lawsuits against us could cause us to incur substantial liabilities. • We may not realize the full commercial potential of our product candidates if we are unable to source and develop effective biomarkers. • We rely on third parties to conduct our nonclinical and clinical studies and perform other tasks for us. • We are dependent on KKC for the **commercialization** ~~clinical and commercial supply~~ of Crysvita ~~for all~~ **in certain** major markets ~~and for~~ **, including** the ~~development~~ **U. S.** and ~~commercialization~~ **Canada, and for our supply** of Crysvita in **our** ~~certain major~~ markets. • We rely on third parties to manufacture our products and product candidates. • The loss of, or failure to supply by, any of any of our single- source suppliers for our drug substance and drug product could adversely affect our business. • The actions of distributors and specialty pharmacies could affect our ability to sell or market products profitably. • Our revenue may be adversely affected if the market opportunities for our products and product candidates are smaller than expected. • Our competitors may develop therapies that are similar, more advanced, or more effective than ours. • We may not successfully manage expansion of our company ~~, including building an integrated commercial organization. • After the transition of our commercialization responsibilities for Crysvita in the U. S. and Canada, the success of Crysvita in those territories is dependent on the effectiveness of KKC' s commercialization efforts~~ . • Commercial success of our products depends on the degree of market acceptance. • We face uncertainty related to insurance coverage and reimbursement status of our newly approved products. • If we, or our third- party partners, are unable to maintain effective proprietary rights for our products or product candidates, we may not be able to compete effectively. • Claims of intellectual property infringement may prevent or delay our development and commercialization efforts. • We may not be successful in obtaining or maintaining necessary rights to our product candidates through acquisitions and in- licenses. • We may face competition from biosimilars of our biologics ~~product~~ **products** and product candidates or from generic versions of our small- molecule ~~product~~ **products** and product candidates, which may result in a material decline in sales of affected products. • We could lose license rights that are important to our business if we fail to comply with our obligations in the agreements under which we license intellectual property and other rights from third parties. • We may become involved in lawsuits to protect or enforce our patents or the patents of our licensors, or be subject to claims that challenge the inventorship or ownership of our patents. • Changes to patent laws in the U. S. and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products. • We may not be able to protect our intellectual property rights throughout the world. • We have limited experience as a company operating our own manufacturing facility. • Our success depends in part on our ability to retain our President and Chief Executive Officer and other qualified personnel. • Our revenue may be impacted if we fail to obtain or maintain orphan drug exclusivity for our products. • Our operating results may be adversely impacted if our intangible assets become impaired. • We may not be successful in identifying, licensing, developing, or commercializing additional product candidates. • We may fail to comply with laws and regulations or changes in laws and regulations could adversely affect our business. • We are exposed to risks related to international expansion of our business outside of the U. S. • Our **employees or consultants may engage in**

misconduct which could cause significant liability for us. • If we are found to have promoted off- label uses for our products, we may become subject to significant liability from the FDA and other regulatory agencies. • Our business may be adversely affected in the event of computer system failures or security breaches. • We or our third- party partners may be adversely affected by earthquakes or other serious natural disasters. • We may incur various costs and expenses and risks related to acquisition of companies or products or strategic transactions. • The market price of our common stock is highly volatile. • Future sales and issuances of our common stock could dilute the percentage ownership of our current stockholders and result in a decline in stock price. • Provisions in our amended and restated certificate of incorporation and by- laws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us or increase the cost of acquiring us or could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees. • We face general risks related to our ability to maintain effective internal controls over financial reporting, additional tax liabilities related to our operations, our ability to use our net operating loss carryforwards, costs of litigation, stockholder activism and increased scrutiny regarding our ESG practices and disclosures. Risks Related to Our Financial Condition and Capital Requirements ~~We~~ **Since inception, we have been engaged in substantial research and development and capital investments, and we have operated at an operating loss each year and expect to continue doing so in the near term. While we currently expect to achieve profitability for the year 2027, our expectations** are **based on** a **variety** ~~biopharmaceutical company with a history~~ of **assumptions, and actual results, including whether we achieve profitability on our expected timeline or at all, may materially differ from our expectations. Our** operating **results** ~~losses, and anticipate continuing to incur operating losses for the foreseeable future. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We have devoted substantially all of our financial resources to identifying, acquiring, and developing our products and product candidates~~ , including ~~conducting clinical studies, developing manufacturing processes, manufacturing product candidates for clinical studies, and providing selling, general and administrative support for these operations. The amount of~~ our ~~future net losses~~ **ability to achieve profitability,** will depend, in part, on non- recurring events, the success of our commercialization efforts, and the rate of our future expenditures. We anticipate that our expenses will increase substantially if and as we: • continue our research and nonclinical and clinical development of our product candidates; • expand the scope of our current clinical studies for our product candidates; • advance our programs into more expensive clinical studies; • initiate additional nonclinical, clinical, or other studies for our product candidates; • pursue preclinical and clinical development for additional indications for existing products and product candidates; • change or add additional manufacturers or suppliers; • expand upon our manufacturing- related facilities and capabilities, particularly as we continue to **increase** ~~ramp- up~~ operations at our GMP gene therapy manufacturing facility; • seek regulatory and marketing approvals for our product candidates that successfully complete clinical studies; • continue to establish Medical Affairs field teams to initiate relevant disease education; • continue to establish **or grow** a marketing and distribution infrastructure and field force to commercialize our products and any product candidates for which we may obtain marketing approval; • continue to manage our international subsidiaries and establish new ones; • continue to operate as a public company and comply with legal, accounting and other regulatory requirements; • seek to identify, assess, license, acquire, and / or develop other product candidates, technologies, and / or businesses; • make milestone or other payments under any license or other agreements; • seek to maintain, protect, and expand our intellectual property portfolio; • seek to attract and retain skilled personnel; • create additional infrastructure, including facilities and systems, to support the growth of our operations, our product development, and our commercialization efforts; and • experience any delays or encounter issues with any of the above, including, but not limited to, failed studies, complex results, safety issues, inspection outcomes, or other regulatory challenges that require longer follow-up of existing studies, additional major studies, or additional supportive studies in order to pursue marketing approval. **Even if** ~~The net losses~~ we ~~incur~~ **do achieve profitability, we may not be able to sustain or increase such profitability on a quarterly or yearly basis. Our operating results** may fluctuate significantly from quarter to quarter and year to year, such that a period-to- period comparison of our results of operations may not be a good indication of our future performance. Our ability to generate significant revenue from product sales depends on our ability, alone or with strategic collaboration partners, to successfully commercialize our products and to complete the development of, and obtain the regulatory and marketing approvals necessary to commercialize, our product candidates. Our ability to generate substantial future revenue from product sales, including named patient sales, depends heavily on our success in many areas, including, but not limited to: • obtaining regulatory and marketing approvals with broad indications for product candidates for which we complete clinical studies; • developing a sustainable and scalable manufacturing process for our products and any approved product candidates and establishing and maintaining supply and manufacturing relationships with third parties that can conduct the processes and provide adequate (in amount and quality) product supply to support market demand for our products and product candidates, if approved; • launching and commercializing our products and product candidates for which we obtain regulatory and marketing approval, either directly or with a collaborator or distributor; • obtaining market acceptance of our products and product candidates as viable treatment options; • obtaining adequate market share, reimbursement and pricing for our products and product candidates; • our ability to sell our products and product candidates on a named patient basis or through an equivalent mechanism and the amount of revenue generated from such sales; • our ability to find patients so they can be diagnosed and begin receiving treatment; • addressing any competing technological and market developments; • negotiating favorable terms, including commercial rights, in any collaboration, licensing, or other arrangements into which we may enter, any amendments thereto or extensions thereof; • maintaining, protecting, and expanding our portfolio of intellectual property rights, including patents, trade secrets, and know- how; and • attracting, hiring, and retaining qualified personnel. If the number of our addressable rare disease patients is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect, or the reasonably accepted population for treatment is narrowed by competition, physician choice, or treatment guidelines, or any other reasons, we may not generate significant revenue from sales of our products, even if they

receive regulatory approval. We may need to raise additional capital to fund our activities. Such additional financing may not be available on acceptable terms, if at all. Failure to obtain this necessary capital when needed may force us to delay, limit, or terminate our product development efforts or other activities. As of December 31, ~~2023~~ **2024**, our available cash, cash equivalents, and marketable debt securities were $ ~~777~~ **745**. ~~1~~ **0** million. We **may** ~~expect we will~~ need additional capital to continue to commercialize our products, and to develop ~~and~~ **,** obtain regulatory approval for, and to commercialize, all of our product candidates. In addition, our operating plans may change as a result of many factors that may currently be unknown to us, and we may need to seek additional funds sooner than planned. Our future funding requirements will depend on many factors, including but not limited to: • the scope, rate of progress, results, and cost of our clinical studies, nonclinical testing, and other related activities; • the cost of manufacturing clinical and commercial supplies of our products and product candidates; • the cost of creating additional infrastructure, including facilities and systems, such as systems in our GMP gene therapy manufacturing facility; • the cost of operating and maintaining our gene therapy manufacturing facility; • the number and characteristics of the product candidates that we pursue; • the cost, timing, and outcomes of regulatory approvals; • the cost and timing of establishing and operating our international subsidiaries; • the cost and timing of establishing and operating field forces, marketing, and distribution capabilities; • the cost and timing of other activities needed to commercialize our products; and • the terms and timing of any collaborative, licensing, acquisition, and other arrangements that we may establish, including any required milestone, royalty, and reimbursements or other payments thereunder. Any additional fundraising efforts may divert our management' s attention from their day- to- day activities, which can adversely affect our ability to develop our product candidates and commercialize our products. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all, particularly in light of the current macroeconomic conditions, including **changing interest rates** ~~the general economic slowdown~~ and **inflation** ~~potential recessionary environment~~. The terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities by us, whether equity or debt, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our stockholders. If we incur debt, it could result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell, or license intellectual property rights, and other operating restrictions that could adversely impact our ability to conduct our business. We have in the past sought and may in the future seek funds through a sale of future royalty payments similar to our transactions with Royalty Pharma and OMERS or through collaborative partnerships, strategic alliances, and licensing or other arrangements, such as our transaction with Daiichi Sankyo Co., Ltd., or Daiichi Sankyo, and we may be required to relinquish rights to some of our technologies or product candidates, future revenue streams, research programs, and other product candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results, and prospects. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or if we have specific strategic considerations. In addition, we **purchase** ~~may not be able to access a portion of our~~ **or** ~~existing~~ **enter into a variety of financial instruments and transactions, including investments in commercial paper, the extension of credit to corporations, institutions and governments. If any of the issuers or counterparties to these instruments were to default on their obligations, it could materially reduce the value of the transaction and adversely affect our** cash ~~,~~ **flows. If our** cash ~~equivalents~~ **flows are materially** and **adversely affected** ~~investments due to market conditions. If banks or financial institutions enter receivership or become insolvent in the future, similar to what occurred at Silicon Valley Bank in March 2023,~~ or if ~~there is a concern that they may do so in response to financial conditions affecting the banking system and financial markets, our ability to access our existing cash, cash equivalents and investments may be threatened and the value of our investments may be significantly impaired. If~~ we are unable to access our existing cash, cash equivalents and investments and / or are unable to obtain funding on a timely basis, or at all, we may be required to significantly curtail, delay, or discontinue one or more of our research or development programs or the commercialization of our products and any approved product candidates or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition, and results of operations. Risks Related to the Discovery and Development of Our Product Candidates Clinical drug development involves a lengthy, complex, and expensive process with uncertain outcomes and the potential for substantial delays, and the results of earlier studies may not be predictive of future study results. Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical studies to demonstrate the safety and efficacy of the product candidates in humans. Clinical testing is expensive, complex, time consuming, and uncertain as to outcome. We cannot guarantee that any clinical studies will be conducted as planned or completed on schedule, if at all. We have also had difficulties in recruiting clinical site investigators and clinical staff for our studies, and may continue to experience such difficulties. Additionally, a failure of one or more clinical studies can occur at any stage of testing, and our future clinical studies may not be successful. Product candidates that have shown promising results in early- stage clinical studies may still suffer significant setbacks or fail in subsequent clinical studies. The safety or efficacy results generated to date in clinical studies do not ensure that later clinical studies will demonstrate similar results. Further, we have reported and expect to continue to report preliminary or interim data from our clinical trials. Preliminary or interim data from our clinical trials are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and / or more patient data become available. Such data may show initial evidence of clinical benefit, but as patients continue to be assessed and more patient data become available, there is a risk that any therapeutic effects are no longer durable in patients and / or decrease over time or cease entirely. As a result, preliminary or interim data should be considered carefully and with caution until the final data are available. Results from investigator- sponsored studies or compassionate- use studies may not be confirmed in company- sponsored studies or may negatively impact the prospects for our programs. Additionally, given the nature of the rare diseases we are seeking to treat, we often devise newly- defined endpoints

to be tested in our studies, which can lead to subjectivity in interpreting study results and could result in regulatory agencies not agreeing with the validity of our endpoints, or our interpretation of the clinical data, and therefore delaying or denying approval. Given the illness of the patients in our studies and the nature of their rare diseases, we have also been required to , or have chosen to , conduct certain studies on an open- label basis. We have in the past, and may in the future , elect to review interim clinical data at multiple time points during the studies, which could introduce bias into the study results and potentially result in denial of approval. In the biopharmaceutical industry, there is a high failure rate for drugs and biologics proceeding through clinical studies, and product candidates in later stages of clinical studies may fail to show the desired safety and efficacy despite having progressed through nonclinical studies and initial clinical studies. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical studies due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier studies. Scenarios that can prevent successful or timely completion of clinical development include but are not limited to: • delays or failures in generating sufficient preclinical, toxicology, or other in vivo or in vitro data to support the initiation or continuation of human clinical studies or filings for regulatory approval; • failure to demonstrate a starting dose for our product candidates in the clinic that might be reasonably expected to result in a clinical benefit; • delays or failures in developing gene therapy ~~, messenger RNA, or mRNA, DNA, small interfering RNA, or siRNA~~ , or other novel and complex product candidates, which are expensive and difficult to develop and manufacture; • delays resulting from a shutdown, or uncertainty surrounding the potential for future shutdowns of the U. S. government, including the FDA; • delays or failures in reaching a consensus with regulatory agencies on study design; • delays in reaching agreement on acceptable terms with contract research organizations, or CROs, clinical study sites, and other clinical trial- related vendors; • failure or delays in obtaining required regulatory agency approval and / or IRB or EC approval at each clinical study site or in certain countries; • failure to correctly design clinical studies which may result in those studies failing to meet their endpoints or the expectations of regulatory agencies; • changes in clinical study design or development strategy resulting in delays related to obtaining approvals from IRBs or ECs and / or regulatory agencies to proceed with clinical studies; • imposition of a clinical hold by regulatory agencies after review of an IND application or amendment, another equivalent application or amendment, or an inspection of our clinical study operations or study sites; • delays in recruiting suitable patients to participate in our clinical studies; • difficulty collaborating with patient groups and investigators; • failure by our CROs, other third parties, or us to adhere to clinical study requirements; • failure to perform in accordance with the FDA' s and / or ICH' s good clinical practices requirements or applicable regulatory guidelines in other countries; • delays in patients' completion of studies or their returns for post- treatment follow- up; • patients dropping out of a study; • adverse events associated with the product candidate occurring that are viewed to outweigh its potential benefits; • changes in regulatory requirements and guidance that require amending or submitting new clinical protocols; • greater than anticipated costs associated with clinical studies of our drug candidates, including as a result of inflation; • clinical studies of our drug candidates producing negative or inconclusive results, which may result in us deciding, or regulators requiring us, to conduct additional clinical or nonclinical studies or to abandon drug development programs; • competing clinical studies of potential alternative product candidates or investigator- sponsored studies of our product candidates; and • delays in manufacturing, testing, releasing, validating, or importing / exporting sufficient stable quantities of our product candidates for use in clinical studies or the inability to do any of the foregoing. Any inability to successfully complete nonclinical and clinical development could result in additional costs to us or negatively impact our ability to generate revenue. In addition, if we make manufacturing or formulation changes to our product candidates, we may need to conduct additional toxicology, comparability or other studies to bridge our modified product candidates to earlier versions. Clinical study delays could also shorten any periods during which our products have commercial exclusivity and may allow our competitors to bring products to market before we do, which could negatively impact our ability to obtain orphan exclusivity and to successfully commercialize our product candidates and may harm our business and results of operations. If we do not achieve our projected development goals in the time frames we announce and expect, the commercialization of our products may be delayed and the credibility of our management may be adversely affected and, as a result, our stock price may decline. For planning purposes, we estimate the timing of the accomplishment of various scientific, clinical, regulatory, and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of scientific studies and clinical trials, the timing of patient dosing, the timing, type or clarity of data from clinical trials, the submission or acceptance of regulatory filings, and the potential approval of such regulatory filings. We periodically make public announcements about the expected timing of some of these milestones. All of these milestones are based on a variety of assumptions, but the actual timing of these milestones can vary dramatically from our estimates. If we do not meet these publicly announced milestones, the commercialization of our products may be delayed and the credibility of our management may be adversely affected and, as a result, our stock price may decline. We may find it difficult to identify and enroll patients in our clinical studies due to a variety of factors, including the limited number of patients who have the diseases for which our product candidates are being studied and other unforeseen events. Difficulty in enrolling patients could delay or prevent clinical studies of our product candidates. Identifying and qualifying patients to participate in clinical studies of our product candidates is critical to our success. The timing of our clinical studies depends in part on the speed at which we can recruit patients to participate in testing our product candidates, and we may experience delays in our clinical studies if we encounter difficulties in enrollment. Each of the conditions for which we plan to evaluate our current product candidates is a rare genetic disease. Accordingly, there are limited patient pools from which to draw for clinical studies. For example, we estimate that approximately 6, 000 patients worldwide suffer from GSDIa, for which DTX401 is being studied, and these all may not be treatable if they are immune to the AAV viral vector. In addition to the rarity of these diseases, the eligibility criteria of our clinical studies will further limit the pool of available study participants as we will require patients to have specific characteristics that we can measure or to assure their disease is either severe enough or not too advanced to include them in a study. The process of finding and diagnosing patients is costly and time- consuming, especially since the rare diseases we are

studying are commonly underdiagnosed. We also may not be able to identify, recruit, and enroll a sufficient number of appropriate patients to complete our clinical studies because of demographic criteria for prospective patients, the perceived risks and benefits of the product candidate under study, the proximity and availability of clinical study sites for prospective patients, and the patient referral practices of physicians. The availability and efficacy of competing therapies and clinical studies can also adversely impact enrollment. If patients are unwilling to participate in our studies for any reason (such as drug- related side effects), the timeline for and our success in recruiting patients, conducting studies, and obtaining regulatory approval of potential products may be delayed or impaired, the commercial prospects of our product candidates will be harmed, and our ability to generate product sales from any of these product candidates could be delayed or prevented. Delays in completing our clinical studies will increase our costs, slow down our product candidate development and approval process, and jeopardize our ability to commence product sales and generate revenue. The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming, and inherently unpredictable. Even if we achieve positive results in our pre- clinical and clinical studies, if we are ultimately unable to obtain timely regulatory approval for our product candidates, our business will be substantially harmed. Our future success is dependent on our ability to successfully commercialize our products and develop, obtain regulatory approval for, and then successfully commercialize one or more product candidates. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the FDA or comparable foreign regulatory authorities. We have only obtained regulatory approval for three products that we have developed, and it is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval. Further, as the clinical trial requirements of regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the product candidates, the regulatory approval process for novel product candidates, such as our gene therapy product candidates, can be more expensive and take longer than for other product candidates, leading to fewer product approvals. To date, very few gene therapy products have received regulatory approval in the U. S. or Europe. The regulatory framework and oversight over development of gene therapy products has evolved and may continue to evolve in the future. Within the FDA, the Center for Biologics Evaluation and Research, or CBER, regulates gene therapy products. Within the CBER, the review of gene therapy and related products is consolidated in the Office of Cellular, Tissue and Gene Therapies, and the FDA has established the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its reviews. The CBER works closely with the National Institutes of Health, or NIH. The FDA and the NIH have published guidance with respect to the development and submission of gene therapy protocols. For example, in January 2020, the FDA issued final guidance to set forth the framework for the development, review and approval of gene therapies. The final guidance pertains to the development of gene therapies for the treatment of specific disease categories, including rare diseases, and to manufacturing and long- term follow up issues relevant to gene therapy, among other topics. At the same time the FDA issued guidance describing the FDA' s approach for determining whether two gene therapy products were the same or different for the purpose of assessing orphan drug exclusivity. Within the European Medicines Agency, or EMA, special rules apply to gene therapy and related products as they are considered advanced therapy medicinal products, or ATMPs. Pursuant to the ATMP Regulation, the Committee on Advanced Therapies, or CAT, is responsible in conjunction with the Committee for Medicinal Products for Human Use, or CHMP, for the evaluation of ATMPs. The CHMP and CAT are also responsible for providing guidelines on ATMPs. These guidelines provide additional guidance on the factors that the EMA will consider in relation to the development and evaluation of ATMPs and include, among other things, the preclinical studies required to characterize ATMPs. The manufacturing and control information that should be submitted in a MAA; and post- approval measures required to monitor patients and evaluate the long- term efficacy and potential adverse reactions of ATMPs. Although such guidelines are not legally binding, compliance with them is often necessary to gain and maintain approval for product candidates. In addition to the mandatory risk- management plan, or RMP, the holder of a marketing authorization for an ATMP must put in place and maintain a system to ensure that each individual product and its starting and raw materials, including all substances coming into contact with the cells or tissues it may contain, can be traced through the sourcing, manufacturing, packaging, storage, transport, and delivery to the relevant healthcare institution where the product is used. To obtain regulatory approval in the U. S. and other jurisdictions, we must comply with numerous and varying requirements regarding safety, efficacy, chemistry, manufacturing and controls, clinical studies (including good clinical practices), commercial sales, pricing, and distribution of our product candidates, as described above in " Item 1. Business – Government Regulation ". Even if we are successful in obtaining approval in one jurisdiction, we cannot ensure that we will obtain approval in any other jurisdictions. In addition, approval policies, regulations, positions of the regulatory agencies on study design and / or endpoints, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate' s clinical development, which may cause delays in the approval or the decision not to approve an application. Communications with the regulatory agencies during the approval process are also unpredictable; favorable communications early in the process do not ensure that approval will be obtained and unfavorable communications early on do not guarantee that approval will be denied. Applications for our product candidates could fail to receive regulatory approval, or could be delayed in receiving regulatory approval, for many reasons, including but not limited to the following: • regulatory authorities may disagree with the design, implementation, or conduct of our clinical studies; • regulatory authorities may change their guidance or requirements for a development program for a product candidate; • the population studied in the clinical program may not be sufficiently broad or representative to assure efficacy and safety in the full population for which we seek approval; • regulatory authorities may disagree with our interpretation of data from nonclinical studies or clinical studies; • the data collected from clinical studies of our product candidates may not be sufficient to support the submission of an NDA, or biologics license application, or BLA, or other submission or to obtain regulatory approval; • we may be unable to demonstrate to regulatory authorities that a product candidate' s risk- benefit ratio for its proposed indication is acceptable; • regulatory authorities may fail to approve the

manufacturing processes, test procedures and specifications, or facilities used to manufacture our clinical and commercial supplies; • the U. S. government may be shut down, which could delay the FDA; • the FDA may be delayed in responding to our applications or submissions due to competing priorities or limited resources, including as a result of the lack of FDA funding or personnel; • failure of our nonclinical or clinical development to comply with an agreed upon Pediatric Investigational Plan, or PIP, which details the designs and completion timelines for nonclinical and clinical studies and is a condition of marketing authorization in the EU; and • the approval policies or regulations of regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval. Furthermore, the disease states we are evaluating often do not have clear regulatory paths for approval and / or do not have validated outcome measures. In these circumstances, we work closely with the regulatory authorities to define the approval path and may have to qualify outcome measures as part of our development programs. Additionally, many of the disease states we are targeting are highly heterogeneous in nature, which may impact our ability to determine the treatment benefit of our potential therapies. This lengthy and uncertain approval process, as well as the unpredictability of the clinical and nonclinical studies, may result in our failure to obtain regulatory approval to market any of our product candidates, or delayed regulatory approval. Fast Track, Breakthrough Therapy, Priority Review, or Regenerative Medicine Advanced Therapy, or RMAT, designations by the FDA, or access to the Priority Medicine scheme, or PRIME, by the EMA, for our product candidates, if granted, may not lead to faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval. As described in " Item 1. Business – Government Regulation ", we seek Fast Track, Breakthrough Therapy designation, RMAT designation, PRIME scheme access or Priority Review designation for our product candidates if supported by the results of clinical trials. Designation as a Fast Track product, Breakthrough Therapy, RMAT, PRIME, or Priority Review product is within the discretion of the relevant regulatory agency. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a Fast Track product, Breakthrough Therapy, RMAT, PRIME, or Priority Review product, the agency may disagree and instead determine not to make such designation. The receipt of such a designation for a product candidate also may not result in a faster development process, review or approval compared to drugs considered for approval under conventional regulatory procedures and does not assure that the product will ultimately be approved by the regulatory authority. In addition, regarding Fast Track products and Breakthrough Therapies, the FDA may later decide that the products no longer meet the conditions for qualification as either a Fast Track product, RMAT, or a Breakthrough Therapy or, for Priority Review products, decide that period for FDA review or approval will not be shortened. Furthermore, with respect to PRIME designation by the EMA, PRIME eligibility does not change the standards for product approval, and there is no assurance that any such designation or eligibility will result in expedited review or approval. The FDA Rare Pediatric Disease Priority Review Voucher Program, or PRV Voucher Program, awards Priority Review Vouchers, or PRVs, to sponsors of rare pediatric product applications that meet certain criteria. Under the program, a company that receives an approval for a product for a rare pediatric disease (as determined by the applicable regulations) may qualify for a PRV that can be redeemed to receive Priority Review of a subsequent marketing application for a different product. PRVs may also be sold by the company to third parties. We received PRVs under the PRV Voucher Program in connection with the approval of Mepsevii and Crysvita in 2018 and subsequently sold these two PRVs to third parties for an average amount of $ 105. 3 million for each PRV. The ~~current~~ PRV Voucher Program **began** ~~is scheduled~~ to sunset **on December 20, 2024** such that the FDA may only award a PRV for a product application if a company ~~receives~~ **received** the rare pediatric disease designation from the FDA for the product candidate by ~~September 30~~ **December 20** , 2024 ~~,~~ and the FDA will cease awarding PRVs after September 30, 2026. ~~Extension~~ **Renewal** of the ~~current~~ PRV Voucher Program is subject to approval by Congress and it is currently uncertain whether the program will be ~~extended~~ **renewed and whether any such renewal will be retroactively effective** . If **the PRV program is not renewed by Congress and** our qualifying product candidates are approved by the FDA after the ~~current approval deadlines~~ **deadline of September 30, 2026** , we will not be eligible to receive additional PRVs for our product candidates and accordingly, we would be unable to use such PRV for Priority Review for another one of our programs or to sell such PRV, which sale has the potential to generate significant proceeds. Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any. Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay, or halt clinical studies or further development, and could result in a more restrictive label, the delay or denial of regulatory approval by the FDA or other comparable foreign authorities, or a Risk Evaluation and Mitigation Strategy, or REMS, plan, which could include a medication guide outlining the risks of such side effects for distribution to patients, restricted distribution, a communication plan for healthcare providers, and / or other elements to assure safe use. Our product candidates are in development and the safety profile has not been established. Further, as one of the goals of Phase 1 and / or **Phase** 2 clinical trials is to identify the highest dose of treatment that can be safely provided to study participants, adverse side effects, including serious adverse effects, have occurred in certain studies as a result of changes to the dosing regimen during such studies and may occur in future studies. Results of our studies or investigator- sponsored trials could reveal a high and unacceptable severity and prevalence of these or other side effects. In such an event, our studies could be suspended or terminated, and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny or withdraw approval of our product candidates for any or all targeted indications. Additionally, notwithstanding our prior or future regulatory approvals for our product candidates, if we or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including but not limited to: • regulatory authorities may withdraw approvals of such product; • regulatory authorities may require additional warnings on the product' s label or restrict the product' s approved use; • we may be required to create a REMS plan **; • we may be required to change the way the product is administered** ; • patients and physicians may elect not to use our products, or reimbursement authorities may elect not to reimburse for them; and • our reputation may suffer. Any of these events could prevent us from achieving or maintaining

market acceptance of the particular product candidate, if approved. Serious adverse events in clinical trials involving gene therapy product candidates may damage public perception of the safety of our product candidates, increase government regulation, and adversely affect our ability to obtain regulatory approvals for our product candidates or conduct our business. Gene therapy remains a novel technology. Public perception may be influenced by claims that gene therapy is unsafe, and gene therapy may not gain the acceptance of the public or the medical community. For example, certain gene therapy trials using AAV8 vectors (although at significantly higher doses than those used in our gene therapy product candidates) and other vectors led to several well- publicized adverse events, including cases of leukemia and death. The risk of cancer or death remains a concern for gene therapy and ~~we cannot~~ **there can be no** ~~assure~~ **assurance** ~~you~~ that it will not occur in any of our planned or future clinical studies. In addition, there is the potential risk of delayed adverse events following exposure to gene therapy products due to persistent biological activity of the genetic material or other components of products used to carry the genetic material. Serious adverse events in our clinical trials, or other clinical trials involving gene therapy products, particularly AAV gene therapy products such as candidates based on the same capsid serotypes as our product candidates, or occurring during use of 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 gene therapy product candidates, stricter labeling requirements for those gene therapy product candidates that are approved and a decrease in demand for any such gene therapy product candidates. Gene therapy ~~and mRNA, DNA and siRNA~~ product candidates are novel, complex, expensive and difficult to manufacture. We could experience manufacturing problems that result in delays in developing and commercializing these programs or otherwise harm our business. The manufacturing process used to produce our gene therapy ~~, mRNA, DNA and siRNA~~ product candidates is novel, complex, and has not been validated for commercial use. Several factors could cause production interruptions, including equipment malfunctions, malfunctions of internal information technology systems, regulatory inspections, facility contamination, raw material shortages or contamination, natural disasters, geopolitical instability, disruption in utility services, human error or disruptions in the operations of our suppliers. Further, given that cGMP gene therapy ~~, mRNA, DNA and siRNA~~ manufacturing is a nascent industry, there are a small number of CMOs with the experience necessary to manufacture our gene therapy product candidates and we may have difficulty finding or maintaining relationships with such CMOs or hiring experts for internal manufacturing and accordingly, our production capacity may be limited. Our gene therapy ~~, mRNA, DNA and siRNA~~ product candidates require processing steps that are more complex than those required for most small molecule drugs. Moreover, unlike small molecules, the physical and chemical properties of a biologic such as gene therapy ~~, mRNA, DNA and siRNA~~ product candidates generally cannot be fully characterized. As a result, assays of the finished product candidate may not be sufficient to ensure that the product candidate is consistent from lot to lot or will perform in the intended manner. Accordingly, we employ multiple steps to control the manufacturing process to assure that the process works reproducibly, and the product candidate is made strictly and consistently in compliance with the process. Problems with the manufacturing process, even minor deviations from the normal process, could result in product defects or manufacturing failures that result in lot failures, noncompliance with regulatory requirements, product recalls, product liability claims or insufficient inventory. We may encounter problems achieving adequate quantities and quality of clinical- grade materials that meet FDA, the EMA or other applicable standards or specifications with consistent and acceptable production yields and costs. In addition, FDA, the EMA and other foreign regulatory authorities may require us to submit samples of any lot of any approved product together with the protocols showing the results of applicable tests at any time. Under some circumstances, FDA, the EMA or other foreign regulatory authorities may require that we not distribute a lot until the agency authorizes its release. Slight deviations in the manufacturing process, including those affecting quality attributes and stability, may result in unacceptable changes in the product that could result in lot failures or product recalls. Lot failures or product recalls could cause us to delay product launches or clinical trials, which could be costly to us and otherwise harm our business, financial condition, results of operations and prospects. Even if we obtain regulatory approval for our product candidates, our products remain subject to regulatory scrutiny. Our products and any product candidates that are approved in the future remain subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, distribution, advertising, promotion, sampling, record- keeping, conduct of post- marketing studies, and submission of safety, efficacy, and other post- market information, including both federal and state requirements in the U. S. and requirements of comparable foreign regulatory authorities, as described above in " Item 1. Business – Government Regulation ~~.~~ **.**" Manufacturers and manufacturers' facilities are required to comply with extensive FDA, and comparable foreign regulatory authority, requirements, including ensuring that quality control and manufacturing procedures conform to Good Manufacturing Practices, or GMP, regulations. As such, we and our contract manufacturers are subject to continual review and inspection to assess compliance with GMP and adherence to commitments made in any NDA, BLA, MAA, or other comparable application for approval in another jurisdiction. Although we are not involved in the day- to- day operations of our contract manufacturers, we are ultimately responsible for ensuring that our products are manufactured in accordance with GMP regulations. Regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our products, product candidates or the associated quality systems for compliance with the regulations applicable to the activities being conducted. Due to the complexity of the processes used to manufacture our products and product candidates, we or any of our collaborators or contract manufacturers may be unable to comply with GMP regulations in a cost- effective manner and may be unable to initially or continue to pass a federal, national or international regulatory inspection. If we, our collaborators, such as KKC or Regeneron, or any of our third- party manufacturers fail to maintain regulatory compliance, the FDA or other applicable regulatory authority can impose regulatory sanctions including, among other things, warning or untitled letters, fines, unanticipated compliance expenses, the temporary or permanent suspension of a clinical study or commercial sales, recalls or seizures of product or the temporary or permanent closure of a facility or withdrawal of product approval, enforcement actions and criminal or civil prosecution. If supply from one approved manufacturer is interrupted due to failure to maintain regulatory

compliance, an alternative manufacturer would need to be qualified through an NDA or BLA supplement or MAA variation, or equivalent foreign regulatory filing, which could result in delays in product supply. The regulatory agencies may also require additional studies if a new manufacturer, material, testing method or standard is relied upon for commercial production. Switching manufacturers, materials, test methods or standards may involve substantial costs and may result in a delay in our desired clinical and commercial timelines. Accordingly, we and others with whom we work are required continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, and quality control. Any regulatory approvals that we receive for our product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or other conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical studies, and surveillance to monitor the safety and efficacy of the product candidate. We could also be asked to conduct post- marketing clinical studies to verify the safety and efficacy of our products in general or in specific patient subsets. If original marketing approval was obtained via the accelerated approval or conditional marketing authorization pathways, we would be required to conduct a successful post- marketing clinical study to confirm clinical benefit for our products. An unsuccessful post- marketing study or failure to complete such a study could result in the withdrawal of marketing approval. We will be required to report certain adverse events and manufacturing problems, if any, to the FDA and comparable foreign regulatory authorities. The holder of an approved NDA, BLA, MAA, or other comparable application must submit new or supplemental applications and obtain approval for certain changes to the approved product, product labeling, or manufacturing process. If we fail to comply with applicable regulatory requirements, or there are safety or efficacy problems with a product, a regulatory agency or enforcement authority may, among other things: • issue warning or notice of violation letters; • impose civil or criminal penalties; • suspend or withdraw regulatory approval; • suspend any of our ongoing clinical studies; • refuse to approve pending applications or supplements to approved applications submitted by us; • impose restrictions on our operations, including closing our contract manufacturers' facilities; • seize or detain products, or require a product recall; or • require entry into a consent decree. Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenue from our products. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected. Product liability lawsuits against us could cause us to incur substantial liabilities and could limit commercialization of our approved products or product candidates. We face an inherent risk of product liability exposure related to the testing of our approved products and product candidates in human clinical trials, as well as in connection with commercialization of our current and future products. If we cannot successfully defend ourselves against claims that any of our approved products or product candidates caused injuries, we could incur substantial liabilities. There can be no assurance that our product liability insurance, which provides coverage in the amount of $ 15. 0 million in the aggregate, will be sufficient in light of our current or planned clinical programs. We may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability, or losses may exceed the amount of insurance that we carry. A product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business. In addition, regardless of merit or eventual outcome, product liability claims may result in impairment of our business reputation, withdrawal of clinical study participants, costs due to related litigation, distraction of management' s attention from our primary business, initiation of investigations by regulators, substantial monetary awards to patients or other claimants, the inability to commercialize our product candidates, and decreased demand for our product candidates, if approved for commercial sale. If we are unable to identify, source, and develop effective biomarkers, or our collaborators are unable to successfully develop and commercialize companion diagnostics for our product candidates, or experience significant delays in doing so, we may not realize the full commercial potential of our product candidates. We are developing companion diagnostic tests to identify the right patients for certain of our product candidates and to monitor response to treatment. In certain cases, diagnostic tests may need to be developed as companion diagnostics and regulatory approval obtained in order to commercialize some product candidates. We currently use and expect to continue to use biomarkers to identify the right patients for certain of our product candidates. We may also need to develop predictive biomarkers in the future. We can offer no assurances that any current or future potential biomarker will in fact prove predictive, be reliably measured, or be accepted as a measure of efficacy by the FDA or other regulatory authorities. In addition, our success may depend, in part, on the development and commercialization of companion diagnostics. We also expect the FDA will require the development and regulatory approval of a companion diagnostic assay as a condition to approval of our gene therapy product candidates. There has been limited success to date industrywide in developing and commercializing these types of companion diagnostics. Development and manufacturing of companion diagnostics is complex and there are limited manufacturers with the necessary expertise and capability. Even if we are able to successfully develop companion diagnostics, we may not be able to manufacture the companion diagnostics at a cost or in quantities or on timelines necessary for use with our product candidates. To be successful, we need to address a number of scientific, technical and logistical challenges. We are currently working with a third party to develop companion diagnostics ~~:~~, however, we have little experience in the development and commercialization of diagnostics and may not ultimately be successful in developing and commercializing appropriate diagnostics to pair with any of our product candidates that receive marketing approval. We rely on third parties for the automation, characterization and validation, of our bioanalytical assays, companion diagnostics and the manufacture of ~~its~~ critical reagents. Companion diagnostics are subject to regulation by the FDA and similar regulatory authorities outside the U. S. as medical devices and require regulatory clearance or approval prior to commercialization. In the U. S., companion diagnostics are cleared or approved through FDA' s 510 (k) premarket notification or premarket approval, or PMA, process. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted 510 (k) premarket

notification, PMA or equivalent application types in jurisdictions outside the U. S., may cause delays in the approval, clearance or rejection of an application. Given our limited experience in developing and commercializing diagnostics, we expect to rely in part or in whole on third parties for companion diagnostic design and commercialization. We and our collaborators may encounter difficulties in developing and obtaining approval or clearance for the companion diagnostics, including issues relating to selectivity / specificity, analytical validation, reproducibility, or clinical validation. Any delay or failure by us or our collaborators to develop or obtain regulatory approval of the companion diagnostics could delay or prevent approval of our product candidates. Risks Related to our Reliance on Third Parties We rely on third parties to conduct our nonclinical and clinical studies and perform other tasks for us. If these third parties do not successfully carry out their contractual duties, meet expected deadlines, or comply with regulatory requirements, we may be exposed to sub- optimal quality and reputational harm, we may not be able to obtain regulatory approval for or commercialize our product candidates, and our business could be substantially harmed. We have relied upon and plan to continue to rely upon third parties, including CROs, collaborative partners, and independent investigators to analyze, collect, monitor, and manage data for our ongoing nonclinical and clinical programs. We rely on third parties for execution of our nonclinical and clinical studies, and for estimates regarding costs and efforts completed, and we control only certain aspects of their activities. We and our CROs and other vendors and partners are required to comply with GMP, GCP, and GLP, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area, and comparable foreign regulatory authorities for all of our product candidates in development. Regulatory authorities enforce these regulations through periodic inspections of study sponsors, principal investigators, study sites, and other contractors. If we or any of our CROs or other vendors and partners, including the sites at which clinical studies are conducted, fail to comply with applicable regulations, the data generated in our nonclinical and clinical studies may be deemed unreliable and the FDA, EMA, or comparable foreign regulatory authorities may deny approval and / or require us to perform additional nonclinical and clinical studies before approving our marketing applications, which would delay the approval process. We cannot make assurances that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical studies comply with GCP regulations or that nonclinical studies comply with GLP regulations. In addition, our clinical studies must be conducted with products produced under GMP regulations. If the regulatory authorities determine that we have failed to comply with GLP, GMP, or GCP regulations, they may deny approval of our product candidates and / or we may be required to repeat clinical or nonclinical studies, which would delay the regulatory approval process. Our CROs and other vendors and partners are not our employees **,** and we cannot control whether or not they devote sufficient time and resources to our on- going nonclinical and clinical programs, except for the limited remedies available to us under our agreements with such third parties. If our vendors and partners 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 data they obtain is compromised due to the failure to adhere to our protocols, regulatory requirements, or for other reasons, our clinical studies may be extended, delayed, or terminated, and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. CROs and other vendors and partners have also generated higher costs than anticipated as a result of changes in scope of work or otherwise. As a result, the commercial prospects for our product candidates could be harmed, our costs could increase, and our ability to generate revenue could be delayed. If any of our relationships with these third parties terminate, we may not be able to enter into arrangements with alternative vendors or do so on commercially reasonable terms. Switching or adding additional vendors involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new vendor commences work. As a result, delays may occur, which can materially impact our ability to meet our desired clinical development timelines. Our efforts to manage our relationships with our vendors and partners can provide no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition, and business prospects. We also rely on third parties in other ways, including efforts to support patient diagnosis and identify patients, to assist our finance and legal departments, and to provide other resources for our business. Use of these third parties could expose us to sub- optimal quality, missed deadlines, and non- compliance with applicable laws, all of which could result in reputational harm to us and negatively affect our business. We are dependent on KKC for the ~~clinical~~ **commercialization of Crysvita in our markets, including the U. S.** and ~~commercial~~ **Canada, and for our** supply of Crysvita **in our** ~~for all major~~ markets **. Failure by** ~~and for the development and commercialization of Crysvita in certain major markets, and~~ KKC ~~' s failure to provide an adequate supply of Crysvita or~~ to commercialize Crysvita in those markets **, or to supply Crysvita to us,** could result in a material adverse effect on our business and operating results. ~~Under~~ **Pursuant to the terms of** our **collaboration and license** agreement with KKC, **or the collaboration agreement, commercialization responsibilities for Crysvita in the U. S. and Canada transitioned from us to** KKC **in April 2023. KKC also** has the sole right to commercialize Crysvita in Europe and, at certain specified times, in ~~the U. S., Canada, and~~ Turkey, subject to certain rights retained **. A substantial portion of our total revenue has been based on revenue from Crysvita, including royalty revenue we receive from KKC for sales of the product in the U. S. and Canada. The commercial success of Crysvita in territories in which KKC owns commercialization responsibilities, such as in the U. S. and Canada depends on, among other things, the efforts and allocation of resources of KKC in those territories, which we do not control. KKC has no obligation under the collaboration agreement to use diligent efforts to commercialize Crysvita in those territories** . Our partnership with KKC may not be successful, and we may not realize the expected benefits from such partnership, due to a number of important factors, including but not limited to the following: ~~• KKC has no obligation under our agreement to use diligent efforts to commercialize Crysvita in Europe. The timing and amount of any royalty payments that are made by KKC based on sales of Crysvita in Europe will depend on, among other things, the efforts, allocation of resources, and successful commercialization of Crysvita by KKC in Europe; • the timing and amount of any payments we may receive under our agreement with KKC will depend on, among other things, the efforts, allocation of resources, and successful~~

~~commercialization of Crysvita by KKC in the U. S. and Canada under our agreement; •~~ KKC may change the focus of its commercialization efforts or pursue higher priority programs; • KKC may make decisions regarding the indications for our product candidates in countries where it has the sole right to commercialize the product candidates that limit commercialization efforts in those countries or in countries where we have the right to commercialize our product candidates; • KKC may make decisions regarding market access and pricing in countries where it has the sole right to commercialize our product candidates which can negatively impact our commercialization efforts in countries where we have the right to commercialize our product candidates; • KKC may fail to manufacture or supply sufficient drug product of Crysvita in compliance with applicable laws and regulations or otherwise for our development and clinical use or commercial use, which could result in program delays or lost revenue; • KKC may elect to develop and commercialize Crysvita indications with a larger market than XLH and at a lower price, thereby reducing the profit margin on sales of Crysvita for any orphan indications, including XLH; • if KKC were to breach or terminate the agreement with us, we would no longer have any rights to develop or commercialize Crysvita or such rights would be limited to non- terminated countries; • KKC may terminate its agreement with us, adversely affecting our potential revenue from licensed products; and • the timing and amounts of expense reimbursement that we may receive are uncertain, and the total expenses for which we are obligated to reimburse KKC may be greater than anticipated. We rely on third parties to manufacture our products and our product candidates and we are subject to a multitude of manufacturing risks, any of which could substantially increase our costs and limit the supply of our ~~product~~ **products** and product candidates. As we currently lack the resources and the full capability to manufacture all of our products and product candidates on a clinical or commercial scale, we rely on third parties to manufacture **, store and distribute** our products and product candidates. Although we oversee the contract manufacturers, we cannot control the manufacturing process of, and are substantially dependent on, our contract manufacturing partners for compliance with the regulatory requirements. See **the risk factor above entitled** "- Even if we obtain regulatory approval for our product candidates, our products remain subject to regulatory scrutiny " ~~risk factor above~~ . Further, we depend on our manufacturers to purchase from third- party suppliers the materials necessary to produce our products and product candidates. There are a limited number of suppliers for raw materials that we use to manufacture our drugs, placebos, or active controls, and there may be a need to identify alternate suppliers to prevent or mitigate a possible disruption of the manufacture of the materials necessary to produce our products and product candidates for our clinical studies, and, if approved, ultimately for commercial sale. We also do not have any control over the process or timing of the acquisition of these raw materials by our manufacturers. We may also experience interruptions in supply of product if the product or raw material components fail to meet our quality control standards or the quality control standards of our suppliers. Further, manufacturers that produce our products and product candidates may not have experience producing our products and product candidates at commercial levels and may not produce our products and product candidates at the cost, quality, quantities, locations, and timing needed to support profitable commercialization. We have not yet secured manufacturing capabilities for commercial quantities of all of our product candidates and may be unable to negotiate binding agreements with manufacturers to support our commercialization activities on commercially reasonable terms. Even if our third- party product manufacturers develop acceptable manufacturing processes that provide the necessary quantities of our products and product candidates in a compliant and timely manner, the cost to us for the supply of our products and product candidates manufactured by such third parties may be high and could limit our profitability. For instance, KKC is our sole supplier of commercial quantities of Crysvita. The supply price to us for commercial sales of Crysvita in Latin America **is 30** ~~and the transfer price for commercial sales of the product in the U. S. and Canada was 35~~ % of net sales ~~through December 31, 2022 and 30 % thereafter~~ , which is higher than the typical cost of sales for companies focused on rare diseases. The process of manufacturing our products and product candidates is complex, highly regulated, and subject to several risks, including but not limited to those listed below. • The process of manufacturing our products and product candidates is extremely susceptible to product loss due to contamination, equipment failure or improper installation or operation of equipment, or vendor or operator error. Even minor deviations from normal manufacturing processes for our products and any of our product candidates could result in reduced production yields, product defects, and other supply disruptions. If microbial, viral, or other contaminations are discovered in our products and product candidates or in the manufacturing facilities in which our products and product candidates are made, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination. • The manufacturing facilities in which our products and product candidates are made could be adversely affected by equipment failures, labor shortages, raw material shortages, natural disasters, power failures, actual or threatened public health emergencies, and numerous other factors. Any adverse developments affecting manufacturing operations for our products and product candidates may result in shipment delays, inventory shortages, lot failures, withdrawals or recalls, or other interruptions in the supply of our products and product candidates. Due to their stage of development, small volume requirements, and infrequency of batch production runs, we carry limited amounts of safety stock for our products and product candidates. We have, and may in the future, be required to take inventory write- offs and incur other charges and expenses for products and product candidates that fail to meet specifications, undertake costly remediation efforts, or seek more costly manufacturing alternatives. The drug substance and drug product for our products and most of our product candidates are currently acquired from single- source suppliers. The loss of these suppliers, or their failure to supply us with the necessary drug substance or drug product, could materially and adversely affect our business. We acquire most of the drug substances and drug products for our products and product candidates from single sources. If any single source supplier breaches an agreement with us, or terminates the agreement in response to an alleged breach by us **, ceases operations, is acquired, enters into exclusive arrangements with a competitor** or otherwise becomes unable or unwilling to fulfill its supply obligations, we would not be able to manufacture and distribute the product or product candidate until a qualified alternative supplier is identified, which could significantly impair our ability to commercialize such product or delay the development of such product candidate. For example, the drug substance and drug product for Crysvita and Evkeeza are made, respectively, by KKC pursuant to a license and

collaboration agreement and **supply agreements and** Regeneron pursuant to a supply agreement. **Further** ~~The drug substance and drug product for Mepsevii are currently manufactured by Rentschler under a commercial supply and services agreement~~ , ~~accompanying purchase orders, and other agreements. Pharmaceutical- grade drug substance for Dojolvi is manufactured by IOI Oleo pursuant to a supply agreement, and the drug product for Dojolvi is prepared by Haupt Pharma AG, pursuant to a master services agreement. Single~~ **single** source suppliers are also used for our gene therapy programs **and for Dojolvi** ~~. Haupt Pharma closed its Wolfrathshausen~~ , **for** ~~Germany site,~~ which ~~produces the Dojolvi drug product, at the end of 2023. As such,~~ we are in the process of qualifying **our** ~~and conducting transfer activities to an~~ alternative supplier. We cannot provide assurances that qualifying alternate sources, if available at all, for ~~the Dojolvi drug product or for~~ any of our ~~other~~ drug substances and drug products, and establishing relationships with such sources would not result in significant expense, supply disruptions or delay in the commercialization of our products or the development of our product candidates. Additionally, we may not be able to enter into supply arrangements with an alternative supplier on commercially reasonable terms or at all. The terms of any new agreement may also be less favorable or more costly than the terms we have with our current supplier. A delay in the commercialization of our products or the development of our product candidates or having to enter into a new agreement with a different third- party on less favorable terms than we have with our current suppliers could have a material adverse impact upon on our business. **Furthermore, geopolitical tensions with China including the Congressional legislative proposal, titled the BIOSECURE Act, which would, among other things, prohibit U. S. federal funding in connection with biotechnology equipment or services produced or provided by Chinese biotechnology companies, and the recent requests by certain Congressional leaders that WuXi AppTech Co. and its affiliates be added to certain U. S. Government restricted entity lists, could lead to our competitors and other companies moving to suppliers outside of China, including to our current suppliers. Significant increases in business at our single source suppliers resulting from such activities could adversely limit capacity at such suppliers to manufacture our products or result in price increases, interruptions or delays of our products.** The actions of distributors and specialty pharmacies could affect our ability to sell or market products profitably. Fluctuations in buying or distribution patterns by such distributors and specialty pharmacies could adversely affect our revenues, financial condition, or results of operations. We rely on commercial distributors and specialty pharmacies for a considerable portion of our product sales and such sales are concentrated within a small number of distributors and specialty pharmacies. The financial failure of any of these parties could adversely affect our revenues, financial condition or results of operations. Our revenues, financial condition or results of operations may also be affected by fluctuations in buying or distribution patterns of such distributors and specialty pharmacies. These fluctuations may result from seasonality, pricing, wholesaler inventory objectives, or other factors. Risks Related to Commercialization of Our Products and Product Candidates If the market opportunities for our products and product candidates are smaller than we believe they are, our revenue may be adversely affected, and our business may suffer. Because the target patient populations of our products and product candidates are small, and the addressable patient population potentially even smaller, we must be able to successfully identify patients and acquire a significant market share to achieve profitability and growth. We focus our research and product development on treatments for rare and ultrarare genetic diseases. Given the small number of patients who have the diseases that we are targeting, it is critical to our ability to grow and become profitable that we continue to successfully identify patients with these rare and ultrarare genetic diseases. Some of our current products or clinical programs may also be most appropriate for patients with more severe forms of their disease. For instance, while adults make up the majority of the XLH patients, they often have less severe disease that may reduce the penetration of Crysvita in the adult population relative to the pediatric population. Given the overall rarity of the diseases we target, it is difficult to project the prevalence of the more severe forms, or the other subsets of patients that may be most suitable to address with our products and product candidates, which may further limit the addressable patient population to a small subset. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our products and product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including the scientific literature, surveys of clinics, patient foundations, or market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. The effort to identify patients with diseases we seek to treat is in early stages, and we cannot accurately predict the number of patients for whom treatment might be possible. Additionally, the potentially addressable patient population for each of our products and product candidates may be limited or may not be amenable to treatment with our products and product candidates, and new patients may become increasingly difficult to identify or access. Further, even if we obtain significant market share for our products and product candidates, because the potential target populations are very small, we may never become or remain profitable nor generate sufficient revenue growth to sustain our business. We face intense competition and rapid technological change **, including the use of artificial intelligence, or AI,** and the possibility that our competitors may develop therapies that are similar, more advanced, or more effective than ours, which may adversely affect our financial condition and our ability to successfully commercialize our product candidates. The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. We are currently aware of various existing treatments that may compete with our products and product candidates. See “ Item 1. Business – Competition ” above. We have competitors both in the U. S. and internationally, including major multinational pharmaceutical companies, specialty pharmaceutical companies, biotechnology companies, startups, academic research institutions, government agencies, and public and private research institutions. Many of our competitors have substantially greater financial, technical, and other resources, such as larger research and development staff and experienced marketing and manufacturing organizations. Additional mergers and acquisitions in the biotechnology and pharmaceutical industries can often result in even more resources being concentrated in our competitors. As a result, these companies may obtain regulatory approval more rapidly than we are able to and may be more effective in selling and marketing their products as well. Smaller or early- stage companies may also prove to be significant competitors,

particularly through collaborative arrangements with large, established companies. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring, or licensing on an exclusive basis, products that are more effective or less costly than any product candidate that we may develop, or achieve earlier patent protection, regulatory approval, product commercialization, and market penetration than we do. Additionally, technologies developed by our competitors may render our potential products and product candidates uneconomical or obsolete, and we may not be successful in marketing our products and product candidates against competitors **. Moreover, we also face increased competition from other companies that are using AI, some of whom may be able to more quickly and effectively identify and develop novel drug candidates compared to us and our business partners, which could impair our ability to compete effectively and have a material adverse effect on our business, results of operations, or financial condition** . We may not be able to effectively manage the expansion of our organization, including building an integrated commercial organization. If we are unable to expand our existing commercial infrastructure or enter into agreements with third parties to market and sell our products and product candidates, as needed, we may be unable to increase our revenue. We expect to need additional managerial, operational, marketing, financial, legal, and other resources to support our development and commercialization plans and strategies. In order to successfully commercialize our products as well as any additional products that may result from our development programs or that we acquire or license from third parties, we ~~are~~ **expect to** ~~expanding~~ ~~---~~ **expand** our commercial ~~infrastructure~~ **team** in ~~,~~ **the United States as well as in** Europe, Latin America and the Asia- Pacific region. This infrastructure consists of both office-based as well as field teams with technical expertise, and ~~will~~ **is expected to** be expanded as we approach the potential approval dates of additional products that result from our development programs. Our management may need to divert a disproportionate amount of its attention away from our day- to- day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, operational mistakes, loss of business opportunities, loss of employees, and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and / or grow revenue could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth. We, as a company, have limited, ~~recent~~ experience selling and marketing our product and only some of our employees have prior experience promoting other similar products while employed at other companies. As we increase the number and range of our commercialized products, we may experience additional complexities in our sales process and strategy and may encounter difficulties in allocating sufficient resources to sales and marketing of certain products. Further, as we launch additional products or as demand for our products change, our initial estimate of the size of the required field force may be materially more or less than the size of the field force actually required to effectively commercialize our product candidates. As such, we may be required to hire larger teams to adequately support the commercialization of our products and product candidates or we may incur excess costs in an effort to optimize the hiring of commercial personnel. With respect to certain geographical markets, we may enter into collaborations with other entities to utilize their local marketing and distribution capabilities, but we may be unable to enter into such agreements on favorable terms, if at all. If our future collaborators do not commit sufficient resources to commercialize our future products, if any, and we are unable to develop the necessary marketing capabilities on our own, we will be unable to generate sufficient product sales to sustain our business. We face competition from companies that currently have extensive and well- funded marketing and sales operations. Without a large internal team or the support of a third party to perform key commercial functions, we may be unable to compete successfully against these more established companies. ~~Our exclusive rights to promote Crysvita in the U. S. and Canada transitioned back to KKC and the success of Crysvita in those territories are dependent on the effectiveness of KKC' s commercialization efforts. Pursuant to the terms of our collaboration and license agreement with KKC, or the collaboration agreement, we had the sole right to promote Crysvita in the U. S. and Canada, or the profit- share territory, for a specified period of time, with KKC increasingly participating in the promotion of the product until the transition date of April 2023. At the transition date, commercialization responsibilities for Crysvita in the profit- share territory transitioned to KKC, and KKC assumed responsibility for the commercialization of the product in the territory. After the transition date, the commercial success of Crysvita in the profit-share territory depends on, among other things, the efforts and allocation of resources of KKC, which we do not control. Failure by KKC to successfully market and sell Crysvita in the United States could have an adverse effect on our financial results.~~ The commercial success of any current or future product will depend upon the degree of market acceptance by physicians, patients, third- party payors, and others in the medical community. Even with the requisite approvals from the FDA and comparable foreign regulatory authorities, the commercial success of our current and future products will depend in part on the medical community, patients, and payors accepting our current and future products as medically useful, cost- effective, and safe. Any product that we bring to the market may not gain market acceptance by physicians, patients, payors, and others in the medical community. The degree of market acceptance of any of our current and future products will depend on a number of factors, including: • the efficacy of the product as demonstrated in clinical studies and potential advantages over competing treatments; • the prevalence and severity of any side effects, including any limitations or warnings contained in a product' s approved labeling; • the clinical indications for which approval is granted; • relative convenience and ease of administration; • the cost of treatment, particularly in relation to competing treatments; • the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies; • the effectiveness of our field forces and marketing efforts; • the strength of marketing and distribution support and timing of market introduction of competitive products; • publicity concerning our products or competing products and treatments; and • sufficient third- party insurance coverage and reimbursement. Even if a

potential product displays a favorable efficacy and safety profile in nonclinical and clinical studies, market acceptance of the product will not be fully known until after it is launched. Our efforts to educate the medical community and payors on the benefits of the product candidates require significant resources and may never be successful. If our current and future products fail to achieve an adequate level of acceptance by physicians, patients, payors, and others in the medical community, we will not be able to generate sufficient revenue to become or remain profitable. The insurance coverage and reimbursement status of newly approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for new or current products could limit our ability to market those products and decrease our ability to generate revenue. Our target patient populations are small, and accordingly the pricing, coverage, and reimbursement of our products and product candidates, if approved, must be adequate to support our commercial infrastructure. Our per- patient prices must be sufficient to recover our development and manufacturing costs and potentially achieve profitability. We expect the cost of a single administration of gene therapy products, such as those we are developing, to be substantial, when and if they achieve regulatory approval. Accordingly, the availability and adequacy of coverage and reimbursement by governmental and private payors are essential for most patients to afford expensive treatments such as ours, assuming approval. Sales of our products and product candidates, if approved, will depend substantially, both domestically and abroad, on the extent to which their costs will be paid for by health maintenance, managed care, pharmacy benefit, and similar healthcare management organizations, or reimbursed by government authorities, private health insurers, and other payors. If coverage and reimbursement are not available, are available only to limited levels, or are not available on a timely basis, we may not be able to successfully commercialize our products and product candidates, if approved. For example, deteriorating economic conditions and political instability in certain Latin American countries and in Turkey continue to cause us to experience significant delays in receiving approval for reimbursement for our products and consequently impact our product commercialization timelines in such regions. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to sustain our overall enterprise. In addition, we do not know the reimbursement rates until we are ready to market the product and we actually negotiate the rates. There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the U. S., the Centers for Medicare & Medicaid Services, or CMS, an agency within the U. S. Department of Health and Human Services, decides whether and to what extent a new drug will be covered and reimbursed under Medicare. Private payors tend to follow the coverage reimbursement policies established by CMS to a substantial degree. It is difficult to predict what CMS or private payors will decide with respect to reimbursement for products such as ours, especially our gene therapy product candidates as there is a limited body of established practices and precedents for gene therapy products. Outside the U. S., international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost- containment initiatives in Europe, Canada, and other countries will put pressure on the pricing and usage of our products and product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medicinal 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 **foreign** markets ~~outside the U. S.~~ , the reimbursement for our products may be reduced compared with the U. S. and may be insufficient to generate commercially reasonable revenue and profits. The timing to complete the negotiation process in each country is highly uncertain, and in some countries outside of the ~~United States~~ **U. S.** , we expect the process to exceed several months. Even if a price can be negotiated, countries frequently request or require reductions to the price and other concessions over time, including retrospective " clawback " price reductions. Additionally, member states of the EU have regularly imposed new or additional cost containment measures for pharmaceuticals such as volume discounts, cost caps, clawbacks and free products for a portion of the expected therapy period. For example, in France, we estimate clawback reserves on Dojolvi **and Evkeeza** based on current regulations, our estimate of pricing on approval of Dojolvi **and Evkeeza** and other factors. However, if pricing is approved at levels lower than estimated, if at all, or if there are further changes in the regulatory framework, we may be required to pay back amounts higher than clawback reserves and reverse revenue that has been previously recorded. Moreover, increasing efforts by governmental and third- party payors in the U. S. and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for new products and, as a result, they may not cover or provide adequate payment for our products and product candidates. We expect to experience pricing pressures in connection with the sale of any of our products and product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, additional legislative changes, including the impact from the Inflation Reduction Act of 2022, and statements by elected officials. For example, proposals have been discussed to tie U. S. drug prices to the cost in other countries, several states in the U. S. have introduced legislation to require pharmaceutical companies to disclose their costs to justify the prices of their products. Drug pricing is also expected to remain a focus for the current Presidential Administration and Congress. The downward pressure on healthcare costs in general, and with respect to prescription drugs, surgical procedures, and other treatments in particular, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. Risks Related to Our Intellectual Property If we are unable to obtain and maintain effective patent rights for our products, product candidates, or any future product candidates, we may not be able to compete effectively in our markets. We rely upon a combination of patents, trade secret protection, and confidentiality agreements to protect the intellectual property related to our technologies, our products, and our product candidates. Our success depends in large part on our and our licensors' ability to obtain and maintain patent and other intellectual property protection in the U. S. and in other countries with respect to our proprietary technologies, our products, and our product candidates. We have sought to protect our proprietary position by filing patent applications in the U. S. and abroad related to our novel technologies, products and product candidates that are important to our business. This process is expensive and time consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will

fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. The patent position of biotechnology and pharmaceutical companies generally is highly uncertain and involves complex legal and factual questions for which legal principles remain unsettled. The patent applications that we own or in- license may fail to result in issued patents with claims that cover our products or product candidates in the U. S. or in foreign countries. There is no assurance that all potentially relevant prior art relating to our patents and patent applications has been found, which can prevent a patent from issuing from a pending patent application or provide the basis for third parties to challenge the validity of an issued patent. Third parties may challenge the validity, enforceability, or scope of any issued patents, which may result in such patents being narrowed, found unenforceable, or invalidated. Furthermore, even if the patents and patent applications we own or in- license are unchallenged, they may not adequately protect our intellectual property, provide exclusivity for our products or product candidates, or prevent others from designing around our claims. Any of these outcomes could impair our ability to prevent competition from third parties. We, independently or together with our licensors, have filed several patent applications covering various aspects of our products or product candidates. We cannot offer any assurances about which, if any, ~~patents~~ **patent applications** will issue, the breadth of any ~~such~~ **issued** patent, or whether any issued patents will be found invalid and unenforceable or will be threatened by third parties. Any successful opposition to these patents could impair the exclusivity position of our products or deprive us of rights necessary for the successful commercialization of any product candidates that are approved. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced. Our current patents or applications covering methods of use and certain compositions of matter do not provide complete patent protection for our products and product candidates in all territories. For example, there are no issued patents covering the Crysvita composition of matter in Latin America, where we have rights to commercialize this product. Therefore, a competitor could develop the same antibody or a similar antibody as well as other approaches that target FGF23 for potential commercialization in Latin America, subject to any intellectual property rights or regulatory exclusivities awarded to us. If we cannot obtain and maintain effective patent rights for our products or product candidates, we may not be able to compete effectively and our business and results of operations would be harmed. We may not have sufficient patent terms to effectively protect our products and business. Patents have a limited lifespan. In the U. S., the natural expiration of a patent is generally 20 years from its earliest non- provisional filing date. Although various extensions may be available, the life of a patent, and the protection it affords, is limited. Even if patents covering our products or product candidates are obtained, once the patent life has expired for a product, we may be open to competition from generic or biosimilar medications. Patent term extensions under the Hatch- Waxman Act in the U. S. and under supplementary protection certificates in Europe may not be available to extend the patent exclusivity term for our products and product candidates, and we cannot provide any assurances that any such patent term extension will be obtained and, if so, for how long. Furthermore, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents, or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. If we do not have sufficient patent terms or regulatory exclusivity to protect our products, our business and results of operations may be adversely affected. Patent law and rule changes could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. Changes in either the patent laws or interpretation of the patent laws in the U. S. and other countries may diminish the value of our patents or narrow the scope of our patent protection. The laws of foreign countries may not protect our rights to the same extent as the laws of the U. S. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the U. S. and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. We therefore cannot be certain that we or our licensors were the first to make the ~~invention~~ **inventions** claimed in our owned and in- licensed patents or pending applications, or that we or our licensor were the first to file for patent protection of such inventions. In 2011, the Leahy- Smith America Invents Act, or the Leahy- Smith Act, was signed into law and introduced significant changes to the prosecution of U. S. patent applications and to the procedures for challenging U. S. patents. The effects of these changes ~~still~~ remain unclear owing to the evolving nature of the law and the lengthy timelines associated with court system review and interpretation. ~~However~~ **Consequently**, the Leahy- Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition. Outside the U. S., there have been changes to patent laws in certain jurisdictions that could impair our ability to obtain, maintain, or enforce our patents in those territories. For instance, Europe' s new Unitary Patent system and Unified Patent Court ~~(~~**, or** the ~~"~~UPC **,** ~~")~~ may present uncertainties for our ability to protect and enforce our patent rights against competitors in Europe. In 2012, as part of the European Patent Package ~~(~~**, or** the ~~"~~ EU Patent Package ~~")~~, regulations were passed with the goal of providing a single pan- European Unitary Patent system and a new UPC, for litigation involving European patents. Implementation of the EU Patent Package occurred in June 2023. Under the UPC, all European patents, including those issued prior to ratification of the European Patent Package, will by default automatically fall under the jurisdiction of the UPC. The UPC will provide our competitors with a new forum in which to seek central revocation of our European patents and allow for the possibility of a competitor to obtain pan- European injunctions. It will be several years before we will understand the scope of patent rights that will be recognized and the strength of patent remedies that will be provided by the UPC. Under the EU Patent Package, we will have the right to opt our patents out of the UPC over the first seven years of the court' s existence, but doing so may preclude us from realizing the benefits of the new unified court. If we are unable to maintain effective proprietary rights for our products, product candidates, or any future product candidates, we may not be able to compete effectively in our markets. In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know- how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our products or product candidate discovery and development processes that involve proprietary know- how, information, or technology that is not covered by

patents. However, trade secrets can be difficult to protect. The confidentiality agreements entered into with our employees, consultants, scientific advisors, contractors and other third parties that we rely on in connection with the development, manufacture and commercialization of our products may not be sufficient to protect our proprietary technology and processes, which increase the risk that such trade secrets may become known by our competitors or may be inadvertently incorporated into the technology of others. The physical security of our premises and physical and electronic security of our information technology systems may not preserve the integrity and confidentiality of our data and trade secrets. These individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. The assignment agreements we enter into with our employees and consultants to assign their inventions to us, and the confidentiality agreements we enter into with our employees, consultants, advisors, and any third parties who have access to our proprietary know- how, information, or technology may not have been duly executed and we cannot assure that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Misappropriation or unauthorized disclosure of our trade secrets could impair our competitive position and may have a material adverse effect on our business. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret. Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of others. There have been many lawsuits and other proceedings involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, inter partes reviews, post grant reviews, oppositions, and reexamination proceedings before the USPTO and corresponding foreign patent offices. Numerous U. S. and foreign issued patents and pending patent applications, which are owned by other parties, exist in the fields in which we are developing product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our products or product candidates may be subject to claims of infringement of the patent rights of these other parties. Other parties may assert that we are employing their proprietary technology without authorization. There may be patents or patent applications with claims to materials, formulations, methods of manufacture, or methods for treatment relevant to the use or manufacture of our products or product candidates. We have conducted freedom to operate analyses with respect only to our products and certain of our product candidates, and therefore we do not know whether there are any patents of other parties that would impair our ability to commercialize all of our product candidates. We also cannot guarantee that any of our analyses are complete and thorough, nor can we be sure that we have identified each and every patent and pending application in the U. S. and abroad that ~~is~~ **covers technology** relevant or necessary to the commercialization of our products or product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that are relevant to our products or product candidates. We are aware of certain U. S. and foreign patents owned by third parties that a court might construe to be valid and relevant to one or more of our gene therapy product candidates, certain methods that may be used in their manufacture or delivery, or certain formulations comprising one or more of our gene therapy candidates. Regarding our anti- sclerostin antibody product candidate, setrusumab, we are aware of litigation involving patents owned by a third- party, OssiFi- Mab LLC ~~(~~**, or** OMab ~~)~~, relating to methods of using sclerostin antagonists in combination with antiresorptive drugs to increase bone growth, bone formation, and / or bone density. Specifically, in the U. S., OMab has asserted certain patents expiring in 2027 or 2028 against Amgen based on Amgen' s commercialization of an anti- sclerostin antibody, Evenity ®, for the treatment of osteoporosis in postmenopausal women at high risk for fracture; Amgen denies infringement and asserts the OMab patents are invalid. In Europe, OMab was granted two patents with related subject matter; the first patent has been revoked while the second has been opposed by Amgen, UCB, and two anonymous parties. There is a risk that one or more third parties may choose to engage in litigation with us to enforce or to otherwise assert their patent rights against us. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that one or more of these patents is valid, enforceable, and infringed, in which case the owners of any such patents may be able to block our ability to commercialize a product candidate unless we obtain a license under the applicable patents, or until such patents expire. However, such a license may not be available on commercially reasonable terms or at all. Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to continue commercialization of our products, or block our ability to develop and commercialize one or more of our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products, or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure. Because our programs may require the use of proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in- license, or use these proprietary rights. We may be unable to acquire or in- license any compositions, methods of use, processes, or other third- party intellectual property rights from third parties that we identify as necessary for our product candidates. The licensing and acquisition of third- party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third- party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources, and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third- party intellectual property rights on terms that would allow us to make an appropriate return on our investment. We sometimes collaborate with U. S. and foreign academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide us an option to negotiate a license to any of the institution' s rights in technology resulting from the collaboration. Regardless of such option, we

may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program. If we are unable to successfully obtain rights to required third- party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the corresponding program. We may face competition from biosimilars, which may have a material adverse impact on the future commercial prospects of our biological products and product candidates. Even if we are successful in achieving regulatory approval to commercialize a product candidate faster than our competitors, we may face competition from biosimilars with respect to our biological products (Crysvita, Mepsevii and Evkeeza) and our biological product candidates. In the U. S., the Biologics Price Competition and Innovation Act of 2009, or BPCI Act, was included in the Affordable Care Act and created an abbreviated approval pathway for biological products that are demonstrated to be " highly similar, " or biosimilar, to or " interchangeable " with an FDA- approved biological product. The BPCI Act prohibits the FDA from approving a biosimilar or interchangeable product that references a brand biological product until 12 years after the licensure of the reference product, but permits submission of an application for a biosimilar or interchangeable product to the FDA four years after the reference product was first licensed. The BPCI Act does not prevent another company from developing a product that is highly similar to the innovative product, generating its own data, and seeking approval. The law is complex and is still being interpreted and implemented by the FDA. Moreover, aspects of the law are still being evaluated and interpreted by courts. As a result, its ultimate impact, implementation and meaning are subject to uncertainty. Modification of the BPCI Act, or changes to the interpretation or implementation of the BPCI Act, could have a material adverse effect on the future commercial prospects for our biological products and product candidates. In Europe, the European Commission has granted marketing authorizations for several biosimilars pursuant to a set of general and product class- specific guidelines for biosimilar approvals issued over the past few years. In Europe, a competitor may reference data supporting approval of an innovative biological product, but will not be able to get on the market until 10 years after the time of approval of the innovative product. This 10- year marketing exclusivity period will be extended to 11 years if, during the first eight of those 10 years, the marketing authorization holder obtains an approval for one or more new therapeutic indications that bring significant clinical benefits compared with existing therapies. In addition, companies may be developing biosimilars in other countries that could compete with our products. If competitors are able to obtain marketing approval for biosimilars referencing our products, our products may become subject to competition from such biosimilars, with the attendant competitive pressure and consequences ~~.~~Competitors could enter the market with generic versions of Dojolvi or our small- molecule product candidates, which may result in a material decline in sales of affected products. Under the Hatch- Waxman Act, a pharmaceutical manufacturer may file an abbreviated new drug application, or ANDA, seeking approval of a generic copy of an approved **,** innovator **small- molecule** product **such as Dojolvi** . Under the Hatch- Waxman Act, a manufacturer may also submit an NDA under section 505 (b) (2) that references the FDA' s finding of safety and effectiveness of a previously approved ~~drug~~ **innovator small- molecule product** . A 505 (b) (2) NDA product may be for a new or improved version of the original innovator product. Innovative small **-** molecule drugs may be eligible for certain periods of regulatory exclusivity (e. g., five years for new chemical entities, three years for changes to an approved drug requiring a new clinical study, and seven years for orphan drugs), which preclude FDA approval (or in some circumstances, FDA filing and review of) an ANDA or 505 (b) (2) NDA relying on the FDA' s finding of safety and effectiveness for the innovative drug. In addition to the benefits of regulatory exclusivity, an innovator NDA holder may have patents claiming the active ingredient, product formulation or an approved use of the drug, which would be listed with the product in the " Orange Book. " If there are patents listed in the Orange Book, a generic applicant that seeks to market its product before expiration of the patents must include in the ANDA or 505 (b) (2) what is known as a " Paragraph IV certification, " challenging the validity or enforceability of, or claiming non- infringement of, the listed patent or patents. Notice of the certification must be given to the innovator, too, and if within 45 days of receiving notice the innovator sues to enforce its patents, approval of the ANDA is stayed for 30 months, or as lengthened or shortened by the court. ~~Accordingly~~ **During the year ended December 31** , ~~competitors could~~ **2024, Navinta, Aurobindo, and Esjay** ~~file~~ **filed** ANDAs for generic versions of ~~our small~~ **Dojolvi. We have filed a patent infringement suit under the Hatch** - ~~molecule product~~ **Waxman Act against Navinta** , ~~Dojolvi,~~ **Aurobindo and Esjay in the United States District Court** ~~or~~ **for** ~~505 (b) (2) NDAs that reference Dojolvi. For the patents listed for Dojolvi in the Orange Book, those~~ -- **the District of New Jersey in response** ~~ANDAs and 505 (b) (2) NDAs would be required~~ to ~~include a certification as to each listed patent indicating whether~~ the ~~ANDA applicant does~~ **notices. See " Item 3. Legal Proceedings " below** ~~or~~ **for a description of our suit** ~~does not intend to challenge the patent~~ . We cannot predict **the outcome of our suit** ~~how any generic competitor would address such patents~~ , **nor can we predict** whether **there will be additional ANDA filings** ~~we would sue on any such patents, or~~ **for Dojolvi** ~~the outcome of any such suit~~ . There have been a number of recent regulatory and legislative initiatives designed to encourage generic competition for small- molecule pharmaceutical products. For instance, in December 2019, the Creating and Restoring Equal Access to Equivalent Samples Act, or the CREATES Act, was enacted, which provides a legislatively defined private right of action under which eligible product developers can bring suit against companies who refuse to sell sufficient quantities of their branded products on commercially reasonable, market- based terms to support such eligible product developers' marketing applications. It is our policy to evaluate requests for samples of our branded products, and to provide samples in response to bona fide, CREATES Act- compliant requests from qualified third parties, including generic manufacturers. We ~~have received requests for samples of Dojolvi, and when appropriate, we have sold samples of Dojolvi to eligible product developers in compliance with the requirements of the CREATES Act. We~~ may not be successful in securing or maintaining proprietary patent protection for products and technologies we develop or license. Moreover, if any patents that are granted and listed in the Orange Book are successfully challenged by way of a Paragraph IV certification and subsequent litigation, the affected product could more immediately face generic competition and its sales would likely decline materially. For instance, if **the existing ANDA filers or additional** competitors ~~develop generic version of Dojolvi and~~ are able

to enter the market **with generic versions of Dojolvi** , our sales of Dojolvi could materially decline which could have an adverse impact on our financial results. The patent protection and patent prosecution for some of our products and product candidates is dependent on third parties. While we normally seek and gain the right to fully prosecute the patents relating to our products or product candidates, there may be times when patents relating to our products or product candidates are controlled by our licensors. This is the case with our license agreements with KKC and Regeneron, who are primarily responsible for the prosecution of certain patents and patent applications covering Crysvita and Evkeeza, respectively. In addition, we have in- licensed various patents and patent applications owned by the University of Pennsylvania relating to our DTX301, DTX401 and / or UX701 product candidates. Some of these patents and patent applications are licensed or sublicensed by REGENX and sublicensed to us. We do not have the right to control the prosecution of these patent applications, or the maintenance of any of these patents. In addition, under our agreement with REGENX, we do not have the first right to enforce the licensed patents, and our enforcement rights are subject to certain limitations that may adversely impact our ability to use the licensed patents to exclude others from commercializing competitive products. Moreover, REGENX and the University of Pennsylvania may have interests which differ from ours in determining whether to enforce and the manner in which to enforce such patents. If KKC, Regeneron, the University of Pennsylvania, REGENX, or any of our future licensing partners fail to appropriately prosecute, maintain, and enforce patent protection for the patents covering any of our products or product candidates, our ability to develop and commercialize those products or product candidates may be adversely affected and we may not be able to prevent competitors from making, using, and selling competing products. In addition, even where we now have the right to control patent prosecution of patents and patent applications we have licensed from third parties, we may still be adversely affected or prejudiced by actions or inactions of our licensors and their counsel that took place prior to us assuming control over patent prosecution. If we fail to comply with our obligations in the agreements under which we license intellectual property and other rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business. We are a party to a number of intellectual property license agreements that are important to our business and expect to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future license agreements will impose, various diligence, milestone payment, royalty, and other obligations on us. If we fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, we may be required to make certain payments to the licensor, we may lose the exclusivity of our license, or the licensor may have the right to terminate the license, in which event we would not be able to develop or market products covered by the license. Additionally, the milestone and other payments associated with these licenses will make it less profitable for us to develop our product candidates. In certain cases, we control the prosecution of patents resulting from licensed technology. In the event we breach any of our obligations related to such prosecution, we may incur significant liability to our licensing partners. Licensing of intellectual property is of critical importance to our business and involves complex legal, business, and scientific issues. Disputes may arise regarding intellectual property subject to a licensing agreement, including but not limited to: • the scope of rights granted under the license agreement and other interpretation- related issues; • the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement; • the sublicensing of patent and other rights; • our diligence obligations under the license agreement and what activities satisfy those diligence obligations; • the ownership of inventions and know- how resulting from the joint creation or use of intellectual property by our licensors and us and our collaborators; and • the priority of invention of patented technology. If disputes over intellectual property and other rights that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates. ~~We may become~~ **From time to time, we are** involved in lawsuits to protect or enforce our patents or the patents of our licensors, or **may** be subject to claims that challenge the inventorship or ownership of our patents or other intellectual property, which could be expensive, time consuming, and result in unfavorable outcomes. Competitors **have in the past and** may **in the future** infringe our patents or the patents of our licensors. If we or one of our licensing partners were to initiate legal proceedings against a third party to enforce a patent covering our products or one of our product candidates, the defendant could counterclaim that the patent covering our product or product candidate is invalid and / or unenforceable **. For example, in September 2024, we filed a patent infringement suit under the Hatch- Waxman Act against Navinta, Aurobindo and Esjay. See " – Legal Proceedings " below for more information regarding our suit** . In patent litigation in the U. S., defendant counterclaims alleging invalidity and / or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, or non- enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability is unpredictable. Interference proceedings or derivation proceedings now available under the Leahy- Smith Act provoked by third parties or brought by us or declared or instituted by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. In addition, the validity of our patents could be challenged in the USPTO by one of the new post grant proceedings (i. e., inter partes review or post grant review) now available under the Leahy- Smith Act. Our defense of litigation, interference proceedings, or post grant proceedings under the Leahy- Smith Act may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may in the future also be subject to claims that former employees, collaborators, or other third parties have an interest in our patents as an inventor or co- inventor. In addition, we may have ownership disputes arise from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail to successfully defend

against such litigation or claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Even if we are successful in defending against such litigation and claims, such proceedings could result in substantial costs and distract our management and other employees. 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 litigation. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments related to such litigation or claims. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock. We may be subject to claims that our employees, consultants, or independent contractors have wrongfully used or disclosed confidential information of third parties or that our employees have wrongfully used or disclosed alleged trade secrets of their former employers. We employ certain individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Our efforts to vet our employees, consultants, and independent contractors and prevent their use of the proprietary information or know- how of others in their work for us may not be successful, and we may in the future be subject to claims that our employees, consultants, or independent contractors have wrongfully used or disclosed confidential information of third parties. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely impact our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and distract management and other employees. As is the case with other biotechnology and pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology and pharmaceutical industries involves both technological and legal complexity. Therefore, obtaining and enforcing such patents is costly, time consuming, and inherently uncertain. In recent years, the U. S. Supreme Court has ruled on several patent cases, and in some instances, narrowed the scope of patent protection available. In addition, there have been recent proposals for changes to U. S. laws that, if adopted, could impact our ability to obtain or maintain patent protection for our proprietary technologies. Depending on future actions by U. S. courts, U. S. Congress, the USPTO, and the relevant ~~law making~~ **lawmaking** bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents, shorten the term of our existing patents and patents that we might obtain in the future, or impair the validity or enforceability of our patents that may be asserted against our competitors or other third parties. Any of these outcomes could have a material adverse effect on our business ~~. For example, with respect to patent term adjustment (PTA), the Federal Circuit' s recent holding in In re Cellect, LLC, 81 F. 4th 1216 (Fed. Cir. 2023), that the obviousness- type double patenting analysis for a patent that has received PTA must be based on the expiration date of the patent after the PTA has been added, may negatively impact the validity and / or term of certain of our owned or in- licensed U. S. patents~~ . Filing, prosecuting, and defending patents on our products or product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the U. S. can be less extensive than those in the U. S. 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 U. S. Further, licensing partners such as KKC and Regeneron may not prosecute patents in certain jurisdictions in which we may obtain commercial rights, thereby precluding the possibility of later obtaining patent protection in these countries. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the U. S., or from selling or importing products made using our inventions in and into the U. S. or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and may also export infringing products to territories where we have patent protection, but enforcement is not as strong as that in the U. S. These products may compete with our products, 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, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. Risks Related to Our Business Operations We have limited experience as a company operating our own manufacturing facility and may experience unexpected costs or challenges. ~~We completed~~ **Prior to** construction of our **Bedford, Massachusetts** gene therapy manufacturing facility in ~~Bedford, Massachusetts in~~ 2023 ~~. Prior to construction of this facility~~ , we did not previously have experience as a company in operating our own manufacturing facility and at this point, we cannot assure that the facility will be fully utilized at all times **. While** ~~, particularly as we have only recently commenced~~ our **employees may be experienced in running a** manufacturing ~~operations. Our~~ **facility, our** limited experience **as a company** may contribute to unacceptable or inconsistent product quality success rates and yields, and we may be unable to maintain adequate quality control, quality assurance, and qualified personnel. We have incurred and will continue to incur significant expenses and costs to operate the facility, which may be subject to significant impairment if our gene therapy programs are unsuccessful. Before we can begin to commercially manufacture any of our product candidates at the facility, we must obtain regulatory approval from the FDA for our manufacturing processes and for the facility. In order to obtain approval, we will need to ensure that all of our processes, quality systems, methods, equipment, policies and procedures are compliant with cGMP. Until recently, few gene therapy products manufactured by a cGMP gene therapy manufacturing

facility in the U. S. had received approval from the FDA; therefore, the time frame required for us to obtain such approval is uncertain. The cGMP requirements govern quality control of the manufacturing process and documentation policies and procedures. In complying with cGMP, we will be obligated to spend time, money and effort on production, record keeping and quality control to assure that the product meets applicable specifications and other requirements. If we fail to comply with these requirements, we would be subject to possible regulatory action and may not be permitted to sell any products that we may develop. As we seek to optimize and operate our manufacturing process at the facility, we will likely face technical and scientific challenges, considerable capital costs and potential difficulty in recruiting and hiring experienced, qualified personnel at the facility which could result in delays in our production or difficulties in maintaining compliance with applicable regulatory requirements. We may also experience unexpected technical, regulatory, safety, quality or operational issues during manufacturing campaigns. As we expand our commercial footprint to multiple geographies, we may establish multiple manufacturing facilities, which may lead to regulatory delays or prove costly. Even if we are successful, we cannot assure that such additional capacity will be required or that our investment will be recouped. Further, our manufacturing capabilities could be affected by cost- overruns, unexpected delays, equipment failures, lack of capacity, labor shortages, natural disasters, power failures, program failures, actual or threatened public health emergencies, and numerous other factors that could prevent us from realizing the intended benefits of our manufacturing strategy. Our future success depends in part on our ability to retain our Founder, President, and Chief Executive Officer and to attract, retain, and motivate other qualified personnel. We are dependent on Emil D. Kakkis, M. D., Ph. D., our Founder, President, and Chief Executive Officer, the loss of whose services may adversely impact the achievement of our objectives. Dr. Kakkis could leave our employment at any time, as he is an " at will " employee. Recruiting and retaining other qualified employees, consultants, and advisors for our business, including scientific and technical personnel, will also be critical to our success. There is currently a shortage of skilled personnel in our industry, which is likely to continue. As a result, competition for skilled personnel is intense and the turnover rate can be high. In addition, failure to succeed in preclinical or clinical studies may make it more challenging to recruit and retain qualified personnel. ~~Over the last several years, we have also experienced certain executive leadership changes. Leadership transitions are inherently difficult to manage, cause uncertainty and disruption and could increase the likelihood of turnover of other key officers and employees.~~ The inability to recruit and retain qualified personnel, or the loss of the services of Dr. Kakkis or any of other member of our executive leadership team or other key employee, may impede the progress of our research, development, and commercialization objectives. If we fail to obtain or maintain orphan drug exclusivity for our products, our competitors may sell products to treat the same conditions and our revenue will be reduced **. If another party obtains orphan drug exclusivity for a product that is essentially the same as a product we are developing for a particular indication, we may be precluded or delayed from commercializing the product in that indication** . Our business strategy focuses on the development of drugs that are eligible for FDA and EU orphan drug designation. In the U. S., orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical study costs, tax advantages, and user- fee waivers. In addition, if a product receives the first FDA approval for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer is unable to assure sufficient product quantity. In the EU, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity following drug or biological product approval. This period may be reduced to six years if the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. Because the extent and scope of patent protection for our products may in some cases be limited, orphan drug designation is especially important for our products for which orphan drug designation may be available. For eligible drugs, we plan to rely on the exclusivity period under the Orphan Drug Act to maintain a competitive position. If we do not obtain orphan drug exclusivity for our drug products and biologic products that do not have broad patent protection, our competitors may then sell the same drug to treat the same condition sooner than if we had obtained orphan drug exclusivity, and our revenue will be reduced **. Additionally, if a competitor obtains approval of the same drug for the same indication before us, and the FDA grants such orphan drug exclusivity, we would be prohibited from obtaining approval for our product for seven or more years, unless our product can be shown to be clinically superior** . Even though we have orphan drug designation for UX111, UX143, DTX301, DTX401 and UX701 in the U. S. and Europe and for GTX 102 in the U. S., we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical products. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties can be approved for the same condition or the same drug can be approved for a different indication unless there are other exclusivities such as new chemical entity exclusivity preventing such approval. Even after an orphan drug is approved, the FDA or EMA can subsequently approve the same drug with the same active moiety for the same condition if the FDA or EMA concludes that the later drug is safer, more effective, or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process. Our operating results would be adversely impacted if our intangible assets become impaired. We have recorded on our Consolidated Balance Sheets intangible assets for in- process research and development, or IPR & D, related to DTX301 and DTX401 as a result of the accounting for our acquisition of Dimension Therapeutics. We also recorded ~~an~~ intangible ~~asset~~ **assets** related to our ~~license~~ **licenses** ~~from Regeneron~~ for **Dojolvi and** Evkeeza. We test the intangible assets for impairment annually during the fourth quarter and more frequently if events or changes in circumstances indicate that it is more likely than not that the asset is impaired. If the associated research and development effort is abandoned, the related assets will be written-off and we will record a noncash impairment loss on our Consolidated Statement of Operations. We have not recorded any

impairments related to our intangible assets through December 31, ~~2023~~ **2024** . We may not be successful in our efforts to identify, license, discover, develop, or commercialize additional product candidates. The success of our business depends upon our ability to identify, license, discover, develop, or commercialize additional product candidates in addition to the continued clinical testing, potential approval, and commercialization of our existing product candidates. Research programs to identify and develop new product candidates require substantial technical, financial, and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful. Our research programs or licensing efforts may fail to yield additional product candidates for clinical development and commercialization for a number of reasons, including but not limited to the following: • our research or business development methodology or search criteria and process may be unsuccessful in identifying potential product candidates; • we may not be able or willing to assemble sufficient technical, financial or human resources to acquire or discover additional product candidates; • we may face competition in obtaining and / or developing additional product candidates; • our product candidates may not succeed in research, discovery, preclinical or clinical testing; • our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval; • competitors may develop alternatives that render our product candidates obsolete or less attractive; • product candidates we develop may be covered by third parties' patents or other exclusive rights; • the market for a product candidate may change during our program so that such a product may become unreasonable to continue to develop; • 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 regulatory authorities, patients, the medical community, or payors. If any of these events occur, we may be forced to abandon our development efforts for a program or programs, or we may not be able to identify, license, discover, develop, or commercialize additional product candidates, which would have a material adverse effect on our business and could potentially cause us to cease operations. We may expend our limited resources to pursue a particular product, product candidate or indication and fail to capitalize on products, product candidates or indications that may be more profitable or for which there is a greater likelihood of success. Because we have limited financial and managerial resources, we focus our sales, marketing and research programs on certain products, product candidates or for specific indications. As a result, we may forego or delay pursuit of opportunities with other products or product candidates or other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product or product candidate, we may relinquish valuable rights through collaboration, licensing, or other royalty arrangements in cases in which it would have been advantageous for us to retain sole development and commercialization rights or 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. Changes to healthcare and FDA laws, regulations, and policies may have a material adverse effect on our business and results of operations. As described above in " Item 1. Business ~~–~~ – Government Regulation " and in the Risk Factor above entitled " – The insurance coverage and reimbursement status of newly approved products is uncertain " there have been and continue to be a number of legislative initiatives to contain healthcare costs and to modify the regulation of drug and biologic products. We expect that additional state and federal healthcare reform measures and regulations will be adopted in the future, including proposals to reduce the exclusivity protections provided to already approved biological products and to provide biosimilar and interchangeable biologic products an easier path to approval. Any of these measures and regulations could limit the amounts that federal and state governments will pay for healthcare products and services, result in reduced demand for our product candidates or additional pricing pressures and affect our product development, testing, marketing approvals and post-market activities. Failure to comply with laws and regulations could harm our business and our reputation. Our business is subject to **evolving** regulation by various federal, state, local and foreign governmental agencies, including agencies responsible for monitoring and enforcing employment and labor laws, workplace safety, privacy and security laws and regulations, and tax laws and regulations. In certain jurisdictions, these regulatory requirements may be more stringent than those in the U. S., and in other circumstances these requirements may **less** ~~be more~~ stringent **than those** in the U. S. In particular, our operations are directly, and indirectly through our customers, subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti- Kickback Statute, the federal False Claims Act, and physician sunshine laws and regulations; and patient and non- patient privacy regulations, including the GDPR and the California Consumer Privacy Act, or CCPA, including amendments from the California Privacy Rights Act, or CPRA, as described above in " Item 1. Business – Government Regulation ". 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. For instance, one of our programs for sponsored genetic testing to help patients receive an accurate diagnosis was previously the subject of review by applicable governmental authorities of compliance with various fraud and abuse laws. We settled the matter with the governmental authorities for an immaterial settlement amount and without any admission of legal liability. We cannot assure that our other operations or programs will not be subject to review by governmental authorities or found to violate such laws. The GDPR imposes a number of strict obligations and restrictions on the ability to process personal data of individuals, in particular with respect to special categories of personal data like health data (e. g., reliance on a legal basis, information to individuals, notification to relevant national data protection authorities in case of personal data breach and implementation of appropriate security measures). EU member states may also impose additional requirements in relation to special categories of personal data through their national legislation. In addition, the GDPR imposes specific restrictions on the transfer of personal data to countries outside of the EEA that are not considered by the European Commission as providing an adequate level of protection (including the U. S.). Appropriate safeguards are required to enable such transfers (e. g., reliance on standard contractual clauses and transfer risk assessments). There are also several compliance requirements under the federal Health

Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and implementing regulations that create requirements relating to the privacy and security of protected health information. Those requirements are also applicable, in many instances, to business associates of covered entities. In some cases, depending on our business operations and contractual agreements, including through the conduct of clinical trials, we are subject to HIPAA requirements. Also, we may be subject to additional federal, state and local privacy laws and regulations in the U. S., including new and recently enacted laws ~~(such as CCPA and CPRA)~~ , that may apply to us and / or our service providers now or in the future and that require that we take measures to be transparent regarding, honor rights with respect to, and protect the privacy and security of certain information we gather and use in our business, including personal information, particularly personal information that is not otherwise subject to HIPAA. If our operations are found to be in violation of any of the laws described above or any other governmental 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, disgorgement of profits, and the curtailment or restructuring of our operations. If any governmental sanctions, fines, or penalties are imposed, or if we do not prevail in any possible civil or criminal litigation, our business, operating results, financial condition and our reputation could be harmed. In addition, responding to any action will likely result in a significant diversion of management' s attention and resources and an increase in professional fees. Our research and development activities, including our process and analytical development activities in our quality control laboratory, and our and our third- party manufacturers' and suppliers' activities, including activities related to the build- out and operation of our gene therapy manufacturing facility, involve the controlled storage, use, and disposal of hazardous materials, including the components of our product candidates, such as viruses, and other hazardous compounds, which subjects us to laws and regulations governing such activities. In some cases, these hazardous materials and various wastes resulting from their use are stored at our or our manufacturers' facilities pending their use and disposal. We cannot eliminate the risk of contamination, which could cause an interruption of our commercialization efforts, research and development efforts, and business operations or environmental damage that could result in costly clean- up and liabilities under applicable laws and regulations governing the use, storage, handling, and disposal of these materials and specified waste products. We cannot guarantee that the safety procedures utilized by us and our third- party manufacturers for handling and disposing of these materials comply with the standards prescribed by these laws and regulations, or eliminate the risk of accidental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages — and such liability could exceed our resources — and state or federal or other applicable authorities may curtail our use of certain materials and / or interrupt our business operations. Furthermore, environmental laws and regulations are complex, change frequently, and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance. Additionally, as we and our employees increasingly use social media tools as a means of communication with the public, there is a risk that the use of social media by us or our employees to communicate about our products or business may cause to be found in violation of applicable laws, despite our attempts to monitor such social media communications through company policies and guidelines. In addition, our employees may knowingly or inadvertently make use of social media in ways that may not comply with our company policies or other legal or contractual requirements, which may give rise to liability, lead to the loss of trade secrets or other intellectual property, cause reputational harm or result in public exposure of personal information of our employees, clinical trial patients, customers, and others. International expansion of our business exposes us to business, regulatory, political, operational, financial, and economic risks associated with doing business outside of the U. S. Our business strategy includes international expansion. We currently conduct clinical studies and regulatory activities and we also commercialize products outside of the U. S. **An increasing portion of our revenues are based on our international operations, which exposes us to increased financial risks such as longer payment cycles, additional or more burdensome regulatory requirements of financial institutions outside of the U. S. and exposure to foreign currency exchange rate. We may implement currency hedges intended to reduce our exposure to changes in certain foreign currency exchange rates. However, our hedging strategies, if implemented, may not be successful, and any of our unhedged foreign exchange exposures will continue to be subject to market fluctuations. Further, we sell products in countries that face economic volatility and weakness. Although we have historically collected receivables from customers in those countries, continued weakness or additional deterioration of the local economies and currencies may cause customers in those countries to be unable to pay for our products. Additionally, if one or more of these countries were unable to purchase our products, our revenues would be adversely affected.** Doing business internationally involves a number of **additional** risks, including but not limited to: • multiple, conflicting, and changing laws and regulations such as privacy and data regulations, transparency regulations, tax laws, export and import restrictions, employment laws, regulatory requirements, and other governmental approvals, permits, and licenses **; • export and import restrictions, including the impact from new or increased sanctions and tariffs, or threats or changes in policy with respect to sanctions or tariffs, that are contemplated or could be implemented by the current Presidential administration and by other countries against the U. S. in response** ; • introduction of new health authority requirements and / or changes in health authority expectations; • failure by us to obtain and maintain regulatory approvals for the use of our products in various countries; • additional potentially relevant third- party patent rights; • complexities and difficulties in obtaining protection for, 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 on our ability to penetrate international markets; • ~~financial risks, such as longer payment cycles, additional or more burdensome regulatory requirements of financial institutions outside of the U. S., 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 and geopolitical and economic instability, including wars, terrorism, political unrest (including, for example the conflict between Russia and Ukraine, the conflict between Israel and

the surrounding areas, and the rising tensions between China and Taiwan), results of certain elections and votes, actual or threatened public health emergencies and outbreak of disease, ~~rising~~ inflation, ~~the potential recessionary~~ --- **recession** ~~environment, the potential shutdown of the U. S. federal government~~, boycotts and resulting staffing shortages, adoption or expansion of government trade restrictions, and other business restrictions; • certain expenses including, among others, expenses for travel, translation, and insurance; • regulatory and compliance risks that relate to maintaining accurate information and control over commercial operations and activities that may fall within the purview of the U. S. Foreign Corrupt Practices Act, or FCPA, its books and records provisions, or its anti- bribery provisions, including those under the U. K. Bribery Act and similar **anti- corruption** foreign laws and regulations; and • regulatory and compliance risks relating to doing business with any entity that is subject to sanctions administered by the Office of Foreign Assets Control of the U. S. Department of the Treasury. Any of these factors could significantly harm our future international expansion and operations and, consequently, our results of operations. Our **employees or consultants may engage in misconduct or other improper activities, including non- compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation. We are exposed to the risk of employee fraud or other misconduct, including intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide accurate information to the FDA or comparable foreign regulatory authorities, comply with manufacturing standards, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. Employee or consultant misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. This could include violations of HIPAA, other U. S. federal and state law, and requirements of non- U. S. jurisdictions, including the EU Data Protection Directive. It is not always possible to identify and deter employee or consultant 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 governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards, regulations, guidance or codes of conduct. 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 and results of operations, including the imposition of significant fines or other sanctions. The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off- label uses. If we are found to have promoted off- label uses, we may become subject to significant liability. The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription drug products. In particular, a product may not be promoted in the U. S. for uses that are not approved by the FDA as reflected in the product' s approved labeling or prior to regulatory approval. Further, any labeling approved by the FDA for our products or any of our product candidates may include restrictions on use, limit use to specific populations or include various other limitations. The FDA may impose further requirements or restrictions on the distribution or use of any of our other product candidates as part of a REMS plan. Physicians may nevertheless prescribe such products to their patients in a manner that is inconsistent with the approved label provided the company did not promote such use. If we are found to have promoted such off- label uses, we may become subject to significant liability. Similarly, the FDA strictly regulates the promotion of investigational products prior to approval, known as pre- approval promotion. The federal government has levied large civil and criminal fines and / or other penalties against companies for alleged improper promotion and has investigated and / or prosecuted several companies in relation to off- label and / or pre- approval promotion. The FDA has also requested that certain companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed, curtailed or prohibited or have delayed approval of investigational products due to pre- approval conduct. Inappropriate promotional activities may also subject a company to investigations, prosecutions and litigation by other government entities or private citizens Our** business and operations may be materially adversely affected in the event of computer system failures or security breaches. Cybersecurity incidents, including phishing attacks and attempts to misappropriate or compromise confidential or proprietary information or sabotage enterprise IT systems are becoming increasingly frequent and more sophisticated. **Cybersecurity incidents increasingly involve the use of AI and machine learning to launch more automated, targeted and coordinated attacks on targets.** The information and data processed and stored in our technology systems, and those of our strategic partners, CROs, contract manufacturers, suppliers, distributors or other third parties for which we depend to operate our business, may be vulnerable to loss, damage, denial- of- service, unauthorized access or misappropriation. Data security breaches can occur as a result of malware, hacking, business email compromise, ransomware attacks, phishing or other cyberattacks directed by third parties. We, and certain of the third parties for which we depend on to operate our business, have experienced cybersecurity incidents, including third party unauthorized access to and misappropriation of financial information **and clinical data**, and may experience similar incidents in the future. Further, risks of unauthorized access and cyber- attacks have increased as most of our personnel, and the personnel of many third ~~-~~parties with which we do business, have adopted hybrid working arrangements ~~following the COVID- 19 pandemic~~. Improper or inadvertent behavior by employees, contractors and others with permitted access to our systems **, including through the use of generative AI technologies**, pose a risk that sensitive data may be exposed to unauthorized persons or to the public. A system failure or security breach that interrupts our operations or the operations at one of our third- party vendors or partners could result in intellectual property and other proprietary or confidential information being lost or stolen or a material disruption of our drug development programs and commercial operations. For example, the loss of clinical trial data from ongoing or planned 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 results in a loss of or damage to our data or applications, loss of trade secrets or inappropriate disclosure of confidential or

proprietary information, including protected health information, or personal information of employees or former employees, access to our clinical data, or disruption of the manufacturing process, we could incur liability and the further development of our drug candidates could be delayed. Further, we could incur significant costs to investigate and mitigate such cybersecurity incidents **. In addition, there can be no assurance that our insurance coverage will be sufficient to cover the financial, legal, business or reputational losses that may result from a cybersecurity incident** . A security breach that results in the unauthorized access, use or disclosure of personal information also requires us to notify individuals, governmental authorities, credit reporting agencies, or other parties, as applicable, pursuant to privacy and security laws and regulations or other obligations. Such a security breach could harm our reputation, erode confidence in our information security measures, and lead to regulatory scrutiny and result in penalties, fines, indemnification claims, litigation and potential civil or criminal liability. We or the third parties upon whom we depend may be adversely affected by earthquakes or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster. Our corporate headquarters and one of our laboratories are located in the San Francisco Bay Area, and our collaboration partner for Crysvita, KKC, is located in Japan, which have both in the past experienced severe earthquakes and other natural disasters. We do not carry earthquake insurance. Earthquakes or other natural disasters could severely disrupt our operations or those of our collaborators, and have a material adverse effect on our business, results of operations, financial condition, and prospects. We have also experienced power outages as a result of wildfires in the San Francisco Bay Area which are likely to continue to occur in the future. 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 the manufacturing facilities of our third- party contract manufacturers) or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and may be inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business. We may acquire companies or products or engage in strategic transactions, which could divert our management' s attention and cause us to incur various costs and expenses, or result in fluctuations with respect to the value of such investment, which could impact our operating results. We may acquire or invest in businesses or products that we believe could complement or expand our business or otherwise offer growth opportunities. For example, we acquired Dimension in November 2017 and GeneTx in July 2022. The pursuit of potential acquisitions or investments may divert the attention of management and may cause us to incur various costs and expenses in identifying, investigating, and pursuing them, whether or not they are consummated. We may not be able to identify desirable acquisitions or investments or be successful in completing or realizing anticipated benefits from such transactions. We may experience difficulties in assimilating the personnel, operations and products of the acquired companies, management' s attention may be diverted from other business concerns and we may potentially lose key employees of the acquired company. If we are unable to successfully or timely integrate the operations of acquired companies with our business, we may incur unanticipated liabilities and be unable to realize the revenue growth, synergies and other anticipated benefits resulting from the acquisition, and our business, results of operations and financial condition could be materially and adversely affected. The value of our investments in other companies or businesses may also fluctuate significantly and impact our operating results quarter to quarter or year to year. We purchased 7, 825, 797 shares of common stock of Solid in October 2020. Our investment in Solid is being accounted for at fair value, as the fair value is readily determinable. As a result, increases or decreases in the stock price of equity investments have resulted in and will result in accompanying changes in the fair value of our investments, and cause substantial volatility in, our operating results for the reporting period. As the fair value of our investment in Solid is dependent on the stock price of Solid, which has recently seen wide fluctuations, the value of our investments and the impact on our operating results may similarly fluctuate significantly from quarter to quarter and year to year such that period- to- period comparisons may not be a good indication of the future value of the investments and our future operating results. Risks Related to Ownership of Our Common Stock The market price of our common stock may be highly volatile. The market price of our common stock has been, and is likely to continue to be, volatile, including for reasons unrelated to changes in our business. Our stock price could be subject to wide fluctuations in response to a variety of factors, including but not limited to the following: • adverse results or delays in preclinical or clinical studies; • any inability to obtain additional funding; • any delay in filing an IND, NDA, BLA, MAA, or other regulatory submission for any of our product candidates and any adverse development or perceived adverse development with respect to the applicable regulatory agency' s review of that IND, NDA, BLA, MAA, or other regulatory submission; • the perception of limited market sizes or pricing for our products and product candidates; • decisions by our collaboration partners with respect to the indications for our products and product candidates in countries where they have the right to commercialize the products and product candidates; • decisions by our collaboration partners regarding market access and pricing in countries where they have the right to commercialize our products and product candidates; • failure to successfully develop and commercialize our products and product candidates; • the level of revenue we receive from our commercialized products or from named patient sales; • post- marketing safety issues; • failure to maintain our existing strategic collaborations or enter into new collaborations; • failure by us or our licensors and strategic collaboration partners to prosecute, maintain, or enforce our intellectual property rights; • changes in laws or regulations applicable to our products; • any inability to obtain adequate product supply for our products and product candidates or the inability to do so at acceptable prices; • adverse regulatory decisions; • introduction of new products, services, or technologies by our competitors; • changes in or failure to meet or exceed financial projections or other guidance we may provide to the public; • changes in or failure to meet or exceed the financial projections or other expectations of the investment community; • the perception of the pharmaceutical industry or our company by the public, legislatures, regulators, and the investment community; • the perception of the pharmaceutical industry' s approach to drug pricing; • announcements of significant acquisitions, strategic partnerships, joint ventures, or capital

commitments by us, our strategic collaboration partners, or our competitors; • the integration and performance of any businesses we have acquired or may acquire; • disputes or other developments relating to proprietary rights, including patents, litigation matters, and our ability to obtain patent protection for our technologies; • additions or departures of key scientific or management personnel; • significant investigations, regulatory proceedings or lawsuits, including patent or stockholder litigation; • securities or industry analysts' reports regarding our stock, or their failure to issue such reports; • changes in the market valuations of similar companies; • general market, macroeconomic conditions or geopolitical developments, ~~rising~~ **changing interest rates and** inflation ~~, and the potential recessionary environment~~ ; • sales of our common stock by us or our stockholders in the future; and • trading volume of our common stock. In addition, biotechnology and biopharmaceutical companies in particular have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall. We will need additional capital in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities, or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities, or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders. **Pursuant to** ~~In June 2023, we adopted~~ our 2023 Incentive Plan, **as amended** ~~or the 2023 Plan~~ , ~~which replaced our~~ - **or** ~~2014 Incentive Plan, following stockholder approval of~~ the ~~plan. Pursuant to our~~ 2023 Plan, our management is authorized to grant stock options and other equity- based awards to our employees, directors, and consultants. At December 31, ~~2023~~ **2024** , there were ~~5~~ **6** , ~~359~~ **139** , ~~901~~ **766** shares available for future grants under the 2023 Plan. Pursuant to our 2014 Employee Stock Purchase Plan, ~~which was~~ - **as** amended ~~and restated in June 2023~~ , or the A & R ESPP, eligible employees can acquire shares of our common stock at a discount to the prevailing market price. At December 31, ~~2023~~ **2024** , there were 6, ~~609~~ **409** , ~~795~~ **256** shares available for issuance under the A & R ESPP. Our board of directors has adopted an Employment Inducement Plan, which was amended in ~~June~~ **July** ~~2023~~ **2024** , or the Inducement Plan, with a maximum of ~~850~~ **1, 200** , 000 shares available for grant under the plan. At December 31, ~~2023~~ **2024** , there were ~~130~~ **211** , ~~996~~ **628** shares available for issuance under the Inducement Plan. If our board of directors elects to increase the number of shares available for future grant under the 2023 Plan, the A & R ESPP, or the Inducement Plan, our stockholders may experience additional dilution, which could cause our stock price to fall. Provisions in our amended and restated certificate of incorporation and by- laws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders, or remove our current management. Our amended and restated certificate of incorporation, amended and restated by- laws, and Delaware law contain provisions that may have the effect of delaying or preventing a change in control of us or changes in our management. Our amended and restated certificate of incorporation and by- laws include provisions that: • authorize " blank check " preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend, and other rights superior to our common stock; • create a classified board of directors whose members serve staggered three- year terms; • specify that special meetings of our stockholders can be called only by our board of directors or the chairperson of our board of directors; • prohibit stockholder action by written consent; • establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors; • provide that our directors may be removed only for cause; • provide that vacancies on our board of directors may be filled only by a resolution adopted by the board of directors; • expressly authorize our board of directors to modify, alter or repeal our amended and restated ~~by- laws~~ **bylaws** ; and • require holders of 75 % of our outstanding common stock to amend specified provisions of our amended and restated certificate of incorporation and amended and restated by- laws. These provisions, alone or together, could delay, deter, or prevent hostile takeovers and changes in control or changes in our management. In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15 % of our outstanding voting stock to merge or combine with us. Further, no stockholder is permitted to cumulate votes at any election of directors because this right is not included in our amended and restated certificate of incorporation. Any provision of our amended and restated certificate of incorporation or amended and restated by- laws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock. Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the sole and exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees. Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of fiduciary duty owed by any of our directors, officers, or other employees to us or to our stockholders, (3) any action asserting a claim against us arising under the Delaware General Corporation Law or under our amended and restated certificate of incorporation or bylaws, or (4) any action against us asserting a claim governed by the internal affairs doctrine. The choice of forum provision may limit a stockholder' s ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, or other employees, which may discourage such lawsuits against us and our directors, officers, and other employees. Alternatively, if a court were to find the choice of forum provision contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated

with resolving such action in other jurisdictions, which could harm our business, operating results and financial condition. General Risk Factors If we are unable to maintain effective internal control over financial reporting, investors may lose confidence in the accuracy and completeness of our financial reports and the market price of our stock may decrease. The Sarbanes- Oxley Act requires, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures. In particular, we are required to perform system and process evaluation and testing of our internal controls over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting, as required by Section 404 (a) of the Sarbanes- Oxley Act. Section 404 (b) of the Sarbanes- Oxley Act also requires our independent auditors to attest to, and report on, this management assessment. Ensuring that we have adequate internal controls in place so that we can produce accurate financial statements on a timely basis is a costly and time- consuming effort that will need to be evaluated frequently. If we are not able to comply with the requirements of Section 404 or if we or our independent registered public accounting firm are unable to attest to the effectiveness of our internal control over financial reporting, investors may lose confidence in the accuracy and completeness of our financial reports, the market price of our stock could decline and we could be subject to sanctions or investigations by Nasdaq, the SEC, or other regulatory authorities, which would require additional financial and management resources. We may incur additional tax liabilities related to our operations. We have a multinational tax structure and are subject to income tax in the U. S. and various foreign jurisdictions. Our effective tax rate is influenced by many factors including changes in our operating structure, changes in the mix of our earnings among countries, our allocation of profits and losses among our subsidiaries, our intercompany transfer pricing agreements and rules relating to transfer pricing, the availability of U. S. research and development tax credits, and future changes in tax laws and regulations in the U. S. and foreign countries. Significant judgment is required in determining our tax liabilities including management' s judgment for uncertain tax positions. The Internal Revenue Service, other domestic taxing authorities, or foreign taxing authorities may disagree with our interpretation of tax laws as applied to our operations. Our reported effective tax rate and after- tax cash flows may be materially and adversely affected by tax assessments in excess of amounts accrued for our financial statements. This could materially increase our future effective tax rate thereby reducing net income and adversely impacting our results of operations for future periods. Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited. We have incurred substantial losses during our history. To the extent that we continue to generate taxable losses, unused taxable losses will, subject to certain limitations, carry forward to offset future taxable income, if any, until such unused losses expire. Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the IRC, if a corporation undergoes an " ownership change, " generally defined as a greater than 50 % change (by value) in its equity ownership over a three- year period, the corporation' s ability to use its pre- change net operating loss carryforwards, or NOL carryforwards, and other pre- change tax attributes (such as research tax credits) to offset its post- change income may be limited. An analysis to determine limitations upon our NOL carryforwards and other pre- change tax attributes for ownership changes that have occurred previously has been performed, resulting in a permanent decrease of federal and state NOL carryforwards in the amount of $ 7. 2 million and a permanent decrease in federal research tax credit carryforwards in the amount of $ 0. 2 million. As a result of these decreases and others that may occur as a result of future ownership changes, our ability to use our pre- change NOL carryforwards and other tax attribute carryforwards to offset U. S. federal taxable income and tax liabilities is limited and may become subject to even greater limitations, which could potentially accelerate or permanently increase future federal tax liabilities for us. In addition, there may be periods during which the use of state income tax NOL carryforwards and other state tax attribute carryforwards (such as state research tax credits) are suspended or otherwise limited, which could potentially accelerate or permanently increase future state tax liabilities for us. Litigation may substantially increase our costs and harm our business. We have been, and may in the future become, party to lawsuits including, without limitation, actions, claims and proceedings in the ordinary course of business relating to our directors, officers, stockholders, intellectual property, and employment matters and policies, which will cause us to incur legal fees and other costs related thereto, including potential expenses for the reimbursement of legal fees of officers and directors under indemnification obligations. **For example, we have been defending a lawsuit filed in the U. S. District Court for the District of Maryland by the Estate of Henrietta Lacks alleging unjust enrichment arising from our receipt and use of HeLa cells.** The expense of defending against such claims or litigation may be significant and there can be no assurance that we will be successful in any defense. Further, the amount of time that may be required to resolve such claims or lawsuits is unpredictable, and these actions may divert management' s attention from the day- to- day operations of our business, which could adversely affect our business, results of operations, and cash flows. Litigation is subject to inherent uncertainties, and an adverse result in such matters that may arise from time to time could have a material adverse effect on our business, results of operations, and financial condition. Our business and operations could be negatively affected if we become subject to stockholder activism or hostile bids, which could cause us to incur significant expense, hinder execution of our business strategy and impact our stock price. Stockholder activism, which takes many forms and arises in a variety of situations, has been increasingly prevalent. Stock price declines may also increase our vulnerability to unsolicited approaches. If we become the subject of certain forms of stockholder activism, such as proxy contests or hostile bids, the attention of our management and our board of directors may be diverted from execution of our strategy. Such stockholder activism could give rise to perceived uncertainties as to our future strategy, adversely affect our relationships with business partners and make it more difficult to attract and retain qualified personnel. Also, we may incur substantial costs, including significant legal fees and other expenses, related to activist stockholder matters. Our stock price could be subject to significant fluctuation or otherwise be adversely affected by the events, risks and uncertainties of any stockholder activism. Increased scrutiny regarding ESG practices and disclosures **, as well as existing and proposed laws related to these topics,** could result in additional costs and adversely impact our business and reputation. Companies across all industries are facing increasing scrutiny relating to their Environmental, Social and Governance, or " ESG, " practices and disclosures and institutional and individual investors are increasingly using ESG screening criteria in making investment

decisions. Investors who are focused on ESG matters may seek enhanced ESG disclosures or to implement policies adverse to our business, and there can be no assurances that stockholders will not advocate, via proxy contests, media campaigns or other public or private means, for us to make corporate governance changes or engage in certain corporate actions. Our disclosures on these matters or a failure to satisfy evolving stakeholder expectations for ESG practices and reporting may potentially harm our reputation and impact employee retention and access to capital. In addition, our failure, or perceived failure, to pursue or fulfill our goals, targets, and objectives or to satisfy various reporting standards within the timelines we announce, or at all, could expose us to government enforcement actions and private litigation. Our ability to achieve any goal or objective, including with respect to environmental and ~~diversity~~ **culture** initiatives and compliance with ESG reporting standards, is subject to numerous risks, many of which are outside of our control. Examples of such risks include the availability and cost of technologies and products that meet sustainability and ethical supply chain standards, evolving regulatory requirements affecting ESG standards or disclosures, our ability to recruit, develop, and retain ~~diverse~~ talent in our labor markets, and our ability to develop reporting processes and controls that comply with evolving standards for identifying, measuring and reporting ESG metrics. As ESG best-practices, reporting standards, and disclosure requirements continue to develop, we may incur increasing costs related to maintaining or achieving our ESG goals in addition to ESG monitoring and reporting. ~~65~~