Risk Factors Comparison 2024-02-28 to 2023-02-27 Form: 10-K

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An investment in our ordinary shares involves a high degree of risk. You should carefully consider the following information about these risks, together with the other information appearing elsewhere in this Annual Report on Form 10- K, including our financial statements and related notes thereto, before deciding to invest in our ordinary shares. We operate in a dynamic and rapidly changing industry that involves numerous risks and uncertainties. The risks and uncertainties described below are not the only ones we face. Other risks and uncertainties, including those that we do not currently consider material, may impair our business. If any of the risks discussed below actually occur, our business, financial condition, operating results, or cash flows could be materially adversely affected. This could cause the value of our securities to decline, and you may lose all or part of your investment. Risks Related to the ~~Current Covid Pandemic Our business, operations, human resources and supply chain have been, and may continue to be, materially and adversely affected by the ongoing Covid pandemic. On March 11, 2020, the World Health Organization (" WHO ") declared the ongoing outbreak of coronavirus disease (" Covid ") a pandemic. The Covid pandemic is affecting the U. S. and global economies and has affected and may continue to affect our operations and those of third parties on which we rely. The Covid pandemic has caused and may continue to cause disruptions in our raw material supply, our commercial- scale manufacturing capabilities for AAV- based gene therapies, the development of our product candidates, employee productivity and the conduct of current and future clinical trials. In addition, the Covid pandemic has affected and may continue to affect the operations of the FDA, EMA, and other health authorities, which could result in delays of reviews and approvals, including with respect to our product candidates. Global supply chains have been disrupted, causing shortages, which could further impact our clinical trials. This disruption of our employees, distributors and suppliers has historically impacted and may continue to impact our future operating results. Additionally, to the extent that inspections of facilities by governmental authorities are required, the review of our marketing applications or supplements may further be delayed as regulatory authorities, such as FDA, have significantly limited facility inspections during the pandemic. We may also be subject to further laws, regulations, guidelines, executive orders and other requirements at the federal, state and local levels related to the pandemic, which we may be required to undertake or that we choose to undertake. Any such requirements or guidelines that we adopt could have a material impact on our business operations. Risks Related to the~~ Development of Our Product Candidates ~~Our~~ **We are dependent on the success of our lead product candidate in clinical development, AMT- 130 for the treatment of Huntington' s disease. A failure of AMT- 130 in clinical development, challenges associated with its regulatory pathway, or its inability to demonstrate sufficient efficacy to warrant further clinical development could adversely affect our business. We have invested a significant portion of our development efforts and financial resources in the development of our lead clinical product candidate, AMT- 130. In December 2023, we announced updated interim data from our ongoing Phase I / II clinical trials of AMT- 130, including 30 months of follow- up data from the 39 patients then enrolled in our trials in the U. S. and in Europe. We also announced our plans to continue enrollment in a third cohort to investigate AMT- 130 in combination with perioperative immune suppression to evaluate near- term safety, along with our plans to initiate regulatory interactions with the FDA and EMA to discuss the interim data and strategies for ongoing development of AMT- 130. There are numerous factors that could impede or otherwise negatively impact our further development of AMT- 130, including, but not limited to, patient safety issues, our failure to demonstrate sufficient clinical efficacy or durability of response data to warrant further development, delays in our ability to enroll patients or challenges with regulatory authorities. Any one or combination of these factors could force us to halt or discontinue the ongoing clinical trials of AMT- 130. Certain of these risk factors are heightened in the context of drug development for rare diseases like Huntington' s disease in which non- traditional study designs are utilized to demonstrate efficacy and safety, including open- label studies, single arm studies, studies utilizing active comparators or natural history data, biomarkers or other forms of surrogate endpoints, which may be utilized due to the challenges inherent in designing and conducting clinical trials for severe diseases that progress slowly and that affect small patient populations. For example, in the course of our interactions with the FDA and EMA, the regulatory authorities may disagree with our interpretation of the interim safety and efficacy data we have received to date. Since AMT- 130 is based on our novel gene therapy technology, we are unable predict how regulatory authorities will interpret our data or whether they will agree with our interim conclusions or trial design or whether those data may be utilized in later- stage or registrational trials. We may be required by such regulatory authorities to conduct additional randomized studies of AMT- 130 beyond our existing clinical trials, which would be costly and would significantly delay the potential approval of AMT- 130. We may not be able to commit sufficient capital to support additional clinical studies of AMT- 130, in which case we may need to secure a development partner for AMT- 130. Such partnerships may not be available, in which case we may not be able to fully fund the AMT- 130 program. If AMT- 130 fails in development as a result of any underlying problem with our technology, then we may be required to discontinue development of other** product candidates **that are based on ~~in development have not yet been approved for commercial sale and they~~ the ~~might never~~ same novel therapeutic approach. We cannot be certain that AMT- 130, or any of our product candidates, will be successful in clinical trials or** receive regulatory approval ~~or become commercially viable~~. **If we were required to, ~~We have never generated any significant revenue from product sales and may never be profitable. Our pipeline consists of product candidates in research~~** or **if we chose to, discontinue** development ~~that have not been approved for commercial sale. We have not generated any revenues from the sale~~ of ~~products or manufacturing of a product for a third party and do not expect to generate any such~~

~~revenue until this year, at the earliest. Our product candidates including~~ AMT- 130 ~~and~~ **or** any ~~of our~~ other ~~potential~~ **future** product candidates ~~will require extensive preclinical and / or clinical testing~~ , **or** ~~manufacture development and regulatory approval prior to commercial use. Our research and development efforts may not be successful. Even~~ if **any of them were to fail to** ~~our clinical development efforts result in positive data, our product candidates may not~~ receive regulatory approval or **achieve sufficient** ~~be successfully introduced and marketed~~ -- **market** ~~at prices that~~ **acceptance, we could be prevented from or significantly delayed in achieving profitability and our business** would **be adversely affected** ~~permit us to operate profitably~~ . We have encountered and may encounter future delays in and impediments to the progress of our clinical trials or fail to demonstrate the safety and efficacy of our product candidates. **Drug** ~~Clinical and non- clinical~~ development is expensive, time- consuming, and uncertain as to **the** outcome. Our product candidates are in different stages of clinical or preclinical development, and there is a significant risk of failure or delay in each of these programs **. We are currently conducting Phase I / II clinical trials in the U. S. and Europe for AMT- 130, our investigational gene therapy for the treatment of Huntington' s disease. We are also advancing three other product candidates into clinical development – AMT- 260 for the treatment of refractory mesial temporal lobe epilepsy, AMT- 162 for the treatment of SOD1- ALS and AMT- 191 for the treatment of Fabry disease. We have experienced clinical setbacks in the past and may experience setbacks in the future** . For example, we experienced an immaterial but unexpected delay when our clinical trials of HEMGENIX ~~™~~ ® were placed on clinical hold by the FDA from December 2020 to April 2021 ~~,~~ following a preliminary diagnosis of hepatocellular carcinoma in one patient. Similarly, we experienced an unexpected delay in the enrollment of our Phase Ib / II clinical trial **of AMT- 130** for **the treatment of** Huntington' s disease between July and October 2022 **due to** ~~as a result of~~ our voluntary postponement and comprehensive safety investigation into suspected unexpected serious adverse reactions in three patients. ~~We cannot guarantee that any preclinical tests or clinical trials will be completed as planned or completed on schedule, if at all.~~ A failure of one or more ~~preclinical tests or~~ clinical trials can occur at any stage **and for a variety** of ~~testing~~ **reasons that we cannot predict with accuracy and that are out of our control** . Events that may prevent successful or timely completion of clinical development, as well as product candidate approval, include, but are not limited to: ● occurrence of serious adverse events associated with a product candidate that are viewed to outweigh its potential benefits; ● **insufficient number of patients treated with the product candidate or study period for assessing the effectiveness of the product candidate insufficient in length to assess potential clinical development; ● failures or** delays in reaching **agreement** ~~a consensus~~ with regulatory agencies on study design **, particularly with respect to our novel gene therapies for which regulatory pathways remain untested** ; ● **failures or delays in hiring sufficient personnel with the requisite expertise to execute multiple clinical programs simultaneously; ● failures or** delays in reaching agreement on acceptable terms with ~~prospective~~ clinical research organizations (" CROs ") and clinical trial sites; ● **failures or delays in patient recruiting into clinical trials or in the addition of new investigators; ●** delays in receiving regulatory authorization to conduct ~~the~~ **our** clinical trials or a regulatory authority decision that the clinical trial should not proceed; ● **failures or** delays in obtaining or failure to obtain required IRB and IBC approval at each clinical trial site; ● requirements of regulatory authorities, IRBs, or IBCs to modify a study in such a way that it makes the study impracticable to conduct; ● regulatory authority requirements to perform additional or unanticipated clinical trials **or testing** ; ● changes in standards of care which may necessitate the modification of our clinical trials or the conduct of new trials; ● regulatory authority refusal to accept data from foreign clinical study sites; ● disagreements with regulatory authorities regarding our study design, including endpoints, our chosen indication, ~~or~~ **our chosen bases for comparison as it relates to clinical efficacy,** our interpretation of data from preclinical studies and clinical trials or a finding that a product candidate' s benefits do not outweigh its safety risks; ● recommendations from DSMBs to discontinue, pause, or modify the trial; ● imposition of a clinical hold by regulatory agencies after an inspection of our clinical trial operations or trial sites; ● suspension or termination of clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks, undesirable side effects, or other unexpected characteristics (alone or in combination with other products) of the product candidate, or due to findings of undesirable effects caused by a chemically or mechanistically similar therapeutic or therapeutic candidate; ● failure by CROs, other third parties or us to adhere to clinical trial requirements or otherwise properly manage the clinical trial process, including meeting applicable timelines, properly documenting case files, including the retention of proper case files, and properly monitoring and auditing clinical sites; ● failure of sites or clinical investigators to perform in accordance with Good Clinical Practice or applicable regulatory guidelines in other countries; ● failure of patients to abide by clinical trial requirements; ● ~~difficulty or delays in patient recruiting into clinical trials or in the addition of new investigators; ●~~ delays or deviations in the testing, validation, manufacturing, and delivery of our product candidates to the clinical sites; ● delays in having patients complete participation in a study or return for post- treatment follow- up; ● clinical trial sites or patients dropping out of a study; ● the number of patients required for clinical trials of our product candidates being larger than we anticipate; ● clinical trials producing negative or inconclusive results, or our studies failing to reach the necessary level of statistical significance, requiring that we conduct additional clinical trials or abandon product development programs; ● interruptions in manufacturing clinical supply of our product candidates or issues with manufacturing product candidates that meet the necessary quality requirements; ● unanticipated clinical trial costs or insufficient funding, including **paying** ~~to pay~~ substantial application user fees; ● ~~occurrence of serious adverse events or other undesirable side effects associated with a product candidate that are viewed to outweigh its potential benefits; ● disagreements with regulatory authorities regarding the interpretation of our clinical trial data and results, or the~~ emergence of new information about or impacting our product candidates **or the field of gene therapy** ; ● **with respect to the product candidates for which we manufacture drug product in- house,** determinations that there are issues with our manufacturing facility or process; or ● changes in regulatory requirements and guidance, as well as new, revised, postponed, or frozen regulatory requirements (such as the EU Clinical Trials Regulation), that require amending or submitting new clinical protocols, undertaking additional new tests or analyses, or submitting new types or amounts of clinical data. Before

obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidates in humans. Such trials and regulatory review and approval take many years. It is impossible to predict when or if any of our clinical trials will demonstrate that product candidates are effective or safe in humans. If the results of our clinical trials are inconclusive, or fail to meet the level of statistical significance required for **regulatory** approval or if there are safety concerns **, concerns around durability of response** or **other** adverse events associated with our product candidates, we may: ● be delayed in or altogether prevented from obtaining marketing approval for our product candidates; ● obtain approval for indications or patient populations that are not as broad as intended or desired; ● obtain approval with labeling that includes significant use or distribution restrictions ~~or~~ **,** safety warnings **, labeling statements or contraindications** ; ● be subject to changes ~~with~~ **in** the way ~~the~~ **our** ~~product~~ **products** ~~is~~ **are** administered; ● be required to perform additional clinical trials to support approval or be subject to additional post- marketing testing requirements; ● have regulatory authorities withdraw their approval of the product or impose restrictions on its distribution in the form of a modified risk evaluation and mitigation strategy; ● be subject to **legal action or** ~~the~~ **other challenges** ~~addition of labeling statements, such as warnings or contraindications; ● be sued~~ ; or ● experience damage to our reputation. Because of the nature of the gene therapies we are developing, regulators may also require us to demonstrate long- term gene expression, clinical efficacy **,** and safety, which may require additional or longer clinical trials **for** ~~, and~~ which **we** may not be able to **meet** ~~be demonstrated to~~ the regulatory authorities' standards. Our ability to recruit patients for our **clinical** trials is ~~often~~ **heavily** reliant on third parties, such as clinical trial sites. Clinical trial sites may not have the adequate infrastructure established to handle **the administration of our** gene therapy products **, related surgeries or other means of product administration,** or may have difficulty finding eligible patients to enroll into a **clinical** trial **, which may delay or impede our planned trials** . In addition, we ~~,~~ or any **of our** collaborators ~~we may have~~ may not be able to locate and enroll enough eligible patients to participate in these trials as required by the FDA, the EMA or similar regulatory authorities outside the U. S. and the European Union. This may result in our failure to initiate or continue clinical trials for our product candidates or may cause us to abandon one or more clinical trials altogether. Because our programs are focused on the treatment of patients with rare or orphan or ultra- orphan diseases, our ability to enroll eligible patients in these trials may be limited or slower than we anticipate considering the small patient populations involved and the specific age range required for treatment eligibility in some indications. In addition, our potential competitors, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions, may seek to develop competing therapies, which would further limit the small patient pool available for our studies. Also, patients may be reluctant to enroll in gene therapy trials where there are other therapeutic alternatives available or that may become available ~~, which may be~~ for various reasons **,** including **, but not limited to,** uncertainty about the safety or effectiveness of a new therapeutic such as a gene therapy and the possibility that treatment with a gene therapy therapeutic could preclude future gene therapy treatments due to the formation of antibodies following and in response to the treatment. Any inability to successfully initiate or complete preclinical and clinical development could result in additional costs to us or impair our ability to receive marketing approval, to generate revenues from product sales or obtain regulatory and commercialization milestones and royalties. In addition, if we make manufacturing or formulation changes to our product candidates, including changes in the vector or manufacturing process used, we may need to conduct additional studies to bridge our modified product candidates to earlier versions. It is also possible that any such manufacturing or formulation changes may have an adverse impact on the performance of the product candidate. Clinical trial delays could also shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may materially harm our business, financial condition, and results of operations. Our progress in early- stage clinical trials may not be ~~indicative~~ **predictive** of long- term efficacy in late- stage clinical trials, and our progress in trials for one product candidate may not be ~~indicative~~ **predictive** of progress in trials for other product candidates ~~. Study designs and results from previous studies are not necessarily predictive of our future clinical study designs or results, and initial, top- line, or interim results may not be confirmed upon full analysis of the complete study data~~ . Our product candidates may fail to show the required level of safety and efficacy in later stages of clinical development despite having successfully advanced through initial clinical studies. **For example, the results from early clinical trials of AMT- 130, our product candidate targeting Huntington' s disease, may not be predictive of the results of later- stage trials. In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the clinical trial protocols and the rate of dropout among clinical trial participants. Moreover, should there be an issue with the design of any of our clinical trials, our results may be impacted. We may not discover such a flaw until the clinical trial is at an advanced stage.** Changes to product candidates **, whether as a result of regulatory feedback or changes in clinical trial procedures and protocols,** may also impact their performance in subsequent studies. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later- stage clinical trials even after achieving promising results in early- stage clinical trials. If a larger population of patients does not experience positive results during **our** clinical trials, if ~~these~~ -- **the** results are not reproducible or if our products show diminishing activity over time, our product candidates may not receive approval from the FDA ~~or~~ **,** EMA **or comparable regulatory authorities** . Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit, or prevent regulatory approval. In addition, we may encounter regulatory delays or rejections because of many factors, including changes in regulatory policy during the period of product development. Failure to confirm favorable results from earlier trials by demonstrating the safety and effectiveness of our products in later- stage clinical trials with larger patient populations could have a material adverse effect on our business, financial condition, and results of operations. ~~Fast track~~ **Interim or preliminary data from studies or trials announced or published from time to**

time may change as more data become available and are subject to audit and verification procedures that could result in material changes in the final data. From time to time, we publicly disclose interim or preliminary data from preclinical studies and clinical trials, which are based on a preliminary analysis of then- available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data, the particular study, or trial. We also make assumptions, estimations, calculations, and conclusions as part of our preliminary or interim analyses of data, and we may not have received or had the opportunity to evaluate all data at that time. As a result, the interim or preliminary data that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results once additional data have been received and fully evaluated. Interim or preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, preliminary or interim data should be viewed with caution until the final data are available. From time to time, we also disclose interim data from our preclinical studies and clinical trials. For example, in December 2023, we announced updated interim data from our ongoing Phase I / II clinical trial of AMT- 130, along with our expectation that we will present additional clinical updates with respect to AMT- 130 in the future. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Significant differences between interim data and final data could seriously harm our business. Third parties, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions, or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and ~~, breakthrough therapy, priority review, or~~ our ~~RMAT designation~~ company in general. For example, we plan to initiate regulatory interactions in the first half of 2024 to discuss the U. S. and European data from our ongoing Phase I / II clinical trial of AMT- 130 and potential strategies for ongoing development of AMT- 130. These regulatory authorities may not agree with the assumptions, estimates, calculations, conclusions or analyses underlying the interim data from our ongoing clinical trial of AMT- 130 or any of our future proposals regarding the ongoing development of AMT- 130. Even if the data supporting such regulatory interactions are suggestive of clinical responses, the durability of response may not be sustained over time or may not be sufficient to support regulatory approval. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure. Any information we determine not to disclose may ultimately be deemed significant by ~~the FDA~~ you or others with respect to future decisions , conclusions, views, activities or otherwise regarding a particular product candidate or ~~or~~ our ~~access to~~ business. If the ~~PRIME scheme by the EMA~~ preliminary or interim data that we report differ from final results , or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for ~~our~~ , and commercialize, product candidates may be harmed, which could seriously harm our business. We are making use of exploratory biomarkers and other data that are not scientifically validated, and our reliance on these data may lead us to direct our resources inefficiently. We are making use of experimental biological markers, or biomarkers, in an effort to facilitate our drug development and to optimize our clinical trials. Biomarkers are proteins or other substances which can serve as an indicator of specific cell processes or as evidence of a patient' s biological response to drug product administration. For example, with respect to our ongoing clinical trials of AMT- 130, we are measuring NfL in cerebrospinal fluid (" CSF ") as a potential indicator of neurodegeneration, as well as the pharmacodynamics of mHTT in CSF and changes in total brain volume of patients treated with AMT- 130. While we believe that these biomarkers and data may serve useful purposes for us, including in the evaluation of whether our product candidates are having their intended effects through their assumed mechanisms of action, improving patient selection and monitoring patient compliance with trial protocols, these biomarkers and data have not been scientifically validated and are considered experimental as used in our trials. If our understanding and use of biomarkers is inaccurate or flawed, or if our reliance on specific biomarkers such as NfL and mHTT is otherwise misplaced, then we may fail to realize any benefits from using these data and may also be led to invest time and financial resources inefficiently in attempting to develop inappropriate drug candidates. We may not be successful in our efforts to use our gene therapy technology platform to build a pipeline of additional product candidates or otherwise leverage our research and technology to remain competitive. An element of our strategy is to use our gene therapy technology platform to expand our product pipeline and to progress our product candidates through preclinical and clinical development ourselves or together with collaborators. To date, we have only been successful in obtaining regulatory approval for one product, HEMGENIX ®, our gene therapy for the treatment of hemophilia B, which was approved for commercialization by the FDA and the EMA in November 2022 and February 2023, respectively. AMT- 130 is our investigational gene therapy candidate for the treatment of Huntington' s disease that utilizes our proprietary, gene-silencing miQURE platform and incorporates an AAV vector carrying a miRNA specifically designed to silence the huntingtin gene and the potentially highly toxic exon 1 protein fragment, which is currently in ongoing Phase I / II studies in the U. S. and Europe. In addition to AMT- 130, we are also developing other investigational gene therapies, including AMT- 260 for the treatment of MTLE, AMT- 162 for the treatment of SOD1 ALS and AMT- 191 for the treatment of Fabry' s disease. Although we currently have a pipeline of programs at various stages of development, including an approved product, we may not be able to identify or develop product candidates that are safe and effective. Even if we are successful in continuing to build our pipeline, the potential product candidates that we identify may not be suitable for clinical development. Research programs to identify new product candidates require substantial technical, financial, and human resources. Due to the significant resources required for the development of our product candidates,

we must decide which product candidates to pursue and advance and the resources to allocate to each. For example, as a result of the Reorganization, we discontinued investments in certain of our prior research and development programs, including AMT- 210 for the treatment of Parkinson' s disease, and certain other technology projects, prioritizing instead our early clinical- stage programs, including AMT- 130, AMT- 260, AMT- 162 and AMT- 191. Our decisions concerning the allocation of research, development, collaboration, management, and financial resources toward particular product candidates, including the decisions stemming from our Reorganization, may not lead to ~~faster~~ **the** development **of any viable commercial product and may divert resources away from better opportunities. We or any collaborators may focus** ~~or~~ **our Our gene therapy approach utilizes vectors derived from viruses,which may be perceived as unsafe or may result in unforeseen adverse events.Negative public opinion and increased regulatory scrutiny of gene therapy may damage public perception of the safety of our product and product candidates and adversely affect our ability to conduct our business or obtain regulatory approvals for our product candidates.Gene therapy** remains a ~~concern for gene therapy,and we cannot guarantee~~ **novel technology.Public perception may be influenced by claims** that **gene therapy is unsafe,and gene therapy may** ~~patients treated in any of our planned or future clinical studies will~~ not **gain the acceptance** ~~develop cancer as a result~~ of **the public** ~~being treated with our~~ **or** ~~product candidates.In addition,there~~ **the medical community** ~~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~~ .Public and medical community adoption of any of our gene therapies will **also** depend on ~~other~~ factors ~~,~~ including the ease of administration in comparison to other therapeutics ~~and the extent to which our therapies are successful in slowing disease progression if not acting as a cure for the disease~~ . ~~For~~ **By** example,the need for ~~lengthy and~~ complex surgeries for the administration of a product candidate may impact the acceptance of a product.In particular,our success will depend upon physicians who specialize in the treatment of genetic diseases targeted by our ~~products~~ **product and product candidates,** prescribing treatments that involve the use of our ~~products~~ **product and product candidates,** in lieu of,or in addition to,existing treatments with which they are familiar and for which greater clinical data may be available.More restrictive government ~~regulation~~ **regulations** ~~of gene therapies~~ or negative public opinion ~~may~~ **would** have an adverse effect on our business,financial condition,results of operations and prospects and may delay or impair the development and commercialization of our product candidates or demand for any products we may develop.For example,earlier gene therapy trials led to several well- publicized adverse events,including cases of leukemia and death seen in other trials using other vectors.Serious adverse events in our clinical trials,or other clinical trials involving gene therapy products or our competitors' products,even if not ultimately attributable to the relevant product candidates,and the resulting publicity,could result in increased government regulation,unfavorable public perception,potential regulatory delays in the testing or approval of our product candidates,stricter labeling requirements for those product candidates that are approved and a decrease in demand for any products for which we obtain marketing approval. ~~A small number of~~ regulatory review ~~or~~ **for each submitted product application, may cause delays in the approval or rejection of an application. Regulatory authorities may also be delayed in completing their review of any marketing applications submitted by us or our partners. Regulatory authorities have substantial discretion in the** approval process ~~,~~ and ~~it does~~ **may refuse to accept any application, may decide that our data are insufficient for approval, may require additional preclinical, clinical, or other studies and may** not ~~increase~~ **complete** ~~the~~ **their** ~~likelihood~~ **review in a timely manner. Further, any marketing approval we ultimately obtain may be for only limited indications or be subject to stringent labeling or other restrictions or post- approval commitments** that **render the approved product not commercially viable. The risks associated with the marketing approval process are heightened by the status of** our **products as gene therapies. We believe that all our current** product candidates will ~~receive~~ **be viewed as gene therapy products by the applicable regulatory authorities. While there are several gene therapy product candidates under development in the U. S., the FDA has only approved a limited number of gene therapy products, to date. Accordingly, regulators like the FDA may have limited experience with the review and approval of** marketing ~~.Further,any marketing approval we ultimately obtain may be for only limited indications or be subject to stringent labeling or other restrictions or post- approval commitments that render the approved product not commercially viable.The risks associated with the marketing approval process are heightened by the status of our products as gene therapies.We believe that all our current product candidates will be viewed as gene therapy products by the applicable regulatory authorities.While there are a number of gene therapy product candidates under development,in the U.S.,the FDA has only approved a limited number of gene therapy products,to date.Accordingly,regulators,like the FDA,may have limited experience with the review and approval of marketing~~ applications for gene therapy products **,which may adversely affect the approval prospects for our product candidates** .Both the FDA and the EMA have demonstrated caution in their regulation of gene therapy treatments,and ethical and legal concerns about gene therapy and genetic testing may result in additional regulations or restrictions on the development and commercialization of our product candidates that are difficult to predict.The FDA and the EMA have issued various guidance documents pertaining to gene therapy products, ~~with~~ which ~~we~~ **will** likely ~~must comply~~ **be applicable** to ~~gain regulatory approval of any of~~ our product candidates **prior to our obtaining regulatory approval** in the U.S.or **the** EU ~~,respectively~~ .The close regulatory scrutiny of gene therapy products may result in delays and increased costs and may ultimately lead to the failure to obtain approval for any gene therapy product **.Experiences with existing gene therapies,including any emergent adverse effects,could also impact how the FDA and the EMA view our products and product candidates,making it harder to obtain or maintain regulatory approvals** .Regulatory requirements affecting gene therapy have changed frequently and continue to evolve,and agencies at both the U.S.federal and state level,as well as congressional committees and foreign governments,have sometimes expressed interest in further regulating biotechnology.In the U.S.,there have been a number of ~~recent~~ changes relating to gene therapy development.By example,FDA issued a number of ~~new~~ guidance documents,and continues to issue guidance documents,on human gene therapy development,one of which was specific to human gene therapy

for hemophilia,one that was specific to neurodegenerative diseases,and another of which was specific to rare diseases.Moreover,the European Commission conducted a public consultation in early 2013 on the application of EU legislation that governs advanced therapy medicinal products,including gene therapy products,which could result in changes in the data we need to submit to the EMA for our product candidates to gain regulatory approval or change the requirements for tracking,handling and distribution of the products which may be associated with increased costs.In addition,divergent scientific opinions among the various bodies involved in the review process may result in delays,require additional resources,and ultimately result in rejection.The FDA,EMA,and other regulatory authorities will likely continue to revise and further update their approaches to gene therapies in the coming years.These regulatory agencies,committees and advisory groups and the new regulations and guidelines they promulgate may lengthen the regulatory review process,require us to perform additional studies,increase our development costs,lead to changes in regulatory positions and interpretations,delay or prevent approval and commercialization of our product candidates or **lead to significant post- approval limitations or restrictions.Delay or failure to obtain,or unexpected costs in obtaining,the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product revenues to maintain our business.We may use certain specialized pathways to develop our product candidates or to seek regulatory approval.We may not qualify for these pathways,or such pathways may not ultimately speed the time to approval or result in product candidate** approval. We have obtained and may in the future seek one or more ~~of~~ fast **-** track ~~designation~~ **designations**, breakthrough therapy designation, RMAT designation, PRIME scheme access or priority review designation for our product candidates. A fast **-** track product designation is designed to facilitate the clinical development and expedite the review of drugs intended to treat a serious or life- threatening condition and which demonstrate the potential to address an unmet medical need. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life- threatening disease or condition, where preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. ~~A~~ **An** RMAT designation is designed to accelerate approval for regenerative advanced therapies. Priority review designation is intended to ~~speed~~ **accelerate** the FDA marketing application review timeframe for ~~drugs~~ **drug products** that treat a serious condition and **that**, if approved, would provide a significant improvement in safety or effectiveness. PRIME is a scheme provided by the EMA, similar to the FDA' s breakthrough therapy designation, to enhance support for the development of medicines that target an unmet medical need. For drugs and biologics that have been designated as fast track products, RMAT, or breakthrough therapies, or granted access to the PRIME scheme, interaction and communication between the regulatory agency and the sponsor of the trial can help to identify the most efficient path for clinical development. Sponsors of fast **-** track products, RMAT products, or breakthrough therapies may also be able to submit marketing applications on a rolling basis, meaning that the FDA may review portions of a marketing application before the sponsor submits the complete application to the FDA, if the sponsor pays the user fee upon submission of the first portion of the marketing application and the FDA approves a schedule for the submission of the remaining sections. For products that receive a priority review designation, the FDA ~~'~~**'**s marketing application review goal is shortened to six months, as opposed to ten months under standard review. Designation as a fast **-** track product, breakthrough therapy, RMAT, PRIME, or priority review product is within the discretion of the regulatory agency. Accordingly, even if we believe one of our product candidates meets the relevant criteria, the agency may disagree and instead determine not to make such **a** designation. In any event, the receipt of such a designation for a product candidate 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 ultimate marketing approval by the agency. In addition, the FDA may later decide that the products no longer meet the applicable conditions for qualification as either a fast **-** track product, RMAT, or a breakthrough therapy or, for priority review products, decide that the period for FDA review or approval will not be shortened. Moreover, in the U. S., **the** FDA expects that sponsors with products under these programs will be prepared for a more rapid pace of development, including with respect to manufacturing or any combination medical devices, such as companion diagnostics. If we are unable to meet these expectations, we may not be able to fully avail ourselves of certain advantages of these programs. ~~We may not be successful~~ **Biologics studied for their safety and effectiveness** in **treating serious** ~~our~~ **or** ~~efforts to use our gene therapy technology platform to build a pipeline of additional~~ **life- threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval by the FDA, meaning the agency may approve the** product ~~candidates~~ **candidate** ~~. An element of our strategy~~ **based upon a surrogate endpoint that** is **reasonably likely** to **predict** ~~use our gene therapy technology platform to expand our product pipeline and to progress these candidates through preclinical and~~ clinical **benefit** ~~development ourselves or together with collaborators. Although we currently have a pipeline of programs at various stages of development~~, ~~we may not be able to identify~~ or ~~develop product candidates~~ **on a clinical endpoint** that ~~are safe~~ **is reasonably likely to predict** ~~and~~ **an** ~~effective~~ **effect on irreversible morbidity or mortality or other clinical benefit**. Even if we **do qualify** ~~are successful in continuing to build our pipeline, the potential product candidates that we identify may not be suitable~~ for **accelerated approval, we may be unsuccessful in meeting post- marketing compliance requirements, or fail to conduct required post- approval studies, or to confirm a** clinical **benefit during post- marketing studies** ~~development. Research programs to identify new product candidates require substantial technical, financial, and human resources. We or any collaborators may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful. If we do not continue to successfully develop and commercialize product candidates based upon our technology, we may face difficulty in obtaining product revenues in future periods~~, which could result in **the FDA withdrawing our product from the market. In recent years, the accelerated approval pathway has come under** significant ~~harm to~~ **FDA and public scrutiny. Accordingly, it is uncertain whether the FDA may be more conservative in granting accelerated approval** ~~our~~ **or** ~~business~~, **if granted, more apt** ~~results of operations and financial position and materially adversely affect our share price. Our strategy of obtaining~~

~~rights~~ to **withdraw approval if clinical benefit is** ~~key technologies through in- licenses may~~ not **confirmed** ~~be successful~~. ~~We seek to expand~~ **There is no guarantee that regulatory interactions with FDA** ~~our~~ **or comparable foreign authorities** ~~product pipeline from time to time in part by in- licensing the rights to key technologies, including those related to gene delivery, genes, and gene cassettes. The future growth of our business~~ will ~~depend~~ **result** in ~~significant part on~~ our ability to ~~in- license~~ **avail ourselves of any specialized approval pathways** ~~or~~ **for our** ~~otherwise acquire the rights to additional~~ product candidates or technologies, particularly through our collaborations..... sufficient product revenues to maintain our business. Our failure to obtain or maintain orphan product exclusivity for any of our product candidates for which we seek this status could limit our commercial opportunity, and if our competitors are able to obtain orphan product exclusivity before we do, we may not be able to obtain approval for our competing products for a significant period. Regulatory authorities in some jurisdictions, including the U. S. and the European Union, may designate drugs for relatively small patient populations as orphan drugs. While certain of our product candidates **, including AMT- 130** have received orphan drug designation, there is no guarantee that we will be able to receive such designations in the future. The FDA may grant orphan designation to multiple sponsors for the same compound or active molecule and for the same indication. If another sponsor receives FDA approval for such product before we do, we would be prevented from launching our product in the U. S. for the orphan indication for a period of at least seven years unless we can demonstrate clinical superiority. Moreover, while orphan drug designation neither shortens the development or regulatory review time, nor gives the product candidate advantages in the regulatory review or approval process, generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the relevant indication, the product is entitled to a period of market exclusivity, which precludes the FDA or the EMA from approving another marketing application for the same drug for the same indication for that period. The FDA and the EMA, however, may subsequently approve a similar drug or same drug, in the case of the U. S., for the same indication during the first product ~~'~~ **'** s market exclusivity period if the FDA or the EMA concludes that the later drug is clinically superior in that it is shown to be safer or more effective or makes a major contribution to patient care. Orphan exclusivity in the U. S. also does not prevent the FDA from approving another product that is considered to be the same as our product candidates for a different indication or a different product for the same orphan indication. If another product that is the same as ours is approved for a different indication, it is possible that third- party payors will reimburse for products off- label even if not indicated for the orphan condition. Moreover, in the U. S. the exact scope of orphan **drug** exclusivity is currently uncertain and evolving due to a recent court decision. Orphan drug exclusivity may be lost if the FDA or the EMA determines that the request for designation was materially defective, or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition or if the incidence and prevalence of patients who are eligible to receive the drug in these markets materially increase. The inability to obtain or failure to maintain adequate product exclusivity for our product candidates could have a material adverse effect on our business prospects, results of operations and financial condition. ~~Additionally,~~ **Our focus on developing gene therapies makes it difficult to determine the availability and utility of the orphan drug regime to our product candidates.** ~~regulatory~~ **Regulatory** criteria with respect to orphan products ~~is~~ **are** evolving, especially in ~~the area of~~ gene therapy. By example, in the U. S., whether two gene therapies are considered to be the same for the purpose of determining clinical superiority was ~~recently~~ updated via a final guidance document specific to gene therapies, and depends on a number of factors, including the expressed transgene, the vector, and other product or product candidate features. Depending on the products, whether two products are ultimately considered to be the same may be determined by FDA on a case- by- case basis, making it difficult to make predictions regarding when **the** FDA might be able to make an approval of a product effective and whether periods of exclusivity will effectively block competitors seeking to market products that are the same or similar to ours for the same intended use. Accordingly, whether any of our ~~product candidates~~ **gene therapies** will be deemed to be the same as another product or product candidate is uncertain. As appropriate, we intend to seek available periods of regulatory exclusivity for our product candidates. However, there is no guarantee that we will be granted these periods of regulatory exclusivity or that we will be able to maintain these periods of exclusivity. The FDA grants product sponsors certain periods of regulatory exclusivity, during which the agency may not approve, and in certain instances, may not accept, certain marketing applications for competing drugs. For example, biologic product sponsors may be eligible for twelve years of exclusivity from the date of approval, seven years of exclusivity for drugs that are designated to be orphan drugs, and / or a six- month period of exclusivity added to any existing exclusivity period for the submission of FDA requested pediatric data. While we intend to apply for all periods of market exclusivity that we may be eligible for, there is no guarantee that we will be granted any such periods of market exclusivity. By example, regulatory authorities may determine that our product candidates are not eligible for periods of regulatory exclusivity for various reasons, including a determination by the FDA that a BLA approval does not constitute a first licensure of the product. Additionally, under certain circumstances, the FDA may revoke the period of market exclusivity. Thus, there is no guarantee that we will be able to maintain a period of market exclusivity, even if granted. In the case of orphan designation, other benefits, such as tax credits and exemption from user fees may be available. If we are not able to obtain or maintain orphan drug designation or any period of market exclusivity to which we may be entitled, we could be materially harmed, as we will potentially be subject to greater market competition and may lose the benefits associated with programs. It is also possible that periods of exclusivity will not adequately protect our product candidates from competition. For instance, even if we receive twelve years of exclusivity from the FDA, other applicants will still be able to submit and receive approvals for versions of our product candidates through a full BLA. If we do not obtain or maintain periods of market exclusivity, we may face competition sooner than otherwise anticipated. For instance, in the U. S., this could mean that a competing biosimilar product may be able to **apply** ~~submit an application~~ to the FDA and obtain approval either as a biosimilar to one of our products or even as an interchangeable product. This may require that we undertake costly and time- consuming patent litigation, to the extent available, or defend actions brought by the biosimilar applicant for declaratory judgment. If a biosimilar product does enter the market, it is possible that it could be substituted for one of our product candidates, especially if

it is available at a lower price. It is also possible that, at the time we obtain approval of our product candidates, regulatory laws and policies around exclusivities may have changed. For instance, there have been efforts to decrease the U. S. period of exclusivity to a shorter timeframe. Future proposed budgets, international trade agreements and other arrangements or proposals may affect periods of exclusivity. If any of our product candidates receive regulatory approval, we and / or our partners will be subject to extensive regulatory requirements. Failure to fulfill and comply with the applicable regulatory requirements could result in regulatory enforcement actions that would be detrimental to our business. Following any regulatory approval, the FDA and the EMA may impose certain post- approval requirements related to a product. Specifically, any approved products will be subject to continuing and comprehensive regulation concerning the product' s design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale **,** and distribution. Regulatory authorities may also require post- marketing testing, known as Phase 4 testing, a risk evaluation and mitigation strategy, and surveillance to monitor the effects of an approved product or place conditions on an approval that could restrict the distribution or use of the product. Failure to comply with any of these requirements could result in regulatory, administrative, or other enforcement action, ~~that~~ **which** would be detrimental to our business. For instance, the FDA and other government agencies closely regulate the post- approval marketing and promotion of approved products, including off- label promotion, industry- sponsored scientific and educational activities, and **on** the Internet and social media. Approved products may be marketed only for the approved indications and in accordance with the provisions of the approved labeling. Failure to comply with regulatory promotional standards could result in actions being brought against us by these agencies. Moreover, if a company obtains FDA approval for a product via the accelerated approval pathway, the company would be required to conduct a post- marketing confirmatory trial to verify and describe the clinical benefit in support of full approval. FDA can require that this confirmatory trial be commenced prior to FDA granting a product accelerated approval. An unsuccessful post- marketing study or failure to complete such a study could result in the expedited withdrawal of the FDA' s marketing approval for a product using a statutorily defined streamlined process. Changes to some of the conditions established in an approved application, including changes in labeling, indications, manufacturing processes or facilities, may require a submission to and approval by the FDA or the EMA, as applicable, before the change can be implemented. A New Drug Application (" NDA ") / BLA or MAA supplement for a new indication typically requires clinical data similar to that in the original application. The applicable regulatory authorities would review such supplement using similar procedures and actions as in reviewing NDAs / BLAs and MAAs. Adverse event reporting and submission of periodic reports is required following marketing approval. Regulatory authorities may withdraw product approvals or request product recalls, as well as impose other enforcement actions, if a company fails to comply with regulatory standards, if it encounters problems following initial marketing, or if previously unrecognized problems are subsequently discovered. In addition, the manufacture, testing, packaging, labeling, and distribution of products after approval will need to continue to conform to cGMPs. Drug and biological product manufacturers **, including us,** and certain of their subcontractors are subject to periodic unannounced inspections by the FDA or the EMA for compliance with cGMPs. Accordingly, manufacturers must continue to expend time, money **,** and effort in the areas of production and quality control to maintain compliance with cGMPs. In addition, prescription drug manufacturers in the U. S. must comply with applicable provisions of the Drug Supply Chain Security Act and provide and receive product tracing information, maintain appropriate licenses, ensure they only work with other properly licensed entities and have procedures in place to identify and properly handle suspect and illegitimate products. **If we or any of our contractors are unable to comply with the requirements that are applicable to drug manufacturers, we or they may be subject to regulatory enforcement, or may need to conduct a recall or take other corrective actions, which could result in material harm to us or our products.** Where we partner with third parties for the development, approval, and marketing of a product, such third parties will be subject to the same regulatory obligations as we will. However, as we will not control the actions of the applicable third parties, we will be reliant on them to meet their contractual and regulatory obligations. Accordingly, actions taken by any of our partners could materially and adversely impact our business. Risks Related to Commercialization If we, or our commercial ~~partner~~ **partners** , are unable to successfully commercialize our product candidates or experience significant delays in doing so, our business could be materially harmed. Our ability to generate revenues from ~~HEMGENIX ™ or~~ **our** ~~any other~~ product **candidates** will depend on the successful development and eventual commercialization of our product candidates. The success of ~~HEMGENIX ™ or~~ **our** ~~other~~ product candidates will depend on many factors, including: ~~● successful execution of our contractual relationship with CSL Behring for the commercialization of HEMGENIX ™;~~ ● successful completion of preclinical studies and clinical trials, and other work required by regulators; ● receipt and maintenance of marketing approvals from applicable regulatory authorities; ● ~~our ability to timely manufacture sufficient quantities of HEMGENIX ™ and other products according to required quality specifications; ●~~ obtaining and maintaining patent and trade secret protection and non- patent **,** exclusivities for our product candidates; ● maintaining regulatory approvals using our manufacturing facility in Lexington, Massachusetts; ● launch and commercialization of our products, if approved, whether alone or in collaboration with others; ● identifying and engaging effective distributors or resellers on acceptable terms in jurisdictions where we plan to utilize third parties for the marketing and sales of our product candidates; ● acceptance of our products, if approved, by patients, the medical community, and third- party payers; ● effectively competing with existing therapies and gene therapies based on safety and efficacy profiles; ● the strength of our marketing and distribution; ● **the** ~~achieve~~ **achievement** optimal pricing based on durability of expression, safety, and efficacy; ● the ultimate content of the regulatory authority approved label, including the approved clinical indications, and any limitations or warnings; ● any distribution or use restrictions imposed by regulatory authorities; ● the interaction of our products with any other medicines that patients may be taking or the restriction on the use of our products with other medicines; ● the standard of care at the time of product approval; ● the relative convenience and ease of administration of our products; ● obtaining ~~and maintaining~~ healthcare coverage and adequate reimbursement **of our** ~~for HEMGENIX ™ and other~~ products; ● any price concessions, rebates, or discounts we may need to provide; ● complying with any applicable post- approval commitments and

requirements, and maintaining a continued acceptable overall safety profile; and ● obtaining adequate reimbursement for the total patient population and each subgroup to sustain a viable commercial business model in U. S. and EU markets. ~~CSL Behring may not receive a conditional marketing authorization based on an accelerated assessment by the EMA for AMT- 061 product candidate to facilitate a first commercial sale in the European Union prior to July 2, 2023, and we, thus, may not receive the $ 75. 0 million first commercial sale milestone in any of the five contractually defined European countries prior to July 2, 2023 under the CSL Behring Agreement.~~ Even if our product candidates are approved, they may be subject to limitations that make commercialization difficult. There may be limitations on the indicated uses and populations for which the products may be marketed. They may also be subject to other conditions of approval, may contain significant safety warnings, including boxed warnings, contraindications, and precautions, may not be approved with label statements necessary or desirable for successful commercialization, or may contain requirements for costly post- market testing and surveillance, or other requirements, including the submission of a risk evaluation and mitigation strategy ~~, or~~ **(“** REMS ~~,~~ **”)** to monitor the safety or efficacy of the products. Failure to achieve or implement any of the above elements could result in significant delays or an inability to successfully commercialize our product candidates, which could materially harm our business. The affected populations for our gene therapies may be smaller than we or third parties currently project, which may affect the size of our addressable markets. Our projections of the number of people who have the diseases we are seeking to treat, as well as the subset of people with these diseases who have the potential to benefit from treatment with our therapies, are estimates based on our knowledge and understanding of these diseases **and may change** . The total addressable market opportunities for these therapies will ~~ultimately~~ depend upon many factors, including the diagnosis and treatment criteria included in the final label, if approved for sale in specified indications, acceptance by the medical community, patient consent, patient access and product pricing and reimbursement **, among other factors** . Prevalence estimates are frequently based on information and assumptions that are not exact and may not be appropriate, and the methodology is forward- looking and speculative. ~~The use of such data involves risks and uncertainties and is subject to change based on various factors. Our estimates may prove to be incorrect and new studies may change the estimated incidence or~~ **For example** ~~prevalence of the diseases we seek to address. The number of patients with the diseases we are targeting may turn out to be lower than expected or may not be otherwise amenable to treatment with our products~~ , **the** ~~reimbursement may not be sufficient to sustain a viable business for all sub populations being studied, or new patients may become increasingly difficult to identify or access, any of which could adversely affect our results of operations and our business. The~~ addressable markets for **certain of our** AAV- based gene therapies may be impacted by the prevalence of neutralizing antibodies to the capsids, which are an integral component of our gene therapy constructs. Patients that have pre-existing antibodies to a particular capsid ~~may~~ **might** not be eligible for administration of a gene therapy that includes this particular capsid. **Moreover, neutralizing antibodies may be developed by a patient following administration of the product, which may render the patient ineligible for subsequent dosing. The use of such data to support addressable market estimates involves risks and uncertainties and is subject to change based on various factors. Our estimates may prove to be incorrect and new studies and information may change the estimated incidence or prevalence of the diseases we seek to address. The number of patients with the diseases we are targeting may turn out to be lower than expected or may not be otherwise amenable to treatment with our products, reimbursement may not be sufficient to sustain a viable business for all sub- populations being studied, or new patients may become increasingly difficult to identify or access, any of which could adversely affect our results of operations and our business.** Any approved gene therapy we seek to offer may fail to achieve the degree of market acceptance by physicians, patients, third party payers and others in the medical community necessary for commercial success. Doctors may be reluctant to accept ~~a~~ gene therapy as a treatment option or, where available, choose to continue to rely on existing treatments. The degree of market acceptance of any of our product candidates that receive marketing approval in the future will depend on many factors, including: ● the efficacy and potential advantages of our therapies compared with alternative treatments; ● our ability to convince payers of the long- term cost- effectiveness of our therapies and, consequently, the availability of third- party coverage and adequate reimbursement; ● the cost of treatment with gene therapies, including ours, in comparison to traditional chemical and small ~~-~~ molecule treatments; ● the limitations on use and label requirements imposed by regulators; ● the convenience and ease of administration of our gene therapies compared with alternative treatments; ● the willingness of the target patient population to try new therapies, especially a gene therapy, and of physicians to administer these therapies; ● the strength of marketing and distribution support; ● the prevalence and severity of any side effects; ● limited access to site of service that can perform the product preparation and administer the infusion; and ● any restrictions by regulators on the use of our products. A failure to gain market acceptance for any of the above reasons, or any reasons at all, by a gene therapy for which we receive regulatory approval would likely hinder our ability to recapture our substantial investments in that and other gene therapies and could have a material adverse effect on our business, financial condition, and results of operation. If the market opportunities for our product candidates are smaller than we believe they are, our product revenues may be adversely affected, and our business may suffer. We focus our research and product development on treatments for severe genetic and orphan diseases. Our understanding 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 product candidates, are based on estimates. These estimates may prove to be incorrect and new studies may reduce the estimated incidence or prevalence of these diseases. The number of patients in the U. S., the EU and elsewhere may turn out to be lower than expected, may not be otherwise amenable to treatment with our products or patients may become increasingly difficult to identify and access, any of which could adversely affect our business, financial condition, results of operations and prospects. Further, there are several factors that could contribute to making the actual number of patients who receive other potential products less than the potentially addressable market. These include the lack of widespread availability of, and limited reimbursement for, new therapies in many underdeveloped markets. Further, the severity of the progression of a disease up to the time of treatment, especially in certain degenerative conditions, could diminish the therapeutic benefit conferred by a gene therapy. Lastly, certain

patients' immune systems might prohibit the successful delivery of certain gene therapy products to the target tissue, thereby limiting the treatment outcomes. Our gene therapy approach utilizes vectors derived..... for which we obtain marketing approval. Ethical, legal, and social issues **associated with genetic testing** may reduce demand for any gene therapy products for which we obtain marketing approval. Prior to receiving certain gene therapies, patients may be required to undergo genetic testing. Genetic testing has raised concerns regarding the appropriate utilization and the confidentiality of information provided by genetic testing. Genetic tests for assessing a person' s likelihood of developing a chronic disease have focused public attention on the need to protect the privacy of **patient' s underlying** genetic information. For example, concerns have been expressed that insurance carriers and employers may use these tests to discriminate **based** on ~~the basis of~~ genetic information, resulting in barriers to the acceptance of genetic tests by consumers. This could lead to governmental authorities restricting genetic testing or calling for limits on or regulating the use of genetic testing, particularly for diseases for which there is no known cure. Any of these scenarios could decrease demand for any products for which we obtain marketing approval. If we, or our commercial ~~partner~~ **partners**, obtain approval to commercialize any of our product candidates outside of the U. S., a variety of risks associated with international operations could materially adversely affect our business. We expect that we will be subject to additional risks in commercializing any of our product candidates outside the U. S., including: ● different regulatory requirements for approval of drugs and biologics in foreign countries; ● reduced protection for intellectual property rights; ● unexpected changes in tariffs, trade barriers and regulatory requirements which may make it more difficult or expensive to export or import products and supplies to or from the U. S.; ● economic weakness, including inflation, or political instability in particular foreign economies and markets; ● compliance with tax, employment, immigration, and labor laws for employees living or traveling abroad; ● foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country; ● workforce uncertainty in countries where labor unrest is more common than in the U. S.; ● production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and ● business interruptions resulting from geopolitical actions, including war and terrorism or natural disasters including earthquakes, typhoons, floods, and fires. ~~In February 2022, armed conflict escalated between Russia and Ukraine. The sanctions announced by the U. S. and other countries following Russia' s invasion of Ukraine against Russia to date include restrictions on selling or importing goods, services or technology in or from affected regions and travel bans and asset freezes impacting connected individuals and political, military, business and financial organizations in Russia. The U. S. and other countries could impose wider sanctions and take other actions should the conflict further escalate. It is not possible to predict the broader consequences of this conflict, which could include further sanctions, embargoes, regional instability, geopolitical shifts and adverse effects on macroeconomic conditions, currency exchange rates and financial markets, all of which could impact our business, financial condition and results of operations. We may be adversely affected by the effects of inflation. Inflation has the potential to adversely affect our liquidity, business, financial condition and results of operations by increasing our overall cost structure. The existence of inflation in the economy has resulted in, and may continue to result in, higher interest rates and capital costs, shipping costs, supply shortages, increased costs of labor, weakening exchange rates and other similar effects. As a result of inflation, we have experienced and may continue to experience, cost increases. Although we may take measures to mitigate the impact of this inflation, if these measures are not effective our business, financial condition, results of operations and liquidity could be materially adversely affected. Even if such measures are effective, there could be a difference between the timing of when these beneficial actions impact our results of operations and when the cost inflation is incurred.~~ We face substantial competition, and others may discover, develop, or commercialize competing products before or more successfully than we do. The development and commercialization of new biotechnology and biopharmaceutical products, including gene therapies, is highly competitive. We may face intense competition with respect to our **current and future** product candidates ~~, as well as with respect to any product candidates that we may seek to develop or commercialize in the future,~~ from large and specialty pharmaceutical companies and biotechnology companies worldwide, who **, like us,** currently market and sell products or are pursuing the development of products for the treatment of **rare** ~~many of the disease~~ **diseases** ~~indications for which we are developing our product candidates~~. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing, and commercialization. In recent years, there has been a significant increase in commercial and scientific interest and financial investment in gene therapy as a therapeutic approach, which has intensified the competition in this area. We face worldwide competition from larger pharmaceutical companies, specialty pharmaceutical companies and biotechnology firms, universities and other research institutions and government agencies that are developing and commercializing pharmaceutical products. Our key competitors focused on developing therapies in various indications, include among others, Pfizer, Freeline Therapeutics, Intellia Therapeutics, Sangamo Biosciences, Voyager Therapeutics, Passage Bio, Roche, PTC Therapeutics, Prilenia Therapeutics, CombiGene, Caritas Therapeutics, Alnylam, Wave Life Sciences, Bayer AG **(AskBio)**, Amicus Therapeutics ~~and~~ **,** 4D Molecular Therapeutics **, Sanofi, Idorsia, Amicus, Spark, Takeda, Chiesi, CANbridge, Abeona, Annexon, Vico, Alexion (AZ), Neurona, Combigene, NeuExcell, EpiBlok, Biogen, ionis, Eisai and Lexeo**. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than the products that we develop. Our competitors also may obtain FDA, EMA, or other regulatory approval for their products more rapidly than we do, which could result in our competitors establishing a strong market position before we are able to enter the market. A competitor approval may also prevent us from entering the market if the competitor receives any regulatory exclusivities that block our product candidates. Because we expect that gene therapy patients may generally require only a single administration, we believe that the first gene therapy product to enter the market for a particular indication will likely enjoy a significant commercial advantage and may also obtain market exclusivity under applicable orphan drug regimes. Many of the companies with which we are competing or may

compete in the future have significantly greater financial resources and expertise than we do in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved products. **Moreover, actions taken in connection with the Reorganization to streamline our product portfolio may hamper our ability to remain competitive.** Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in more resources being concentrated among a smaller number of our competitors. Smaller and other early- stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs ~~. If we do not achieve our projected development goals in the timeframes we announce and expect, the commercialization of our product candidates may be delayed 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, or development milestones. These development milestones may include the commencement or completion of scientific studies, clinical trials, the submission of regulatory filings, and approval for commercial sale. From time to time, we publicly announce the expected timing of some of these milestones. All these milestones are based on a variety of assumptions. The actual timing of these milestones can vary dramatically compared to our estimates, in many cases for reasons beyond our control. If we do not meet these milestones, including those that are publicly announced, the commercialization of our products may be delayed and, as a result, our stock price may decline~~ . Risks Related to Our Dependence on Third Parties We rely, and expect to continue to rely, on third parties to conduct, supervise, and monitor our preclinical studies and clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines ~~for~~ **in** the **conduct and** completion of such trials or failing to comply with regulatory requirements. We rely on third parties, study sites, and others to conduct, supervise, and monitor our preclinical and clinical trials for our product candidates and do not currently plan to independently conduct clinical or preclinical trials of any other potential product candidates. We expect to continue to rely on third parties, such as CROs, clinical data management organizations, medical and scientific institutions, and clinical and preclinical investigators, to conduct our preclinical studies and clinical trials. While we have agreements governing the activities of such third parties, we have limited influence and control over their actual performance and activities. For instance, our third- party service providers are not our employees, and except for remedies available to us under our agreements with such third parties we cannot control whether or not they devote sufficient time and resources to our ongoing clinical, non- clinical, and preclinical programs. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our preclinical studies or clinical trials in accordance with regulatory requirements or our stated protocols, 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 trials may be repeated, extended, delayed, or terminated, we may not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates, we may not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates, or we or they may be subject to regulatory enforcement actions. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed. To the extent we are unable to successfully identify and manage the performance of third- party service providers in the future, our business may be materially and adversely affected. Our third- party service providers may also have relationships with other entities, some of which may be our competitors, for whom they may also be conducting trials or other therapeutic development activities that could harm our competitive position. Our reliance on these third ~~-~~parties for development activities ~~will reduce~~ **reduces** our control over these activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory, and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities. For example, we will remain responsible for ensuring that each of our trials is conducted in accordance with the general investigational plan and protocols for the trial. We must also ensure that our preclinical trials are conducted in accordance with GLPs, as appropriate. Moreover, the FDA and comparable foreign regulatory authorities require us to comply with GCPs for conducting, recording, and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity, and confidentiality of trial participants are protected. Regulatory authorities enforce these requirements through periodic inspections of trial sponsors, clinical and preclinical investigators, and trial sites. If we or any of our third- party service providers fail to comply with applicable GCPs or other regulatory requirements, we or they may be subject to enforcement or other legal actions, the data generated in our trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional studies. In addition, we will be required to report **on** certain financial interests of our third- party investigators if these relationships exceed certain financial thresholds or meet other criteria. The FDA or comparable foreign regulatory authorities may question the integrity of the data from those clinical trials conducted by investigators who may have conflicts of interest. We cannot assure that **,** upon inspection by a given regulatory authority, such regulatory authority will determine that any of our trials complies with the applicable regulatory requirements. In addition, our clinical trials must be conducted with product candidates that were produced under GMP conditions. Failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. We also are required to register certain clinical trials and post the results of certain completed clinical trials on a government- sponsored database, ClinicalTrials. gov, within specified timeframes. Failure to do so can result in enforcement actions and adverse publicity. Agreements with third parties conducting or otherwise assisting with our clinical or preclinical studies might terminate for a variety of reasons, including a failure to perform by the third parties. If any of our relationships with these third parties terminate, we may not be able to enter into arrangements with alternative providers or to do so on commercially reasonable terms. Switching or adding additional third parties involves additional ~~cost~~ **costs** and requires management time and focus. In addition, there is a natural transition period when a new third party commences work. As a result, if we need to enter into

alternative arrangements, it could delay our product development activities and adversely affect our business. Though we carefully manage our relationships with our third parties, there can be no assurance that we will not encounter 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 prospects, and results of operations. We also rely on other third parties to store and distribute our products for the clinical and preclinical trials that we conduct. Any performance failure on the part of our distributors could delay **the** development, marketing approval, or commercialization of our product candidates, producing additional losses and depriving us of potential product revenue. We rely on third parties for important aspects of our development programs. If these parties do not perform successfully or if we are unable to enter into or maintain key ~~collaboration~~ **collaborations** or other contractual arrangements, our business could be adversely affected. We have in the past entered into, and expect in the future to enter into, collaborations with other companies and academic research institutions with respect to important elements of our development programs. Any collaboration **we enter into** may pose several risks, including the following: ● collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations; ● we may have limited or no control over the design or conduct of clinical trials sponsored by collaborators; ● we may be hampered from entering into collaboration arrangements if we are unable to obtain consent from our licensors to enter into sublicensing arrangements of technology we have in- licensed; ● if any collaborator does not conduct the clinical trials they sponsor in accordance with regulatory requirements or stated protocols, we will not be able to rely on the data produced in such trials in our further development efforts; ● collaborators may not perform their obligations as expected; ● collaborators may also have relationships with other entities, some of which may be our competitors; ● collaborators may not pursue development and commercialization of any product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators ~~'~~ **'** strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities; ● collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial, or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing; ● collaborators could develop, independently or with third parties, products that compete directly or indirectly with our products or product candidates, if, for instance, the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours; ● our collaboration arrangements may impose restrictions on our ability to undertake other development efforts that may appear to be attractive to us; ● product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates; ● a collaborator with marketing and distribution rights that achieves regulatory approval may not commit sufficient resources to the marketing and distribution of such product or products; ● disagreements with collaborators, including over proprietary rights, contract interpretation or the preferred course of development, could cause delays or termination of the research, development or commercialization of product candidates, lead to additional responsibilities for us, delay or impede reimbursement of certain expenses or result in litigation or arbitration, any of which would be time- consuming and expensive; ● collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our rights or expose us to potential litigation; ● collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and ● collaborations may in some cases be terminated for the convenience of the collaborator and, if terminated, we could be required to expend additional funds to pursue further development or commercialization of the applicable product or product candidates. If any collaboration does not result in the successful development and commercialization of products or if a collaborator were to terminate an agreement with us, we may not receive future research funding or milestone or royalty payments under that collaboration, and we may lose access to important technologies and capabilities of the collaboration. All the risks relating to product development, regulatory approval and commercialization described herein also apply to the activities of any development collaborators. Risks Related to Our Intellectual Property We rely on licenses of intellectual property from third parties, and such licenses may not provide adequate rights **, may be open to multiple interpretations** or may not be available in the future on commercially reasonable terms or at all, and our licensors may be unable to obtain and maintain patent protection for the technology or products that we license from them. We currently are heavily reliant upon licenses of proprietary technology from third parties that ~~is~~ **are** important or necessary to the development of our technology and products, including technology related to our manufacturing process, our vector platform, our gene cassettes **,** and the therapeutic genes of interest we are using. These and other licenses may not provide adequate rights to use such technology in all relevant fields of use. Licenses to additional third- party technology that may be required for our development programs may not be available in the future or may not be available on commercially reasonable terms, which could have a material adverse effect on our business and financial condition. In some circumstances, we may not have the right **, or have otherwise given up the right,** to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we **own or** license from third parties. In addition, some of our agreements with our licensors require us to obtain consent from the licensor before we can enforce patent rights, and our licensor may withhold such consent or may not provide it on a timely basis. Therefore, we cannot be certain that these patents and applications will be prosecuted and enforced in a manner consistent with the best interests of our business **which may materially impact any revenue that may be due to us in connection with such patents** . In addition, if third parties who license patents to us fail to maintain such patents, or lose rights to those patents, the rights we have licensed may be reduced or eliminated. Our intellectual property licenses with third parties may be subject to disagreements over contract interpretation, which could narrow the scope of our rights to the relevant intellectual property or technology or increase our financial or other obligations to our licensors. The agreements under which we license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any

contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology ~~,~~ or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business and financial condition. If we fail to comply with our obligations in our intellectual property licenses with third parties, we could lose rights that are important to our business. Our licensing arrangements with third parties may impose diligence, development and commercialization timelines, milestone payment, royalty, insurance, and other obligations on us. If we fail to comply with these obligations, our counterparties may have the right to terminate these agreements either in part or in whole, in which case we might not be able to develop, manufacture or market any product that is covered by these agreements or may face other penalties under the agreements. Such an occurrence could materially adversely affect the value of the product candidate being developed under any such agreement **or may otherwise result in reputational damage to our business** . Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or amended agreements with less favorable terms or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology. If we are unable to obtain and maintain patent protection for our technology and products, or if the scope of the patent protection is not sufficiently broad, our ability to successfully commercialize our products may be impaired. We rely, in part, upon a combination of forms of intellectual property, including in- licensed and owned patents to protect our intellectual property. Our success depends in ~~a~~ large part on our ability to obtain and maintain this protection in the U. S., the European Union, and other countries, in part by filing patent applications related to our novel technologies and product candidates. Our patents may not provide us with any meaningful commercial protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. **The** ~~Patents~~ **patents** we own currently are and may become subject to future patent opposition or similar proceedings. **Additionally, the patent prosecution process is expensive, time-consuming, and uncertain, and in certain instances we have chosen, and in the future we may choose, not to file and prosecute all necessary or desirable patent applications.** For example, **our defense of certain** ~~we are currently defending a~~ patent ~~case~~ **cases** in each of Canada, the United Kingdom, ~~and the US and have filed Notices of Appeal at the CAFC contesting three~~ -- **the** ~~FWDs~~ **Netherlands and the U. S. pertaining to licensed rights of etranacogene dezaparvovec was assumed by CSL Behring on October 11, 2023** . These oppositions and future patent oppositions may result in loss of scope of some claims or the entire patent **and, with respect to our rights under the CSL Agreement, could affect CSL' s successful commercialization of HEMGENIX ® and, in turn, could negatively impact our financial position** . ~~Our~~ **Additionally, our** competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non- infringing manner. Successful challenges to our patents may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated, or held unenforceable, in whole or in part, which could limit our ability **or the ability of our licensees** to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products ~~. The patent prosecution process is expensive, time- consuming, and uncertain, 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. Additionally, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the U. S ~~.~~. For example, EU patent law with respect to the patentability of methods of treatment of the human body is more limited than U. S. law. Publications of discoveries in the scientific literature often lag the actual discoveries, and patent applications in the U. S. and other jurisdictions are typically not published until 18 months after their priority date, or in some cases at all. Therefore, we cannot know with certainty whether we were the first to make the inventions or that we were the first to file for patent protection of the inventions claimed in our owned or licensed patents or pending patent applications. As a result, the issuance, scope, validity, enforceability, and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued that protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the European Union, the U. S. or other countries may diminish the value of our patents or narrow the scope of our patent protection. Our inability to obtain and maintain appropriate patent protection for any one of our products could have a material adverse effect on our business, financial condition, and results of operations. We may become involved in lawsuits to protect or enforce our patents or other intellectual property, or third parties may assert their intellectual property rights against us, which could be expensive, time consuming and unsuccessful. Competitors may infringe **on** our owned or licensed patents or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated, maintained in **a** more narrowly amended form or interpreted narrowly. Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, increase our operating losses, reduce available resources, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, which could have an adverse effect on the price of our ordinary shares. Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business. For example, outside of the U. S. two of the patents we own are subject to patent opposition. If these or future oppositions are successful or if we are found

to otherwise infringe a third party' s intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our products and technology. We may not be able to obtain the required license on commercially reasonable terms or at all. Even if we could obtain a license, it could be non- exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product or otherwise to cease using the relevant intellectual property. In addition, we could be found liable for monetary damages, including treble damages and attorneys ' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease or materially modify some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business. **In addition, legal proceedings relating to intellectual property claims, with or without merit, are unpredictable and generally expensive and time- consuming and is likely to divert significant resources from our core business, including distracting our technical and management personnel from their normal responsibilities. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.** For example, we are aware of patents **or patent applications** owned by third parties that relate to some aspects of our programs that are still in development. In some cases, because we have not determined the final methods of manufacture, the method of administration or the therapeutic compositions for these programs, we cannot determine whether rights under such third- party ~~patents~~ **positions** will be needed. In addition, in some cases, we believe that the claims of these patents are invalid or not infringed or will expire before commercialization. However, if such patents are needed and found to be valid and infringed, we could be required to obtain licenses, which might not be available on commercially reasonable terms, or to cease or delay commercializing certain product candidates, or to change our programs to avoid infringement. If we are unable to protect the confidentiality of our proprietary information and know- how, the value of our technology and products could be adversely affected. In addition to seeking patent protection, we also rely on other proprietary rights, including protection of trade secrets, know- how and confidential and proprietary information. To maintain the confidentiality of our trade secrets and proprietary information, we enter into confidentiality agreements with our employees, consultants, collaborators and other third parties who have access to our trade secrets. Our agreements with employees also provide that any inventions conceived by the individual while rendering services to us will be our exclusive property. However, we may not obtain these agreements in all circumstances, and individuals with whom we have these agreements may not comply with their terms. The assignment of intellectual property rights may not be self- executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. In addition, in the event of unauthorized use or disclosure of our trade secrets or proprietary information, these agreements, even if obtained, may not provide meaningful protection, particularly for our trade secrets or other confidential information. To the extent that our employees, consultants, or contractors use technology or know- how owned by third parties in their work for us, disputes may arise between us and those third parties as to the rights in related inventions. Adequate remedies may not exist in the event of unauthorized use or disclosure of our confidential information including a breach of our confidentiality agreements. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive, and time consuming, and the outcome is unpredictable. In addition, some courts in and outside of the U. S. are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them from using that technology or information to compete with us. The disclosure of our trade secrets or the independent development of our trade secrets by a competitor or other third party would impair our competitive position and may materially harm our business, financial condition, results of operations, stock price and prospects. Our reliance on third parties may require us to share our trade secrets, which could increase the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed. Because we collaborate from time to time with various organizations and academic research institutions on the advancement of our gene therapy platform, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, materials transfer agreements, collaborative research agreements, consulting agreements or other similar agreements with our collaborators, advisors, and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, such as trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know- how and trade secrets, a competitor' s discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business. In addition, these agreements typically restrict the ability of our collaborators, advisors, and consultants to publish data potentially relating to our trade secrets. Our academic collaborators typically have rights to publish data, if we are notified in advance and may delay publication for a specified time to secure our intellectual property rights arising from the collaboration. In other cases, publication rights are controlled exclusively by us, although in some cases we may share these rights with other parties. We also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development partnerships or similar agreements. Some courts inside and outside the U. S. are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those with whom they communicate, from using that technology or information to compete with us. **Intellectual property rights do not necessarily address all potential threats to our competitive advantage. The degree of future protection afforded by our intellectual property rights is**

uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain a competitive advantage. For example: ● others may be able to make gene therapy products that are similar to our product candidates or utilize similar gene therapy technology but that are not covered by the claims of the patents that we own or have licensed; ● we or our licensors or future collaborators might not have been the first to make the inventions covered issued patents or pending patent applications that we own or have licensed; ● we or our licensors or future collaborators might not have been the first to file patent applications covering certain of our inventions; ● others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights; ● it is possible that our pending patent applications will not lead to issued patents; ● issued patents that we own or have licensed may be held invalid or unenforceable, as a result of legal challenges by our competitors; ● our competitors might conduct activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets; ● we may not develop additional proprietary technologies that are patentable; and ● the patents of others may have an adverse effect on our business. The occurrence of any of these events could seriously harm our business. Risks Related to Business Development Our business development strategy may..... if at all. Risks Related to Pricing and Reimbursement We ~~,~~ and our commercial partner ~~,~~ face uncertainty related to insurance coverage of, and pricing and reimbursement for **,** HEMGENIX ~~™~~ ® and other product candidates for which we may receive marketing approval. We anticipate that the cost of treatment using our product candidates will be significant. We expect that most patients and their families will not be capable of paying for our products themselves. There will be no commercially viable market for our product candidates without reimbursement from third party payers, such as government health administration authorities, private health insurers and other organizations. Even if there is a commercially viable market, if the level of third- party reimbursement is below our expectations, most patients may not be able to afford treatment with our products and our revenues and gross margins will be adversely affected, and our business will be harmed. Government authorities and other third- party payers, such as private health insurers and health maintenance organizations, decide for which medications they will pay and, subsequently, establish reimbursement levels. Reimbursement systems vary significantly by country and by region, and reimbursement approvals must be obtained on a country- by- country basis. Government authorities and third- party payers have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications and procedures and negotiating or requiring payment of manufacturer rebates. Increasingly, third party payers require drug companies to provide them with predetermined discounts from list prices, are exerting influence on decisions regarding the use of particular treatments and are limiting covered indications. ~~Additionally~~ **Moreover** , **payment methodologies may be subject to changes** in **healthcare** ~~the U. S. and some foreign jurisdictions, pending or potential legislative~~ **legislation** and regulatory **initiatives** ~~changes regarding the healthcare system and insurance coverage could result in more rigorous coverage criteria and downward pressure on drug prices, and may affect our ability to profitably sell any products for which we obtain marketing approval~~ . For example, **the Center for Medicare & Medicaid Innovation at the Centers for Medicare & Medicaid Services** ~~on November 27, 2020, CMS issued an interim final rule implementing a Most Favored Nation~~ (" ~~MFN~~ **CMS** ") **may develop new** payment **and delivery** ~~model~~ **models , such as bundled payment models. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several U. S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs** under ~~which reimbursement~~ **government payor programs, and review the relationship between pricing and manufacturer patient assistance programs. Most recently, on August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (with the maximum fair prices for the first year of the negotiation program being initially applicable in 2026), with prices that can be negotiated subject to a cap; imposes rebates** for certain **drugs under** Medicare Part B ~~drugs~~ and ~~biologicals~~ **Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). We expect that additional U. S. federal healthcare reform measures** will be ~~based~~ **adopted in the future, any of which could limit the amounts that the U. S. federal government will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures and could seriously harm our business. Individual states in the U. S. have also increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions** on ~~a~~ **certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Legally mandated** price **controls on payment amounts by third** ~~that reflects the lowest per capita GDP-adjusted price of any~~ **party payors or other restrictions could seriously harm our business. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug healthcare programs. This could reduce the ultimate demand for our product candidates or put pressure** ~~non-~~ **on** ~~-U~~ **our product pricing** . **Furthermore,** ~~S. member country of the~~ **there** ~~OECD with a GDP per capita that is at least sixty percent of the U. S. GDP per capita. While this rule now~~ has been ~~rescinded~~ **increased interest by third- party payors and governmental authorities in reference pricing systems and publication of discounts and list prices. Prescription drugs and biological products that are in violation of these requirements will be included on a public list. These reforms could reduce the ultimate demand for our product candidates or put pressure on our product pricing and could seriously harm our business. In the EU , similar political, economic, and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the**

EU or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever- increasing EU and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to commercialize our product candidates, if approved. In markets outside of the U. S. and EU, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. We cannot predict the likelihood, nature or extent of government **regulation that may arise from future** ~~negotiation of certain Medicare drug pricing continues to be the focus of recent proposed~~ legislation **or administrative or judicial action in the U. S., the EU, or any other jurisdiction. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability** . The pricing review period and pricing negotiations for new medicines take considerable time and have uncertain results. Pricing review and negotiation usually ~~begins~~ **begin** only after the receipt of regulatory marketing approval, and some authorities require approval of the sale price of a product before it can be marketed. In some markets, particularly the countries of the European Union, prescription pharmaceutical pricing remains subject to continuing direct governmental control and to drug reimbursement programs even after initial approval is granted and price reductions may be imposed. Prices of medical products may also be subject to varying price control mechanisms or limitations as part of national health systems if products are considered not cost- effective or where a drug company ~~'~~ **'** s profits are deemed excessive. In addition, pricing and reimbursement decisions in certain countries can lead to mandatory price reductions or additional reimbursement restrictions in other countries. Because of these restrictions, any product candidates for which we may obtain marketing approval may be subject to price regulations that delay or prohibit our or our partners ~~'~~ **'** commercial launch of the product in a particular jurisdiction. In addition, we or any collaborator may elect to reduce the price of our products to increase the likelihood of obtaining reimbursement approvals. If countries impose prices ~~,~~ which are not sufficient to allow us or any collaborator to generate a profit, we or any collaborator may refuse to launch the product in such countries or withdraw the product from the market. If pricing is set at unsatisfactory levels, or if the price decreases, our business could be harmed, possibly materially. If we fail to obtain and sustain an adequate level of coverage and reimbursement for our products by third party payers, our ability to market and sell our products could be adversely affected and our business could be harmed. Due to the generally limited addressable market for our target orphan indications and the potential for our therapies to offer therapeutic benefit in a single administration, we face uncertainty related to **our** ~~pricing and reimbursement for HEMGENIX ™ and other~~ product candidates. The relatively small market size for orphan indications and the potential for long- term therapeutic benefit from a single administration present challenges to pricing review and negotiation of our product candidates for which we may obtain marketing authorization. Most of our product candidates target rare diseases with relatively small patient populations. If we are unable to obtain adequate levels of reimbursement relative to these small markets, our ability to support our development and commercial infrastructure and to successfully market and sell our product candidates for which we may obtain marketing approval could be adversely affected. We also anticipate that many or all our gene therapy product candidates may provide long-term, and potentially curative benefit, with a single administration. This is a different paradigm than that of **many** other pharmaceutical therapies, which often require an extended course of treatment or frequent administration. As a result, governments and other payers may be reluctant to provide the significant level of reimbursement that we seek at the time of administration of our gene therapies or may seek to tie reimbursement to clinical evidence of continuing therapeutic benefit over time. Additionally, there may be situations in which our product candidates will need to be administered more than once, which may further complicate the pricing and reimbursement for these treatments. In addition, considering the anticipated cost of these therapies, governments and other payers may be particularly restrictive in making coverage decisions. These factors could limit our commercial success and materially harm our business. Risks Related to Our Financial Position and Need for Additional Capital We had **net losses in the years ended December 31, 2023 and 2022, have incurred significant losses in previous years and expect to incur losses during the current and over the next several years and may never achieve or maintain profitability. We had** a **net** loss ~~in the current year, gain~~ **of $ 308. 5 million** in the year ended December 31, ~~2021~~ **2023** , ~~but incurred significant losses in previous years~~ and **a** ~~expect to incur losses over the next several years and may never achieve or maintain profitability. We had~~ net loss of $ 126. 8 million in the year ended December 31, 2022 ~~,~~ **. We** incurred a gain of ~~$~~ 329. 6 million in **year ended** ~~2021 and incurred a net loss of $ 125. 0 million in 2020. As of~~ December 31, ~~2022~~ **2021 ; however, such gain was primarily attributable to one- time license revenue from CSL Behring. We have incurred significant losses in the years prior to 2021. As of December 31, 2023** , we had an accumulated deficit of $ ~~581~~ **890** . ~~9~~ **4** million. In the past, we have financed our operations primarily through the sale of equity securities and convertible debt, venture loans, upfront payments from our collaboration partners and, to a lesser extent, subsidies and grants from governmental agencies and fees for services. We expect to finance our operations in ~~2023~~ **2024 and into the second quarter of 2027** primarily from our existing cash **, cash equivalents, and cash** resources ~~including payments we collected and expect to collect in relation to the CSL Behring Agreement~~ . We have devoted substantially all our financial resources and efforts to research and development, including preclinical studies and clinical trials. We expect to continue to incur significant expenses and losses over the next several years, and our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that **we** ~~our~~

~~expenses~~ will ~~increase~~ **continue to incur net losses** for the foreseeable future **as we** ~~and will include costs related to~~ : ● ~~advancing~~ **continue to fund** AMT- 130 ~~for~~ **in its ongoing clinical trials and advance** our **other product candidates** ~~Huntington' s disease gene therapy program~~ into ~~phase III~~ clinical ~~study~~ **development** ; ● ~~advancing our gene therapy programs for rTLE~~ **incur the costs associated with the manufacturing of preclinical** , ~~SOD1- ALS and Fabry disease into Phase I / II~~ clinical ~~studies~~ **and commercial supplies of our product candidates** ; ● ~~potentially acquiring~~ **seek regulatory approvals** ~~or~~ **for any** ~~in- licensing rights to new therapeutic targets,~~ product candidates ~~and technologies~~ **that successfully complete clinical trials** ; ● **maintain** ~~making potential future milestone payments related to the acquisition of Corlieve~~ , ~~if any~~ **expand and protect our intellectual property portfolio** ; ● ~~advancing preclinical research~~ **hire additional personnel to support our business; ● enhance our operational, financial** and ~~development for gene therapy product candidates targeting~~ **management information systems and personnel; and ● incur legal, accounting and** other **expenses operating** ~~diseases; and ● continuing to invest in expanding, developing and optimizing our manufacturing capabilities and other enabling technologies, such~~ as **a public company** ~~next- generation viral vectors, promoters and re- dosing~~ . ~~We~~ **While we expect that, as a result of the Reorganization, we will realize some cost savings and reduce our operating expenses, we** may never succeed in ~~these activities~~ **materially reducing our operating expenses** and, even if we do, may never generate revenues that are sufficient to achieve or sustain profitability. **Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis.** Our failure to become and remain profitable would depress the value of our company and could impair our ability to **raise capital,** expand our business, maintain our research and development efforts, diversify our product offerings, or even continue our operations. We will ~~likely~~ need to raise additional funding **in order to advance the development of our product candidates** , which may not be available on acceptable terms, or at all. Failure to obtain capital when needed may force us to delay, limit or terminate our product development efforts or other operations which could have a material adverse effect on our business, financial condition, results of operations and cash flows. We expect to incur significant expenses in connection with our ~~on- going~~ **ongoing** activities and ~~that~~ we will ~~likely~~ need to obtain substantial additional funding in ~~connection with~~ **order to fund the development of our product pipeline and support** our continuing operations. In addition, we have based our estimate of our financing requirements on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. Adequate capital may not be available to us when needed or may not be available on acceptable terms. Our ability to obtain **additional** debt financing may be limited by covenants we have made under our ~~2021~~ **2023** ~~Restated~~ **Amended** Facility with Hercules ~~Capital Inc. (" Hercules ") that we entered into on December 15, 2021 when the Company and Hercules amended and restated the 2021 Amended Facility (the " 2021 Restated Facility ")~~ and our pledge to Hercules of substantially all our assets as collateral **. Our ability to obtain additional equity financing may be limited by our shareholders' willingness to approve the issuance of additional share capital** . If we raise additional capital through the sale of equity or convertible debt securities, our shareholders ~~'~~ **'** ownership interest could be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of holders of our ordinary shares. If we raise additional funds through collaborations, strategic alliances, ~~or~~ marketing, distribution, or licensing arrangements with third parties, we may have to issue additional equity, relinquish valuable rights to our technologies, future revenue streams, products, or product candidates, or grant licenses on terms that may not be favorable to us. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce, or **further** eliminate our research and development programs or any future commercialization efforts, which would have a negative impact on our financial condition, results of operations and cash flows. Our existing and any future indebtedness could adversely affect our ability to operate our business. As of December 31, ~~2022~~ **2023** , we had $ 100. 0 million of outstanding principal of borrowings under the ~~2021~~ **2023** ~~Restated~~ **Amended** Facility, which we are required to repay in full in ~~December~~ **January** ~~2025~~ **2027 . We might not be able to finance our operations into the second quarter of 2027 from our existing cash, cash equivalents, and cash resources if we are not able to refinance the 2023 Amended Facility prior to the January 2027 maturity date** . We could in the future incur additional debt obligations beyond our borrowings from Hercules. Our existing loan obligations, together with other similar obligations that we may incur in the future, could have significant adverse consequences, including: ● requiring us to dedicate a portion of our cash resources to the payment of interest and principal, reducing money available to fund working capital, capital expenditures, research and development and other general corporate purposes; ● increasing our vulnerability to adverse changes in general economic, industry and market conditions; ● subjecting us to restrictive covenants that may reduce our ability to take certain corporate actions or obtain further debt or equity financing; ● limiting our flexibility in planning for, or reacting to, changes in our business and the industry in which we compete; and ● placing us at a disadvantage compared to our competitors that have less debt or better debt servicing options. We may not have sufficient funds ~~,~~ and may be unable to arrange for additional financing ~~,~~ to pay the amounts due under our existing loan obligations. Failure to make payments or comply with other covenants under ~~our existing debt~~ **2023 Amended Facility** could result in an event of default and acceleration of amounts due. Under the ~~2021~~ **2023** ~~Restated~~ **Amended** Facility, the occurrence of an event that would reasonably be expected to have a material adverse effect on our business, operations, assets, or condition is an event of default. If an event of default occurs and the lender accelerates the amounts due, we may not be able to make accelerated payments, and the lender could seek to enforce security interests in the collateral securing such indebtedness, which includes substantially all our assets **Business Development Our** ~~,enter into strategic transactions consistent with our~~ business development ~~objectives~~ **strategy may not produce the cash flows expected or could result in additional costs and challenges** .Any **business development** ~~acquisition or strategic~~ transaction could expose us to unknown liabilities and risks,and we may incur additional costs and expenses necessary to address an acquired company' s failure to comply with laws and governmental rules and regulations.We could incur additional costs related to resources ~~necessary~~ to align our business practices and operations ~~with that of the acquired company~~ .Moreover,we cannot ~~be sure~~ **assure** that the anticipated ~~or intended~~ benefits of any acquisition ~~or strategic transaction~~ would be realized in a timely manner,if at all **.Risks Related to** . Risks Related to Other Legal Compliance Matters Our relationships with

employees, customers and third ~~–~~parties ~~is~~ **are** subject to applicable laws and regulations, the non- compliance of any of which could have a material adverse effect on our business, financial condition, and results of operations. Healthcare providers, physicians, other practitioners, and third- party payers will play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our future arrangements with third party payers and customers may expose us to broadly applicable anti- bribery laws, including the Foreign Corrupt Practices Act, as well as fraud and abuse and other U. S. and international healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we would be able to market, sell and distribute any products for which we obtain marketing approval. Efforts to ensure that our business arrangements with third parties will comply with applicable laws and regulations could involve substantial costs. If our operations, or the activities of our collaborators, distributors or other third- party agents are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal, and administrative penalties, damages, fines, imprisonment, exclusion from participation in government funded healthcare programs and the curtailment or restructuring of our operations. Additionally, we are subject to various labor and employment laws and regulations. These laws and regulations relate to matters such as employment discrimination, wage and hour laws, requirements to provide meal and rest periods or other benefits, family leave mandates, employee and independent contractor classification rules, requirements regarding working conditions and accommodations to certain employees, citizenship or work authorization and related requirements, insurance and workers' compensation rules, healthcare laws, scheduling notification requirements and anti- discrimination and anti- harassment laws. Complying with these laws and regulations, including ongoing changes thereto, subjects us to substantial expense and non- compliance could expose us to significant liabilities. In particular, we are subject to allegations of Sarbanes- Oxley whistleblower retaliation and employment discrimination and retaliation, and we may in the future be subject to additional claims of non- compliance ~~of~~ **with** similar or other ~~Laws~~ **laws** and regulations. The costs associated with ~~a~~ **an alleged or actual** violation of any of the foregoing could be substantial and could cause irreparable harm to our reputation or otherwise have a material adverse effect on our business, financial condition, and results of operations. We are subject to laws governing data protection in the different jurisdictions in which we operate. The implementation of such data protection regimes is complex, and should we fail to fully comply, we may be subject to penalties that may have an adverse effect on our business, financial condition, and results of operations. Many national **, international,** and state laws govern the privacy and security of health information and other personal and private information. They often differ from each other in significant ways. For instance, the EU has adopted a comprehensive data protection law called the **EU General Data Protection Regulation that took effect in May 2018. The UK has, following its exit from the EU, substantially adopted the EU General Data Protection Regulation into its domestic law through the UK** General Data Protection Regulation (**collectively with the EU General Data Protection Regulation, and related EU and UK e- Privacy laws, the** " GDPR ") ~~that took effect in May 2018~~. The GDPR, together with the national legislation of the **UK (including the Data Protection Act 2018) and** EU member states governing the processing of personal data, impose strict obligations and restrictions on the ability to collect, **use,** analyze and transfer personal ~~data~~ **information** , including health data from clinical trials and adverse event reporting. **GDPR** ~~In particular, these~~ obligations ~~and restrictions concern~~ **applicable to us may include, in many circumstances, obtaining** the **(opt- in)** consent of the individuals to whom the personal data relates ~~, the information provided~~ **; providing GDPR- prescribed data processing notices** to ~~the~~ individuals ~~,~~ **; complying with restrictions regarding** the transfer of personal data out of the EU ~~,~~ **or the UK (as applicable) (including to the US); implementing and maintaining data protection policies and procedures; restrictions regarding the use of certain innovative technologies; providing data** security breach notifications ~~,~~ **to supervisory authorities and affected individuals under tight timescales; and implementing** security and confidentiality ~~of~~ **measures. Supervisory authorities in** the **different EU member states and the UK may interpret the GDPR and national laws differently and impose additional requirements. Guidance on implementation and compliance practices are often updated or otherwise revised. All of this adds to the complexity of processing** personal **information** ~~data,~~ and **remaining compliant with** ~~imposition of substantial potential fines for breaches of~~ the **GDPR** ~~data protection obligations~~. The GDPR **allows EU and UK supervisory authorities to** ~~imposes~~ **impose** penalties for non- compliance of up to the greater of EUR 20. 0 million ~~or~~ **and** 4 % of **annual** worldwide **gross** revenue **of the corporate group in question** . ~~Data protection~~ **(There are similar caps in GBP under the UK GDPR.). Supervisory** authorities **in the EU and UK may potentially levy such fines directly upon on the non- compliant entity and / or on the parent company of the non- compliant entity. Supervisory authorities also possess other wide- ranging powers, including conducting unannounced inspections of our facilities and system (so- called " dawn raids "), and issuing " stop processing " orders to us. Separate** from ~~the different EU member states may interpret the GDPR and national laws differently and impose additional requirements, which add to the complexity of processing personal data in the EU. Guidance on implementation and compliance practices are often updated or otherwise revised. The significant costs of compliance with risk of~~ regulatory enforcement actions **, individuals may bring private actions (including potentially group or representative actions) against us. There is no statutory cap in the GDPR on the amount of compensation or the damages which individuals may recover. Overall, the significant costs of GDPR compliance, risk of regulatory enforcement actions and private litigation** under, and other burdens imposed by the GDPR as well as under other regulatory schemes throughout the world related to privacy and security of health information and other personal and private data could have an adverse impact on our business, financial condition, and results of operations. Product liability lawsuits could cause us to incur substantial liabilities and to limit commercialization of our therapies. We face an inherent risk of product liability related to the testing of our product candidates in human clinical trials and in connection with product sales. If we cannot successfully defend ourselves against claims that our product candidates or products **or the procedures used to administer them to patients** caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in: ● decreased demand for any product candidates or products that we develop or sell; ● injury to our reputation and significant negative media

attention; ● negative publicity or public opinion surrounding gene therapy; ● withdrawal of clinical trial participants or sites, or discontinuation of development programs; ● significant costs to defend the related litigation; ● substantial monetary awards to trial participants or patients; ● loss of revenue; ● initiation of investigations, and enforcement actions by regulators; and product recalls, withdrawals, revocation of approvals, or labeling, marketing, or promotional restrictions; ● reduced resources of our management to pursue our business strategy; and ● the inability to further develop or commercialize any products that we develop. ~~Dependent~~ **Depending** upon the country where the clinical trial is conducted, we currently hold coverages ranging from EUR 500, 000 to EUR 10, 000, 000 per occurrence. Such coverage may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage as we expand our clinical trials. In addition, insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. In the event insurance coverage is insufficient to cover liabilities that we may incur, it could have a material adverse effect on our business, financial condition, and results of operations. Healthcare legislative and regulatory reform measures may have a material adverse effect on our financial operations. Our industry is highly regulated and changes in law may adversely impact our business, operations, or financial results. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or the PPACA, is a sweeping measure intended to, among other things, expand healthcare coverage within the U. S., primarily through the imposition of health insurance mandates on employers and individuals and expansion of the Medicaid program. Several provisions of the law may affect us and increase certain of our costs. In addition, other legislative changes have been adopted since the PPACA was enacted. These changes include aggregate reductions in Medicare payments to providers of 2 % per fiscal year, which went into effect on April 1, 2013, Congress subsequently has extended the period over which these reductions are in effect. While President Biden previously signed legislation temporarily to eliminate this reduction through the end of 2021, ~~recent legislation will restart the reductions~~ **a 1 % payment adjustment was implemented from April 1 – June 30** , ~~which will thereafter remain in~~ **2022, and a 2 % payment adjustment took** effect **beginning July 1, 2022** ~~through 2031 unless additional congressional action is taken~~ . In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on our customers and, accordingly, our financial operations. We anticipate that the PPACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and additional downward pressure on pricing and the reimbursement our customers may receive for our products, and increased manufacturer rebates. Further, there have been, and there may continue to be, judicial and Congressional challenges to certain aspects of the PPACA. For example, the U. S. Tax Cuts and Jobs Act of 2017 includes a provision repealing, effective January 1, 2019, the tax- based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the ~~"~~ **“** individual mandate ~~"~~ **”** . Additional legislative and regulatory changes to the PPACA, its implementing regulations and guidance and its policies, remain possible in the ~~117th~~ **118th** U. S. Congress and under the Biden Administration. However, it remains unclear how any new legislation or regulation might affect the prices we may obtain for any of our product candidates for which regulatory approval is obtained. Any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payers. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products. Our **future growth may depend, in part, on our ability to penetrate markets outside of the U. S. and Europe where we would be subject to additional regulatory burdens and other risks and uncertainties. Our future profitability may depend, in part, on our ability to commercialize current or future drug candidates in foreign markets for which we may rely on collaborations with third parties. We are not permitted to market or promote any of our drug candidates before we receive regulatory approval from the applicable regulatory authority in that foreign market. To obtain separate regulatory approval in many other jurisdictions we must comply with numerous and varying regulatory requirements of such jurisdictions regarding safety and efficacy and governing, among other things, clinical trials, manufacturing, commercial sales, pricing and distribution of our drug candidates, and we cannot predict success in these jurisdictions. Our** internal computer systems, or those of our collaborators or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs. Our internal computer systems and those of our current and any future collaborators and other contractors or consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. The size and complexity of our information technology systems, and those of our collaborators, contractors and consultants, and the large amounts of confidential information stored on those systems, make such systems vulnerable to service interruptions or to security breaches from inadvertent or intentional actions by our employees, third- party vendors and / or business partners, or from cyber- attacks by malicious third parties. Cyber- attacks are increasing in their frequency, sophistication, and intensity, and have become increasingly difficult to detect. Cyber- attacks could include the deployment of harmful malware, ransomware, denial- of- service attacks, social engineering, and other means to affect service reliability and threaten the confidentiality, integrity, and availability of information. Cyber- attacks also could include phishing attempts or e-mail fraud to cause payments or information to be transmitted to an unintended recipient. **Our hybrid** ~~The increased number of employees working remotely -- remote work policy may due to Covid might~~ increase our vulnerability to **such** ~~the above risk~~ **risks** . While we have experienced and addressed system failures, cyber- attacks, and security breaches in the past, we have not experienced a system failure, accident, cyber- attack, or security breach that has resulted in a material interruption in our operations to date. In the future, such events could result in a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets, data, or other proprietary information or other similar disruptions.

Additionally, any such event that leads to unauthorized access, use or disclosure of personal information, including personal information regarding our patients or employees, could harm our reputation, cause us not to comply with federal and / or state breach notification laws and foreign law equivalents and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information. Security breaches and other inappropriate access can be difficult to detect, and any delay in identifying them may lead to increased harm of the type described above **. We may need to devote significant resources to protect against security breaches or to address problems caused by a cyber- attack or security breach** . While we have implemented security measures to protect our information technology systems and infrastructure, there can be no assurance that such measures will prevent service interruptions or security breaches that could adversely affect our business and the further development and commercialization of our product and product candidates could be delayed. **See Part I, Item 1C, Cybersecurity, in this Annual Report on Form 10- K for more information regarding our cybersecurity risk management, strategy and governance.** Climate change **as well as corporate responsibility initiatives** , **including** environmental, social and governance **(ESG) matters** ~~and sustainability initiatives may result in regulatory or structural industry changes that could require significant operational changes and expenditures~~ , **may impose additional costs on** ~~reduce demand for the Company' s products and adversely affect~~ our business ~~, financial condition,~~ and ~~results of operations~~ **expose us to new risks** . Greenhouse gases may have an adverse effect on global temperatures, weather patterns, and the frequency and severity of extreme weather and natural disasters. Such events could have a negative effect on our business. Concern over **the impact of** climate change may result in new or additional legislative and regulatory requirements to reduce or mitigate the effects of climate change on the environment, which could result in ~~future~~ **increases in** ~~tax~~ **taxes** , transportation ~~cost~~ **costs** ~~,~~ and ~~utility~~ **utilities** ~~increases~~ **, among other expenses** . Moreover, natural disasters and extreme weather conditions may impact the productivity of our facilities, the **ability of the patients in our clinical trials to maintain compliance with trial protocols or access clinical trial sites, the** operation of our supply chain, or consumer buying patterns. ~~Any~~ **The occurrence of any** of these ~~risks~~ **events** could have a material adverse effect on our business. **ESG** ~~Climate change, environmental, social and governance~~ and sustainability **initiatives continue to attract** ~~are a growing global movement. Continuing~~ political and social attention **have** ~~to these issues has~~ resulted in both existing and pending international agreements and national, regional **,** and local legislation, regulatory measures, reporting obligations and policy changes. ~~Also, there~~ **There** is increasing societal pressure in some of the ~~areas where~~ **countries in which** we operate ~~,~~ to limit greenhouse gas emissions as well as other global initiatives **focused on climate change** . These agreements and measures, including the Paris Climate Accord, may require, or could result in future legislation, regulatory measures or policy changes that would require operational changes, taxes, or purchases of emission credits to reduce emission of greenhouse gases from our operations, which may **require the that we dedicate additional resources toward compliance with these measures and** result in substantial capital expenditures. Furthermore, increasing attention **on** ~~to climate change,~~ ESG **matters** ~~and sustainability~~ has resulted in governmental investigations, and public and private litigation, which could increase our costs or otherwise adversely affect our business or results of operations. In addition, organizations that provide information to investors on corporate governance and related matters have developed ratings processes for evaluating companies **and investment funds based** on ~~their approach to~~ ESG ~~matters~~ **and sustainability metrics** . Such ratings are used by ~~some~~ investors to inform their investment and voting decisions. Unfavorable ESG ratings may lead to increased negative investor sentiment toward us, which could have a negative impact on the price of our securities and our access to and costs of capital. ~~Any~~ **In addition, investors, particularly institutional investors, use these scores to benchmark companies against their peers and if a company is perceived as lagging, take actions to hold these companies and their boards of directors accountable. Board diversity is an ESG topic that is, in particular, receiving heightened attention by investors, stockholders, lawmakers and listing exchanges. Certain states have passed laws requiring companies to meet certain gender and ethnic diversity requirements on their boards of directors. We may face reputational damage in the event our corporate responsibility initiatives or objectives, do not meet the standards set by our investors, stockholders, lawmakers, listing exchanges or other constituencies, or if we are unable to achieve an acceptable ESG or sustainability rating from third- party rating services. The effects of climate change or any** or all of these ESG and sustainability initiatives may result in significant operational changes and expenditures, reduced demand for our products, cause us reputational harm, and could materially adversely affect our business, financial condition, and results of operations. Risks Related to Employee Matters and Managing **Our** Growth Our future success depends on our ability to retain key executives, technical staff, and other employees and to attract, retain and motivate qualified personnel. Our future growth and success will depend in large part on our continued ability to attract, retain, manage **,** and motivate our employees. The loss of the services of any member of our senior management or the inability to hire or retain experienced management personnel could adversely affect our ability to execute our business plan and harm our operating results. We are highly dependent on hiring, training, retaining **,** and motivating key personnel to lead our research and development, clinical operations, and manufacturing efforts. Although we have entered into employment agreements with our key personnel, each of them may terminate their employment on short notice. We do not maintain key person insurance for any of our senior management or employees. The loss of the services of our key employees could impede the achievement of our research and development objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing senior management and key employees may be difficult and may take an extended period because of the limited number of individuals in our industry with the breadth and depth of skills and experience required to successfully develop gene therapy products. ~~Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms.~~ The competition for qualified personnel in the pharmaceutical field is intense, and there is a limited pool of qualified potential employees to recruit. Due to this intense competition, we may be unable to continue to attract and retain **the** qualified personnel necessary for the development of our business or to recruit suitable replacement personnel. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our business may be harmed and our growth strategy

may be limited. Additionally, we are reliant on our employees, contractors, consultants, vendors **,** and other parties with whom we have relationships to behave ethically and within the requirements of the law. The failure of any employee or other such third parties to act within the bounds of the applicable laws, regulations, agreements, codes and other requirements, or any misconduct or illegal actions or omissions by such persons, could materially damage our business **. Actions that we have taken to restructure our business in alignment with our strategic priorities may not be as effective as anticipated, may not result in cost savings to us and could disrupt our business. In October 2023, we commenced the Reorganization to reprioritize our portfolio of development candidates, conserve financial resources and better align our workforce with current business needs. We may encounter challenges in the execution of these efforts, and these challenges could impact our financial results. Although we believe that these actions will reduce operating costs, we cannot guarantee that the Reorganization will achieve or sustain the targeted benefits, or that the benefits, even if achieved, will be adequate to meet our long- term expectations. As a result of the Reorganization, we will incur additional costs in the near term, including cash expenditures for employee transition, notice period and severance payments, employee benefits, and related facilitation costs. Additional risks associated with the continuing impact of the Reorganization include employee attrition beyond our intended reduction in force and adverse effects on employee morale (which may also be further exacerbated by actual or perceived declining value of equity awards), diversion of management attention, adverse effects to our reputation as an employer (which could make it more difficult for us to hire and retain new employees in the future), potential understaffing and potential failure or delays to meet development targets due to the loss of qualified employees or other operational challenges. If we do not realize the expected benefits of our restructuring efforts on a timely basis or at all, our business, results of operations and financial condition could be adversely affected** . Risks Related to Our Ordinary Shares The price of our ordinary shares has been and may in the future be volatile and fluctuate substantially. Our share price has been and may in the future be volatile. From the start of trading of our ordinary shares on the Nasdaq Global Select Market on February 4, 2014 through February 23, ~~2023~~ **2024** ~~,~~ the sale price of our ordinary shares ranged from a high of $ 82. 49 to a low of $ 4. 72. The closing price on February 23, ~~2022~~ **2024** , was $ ~~20~~ **6** . ~~06~~ **32** per ordinary share. ~~The~~ **In recent years, the** stock market in general and the market for **shares of** smaller biopharmaceutical companies in particular ~~,~~ have experienced ~~extreme volatility~~ **significant price and volume fluctuations** that ~~has~~ **have** often been unrelated **or disproportionate** to **changes in** the operating performance of ~~particular~~ **the** companies **whose stock is experiencing those price and volume fluctuations** . The market price for our ordinary shares may be influenced by many factors, including: ● the success of competitive products or technologies; ● results of clinical trials of our product candidates or those of our competitors; ● public perception **and market reaction to our interim data from clinical trials; ● public perception** of gene therapy **; ● interactions with the FDA on the design of our clinical trials and regulatory endpoints** ; ● regulatory delays and greater government regulation of potential products due to adverse events; ● regulatory or legal developments in the EU, the U. S., and other countries; ● developments or disputes concerning patent applications, issued patents or other proprietary rights; ● the recruitment or departure of key personnel **; ● changes to our business, including pipeline reprioritizations and restructurings** ; ● the level of expenses related to any of our product candidates or clinical development programs; ● the results of our efforts to discover, develop, acquire or in- license additional product candidates or products; ● actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts; ● variations in our financial results or those of companies that are perceived to be similar to us; ● changes in the structure of healthcare payment systems; ● market conditions in the pharmaceutical and biotechnology sectors; ● mergers, acquisitions, licensing, and collaboration activity among our peer companies in the pharmaceutical and biotechnology sectors; ~~and~~ ● general economic, industry and market conditions **; and ● the other factors described in this " Risk Factors " section. Following periods of such volatility in the market price of a company' s securities, securities class action litigation has often been brought against that company. Because of the potential volatility of our stock price, we may become the target of securities litigation in the future. In addition, notwithstanding protective provisions in our articles of association and available to us under Dutch corporate law, market volatility may lead to increased shareholder activism if we experience a market valuation that activist investors believe is not reflective of the intrinsic value of our ordinary shares. Activist campaigns that contest or conflict with our strategic direction or seek changes in the composition of our board of directors could have an adverse effect on our operating results and financial condition. Securities litigation or shareholder activism could result in substantial costs and divert management' s attention and resources from our business** . Our directors, executive officers, and major shareholders, if they choose to act together, will continue to have a significant degree of control with respect to matters submitted to shareholders for approval. Our directors, executive officers and major shareholders holding more than 5 % of our outstanding ordinary shares, in the aggregate, beneficially own approximately ~~39~~ **26** . ~~4~~ **6** % of our issued shares (including such shares to be issued in relation to exercisable options to purchase ordinary shares) as ~~at~~ **of** December 31, ~~2022~~ **2023** . As a result, if these shareholders were to choose to act together, they may be able, as a practical matter, to control many matters submitted to our shareholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, could control the election of the board **of** directors and the approval of any merger, consolidation, or sale of all or substantially all our assets. These shareholders may have interests that differ from those of other of our shareholders and conflicts of interest may arise. Provisions of our articles of association or Dutch corporate law might deter acquisition bids for us that might be considered favorable and prevent or frustrate any attempt to replace our board. **Under Dutch law, various protective measures are possible and permissible within the boundaries set by Dutch statutory and case law.** Certain provisions of our articles of association may make it more difficult for a third party to acquire control of us or effect a change in our board. These provisions include: ● **the** staggered **three- year** terms of our **non- executive** directors **as a result of which only approximately one- third of our non- executive directors may be subject to election or re- election in any one year** ; ● a provision that our directors may only be ~~removed~~ **dismissed or suspected** at a general meeting of

shareholders by a two- thirds majority of votes cast representing more than half of ~~the issued~~ **our outstanding ordinary** ~~share~~ **shares** ~~capital~~ **; ● a provision that our executive directors may only be appointed upon binding nomination** of the ~~Company~~ **non- executive directors, which can only be overruled by the general meeting of shareholders with a two- thirds majority of votes cast representing at least 50 % of our outstanding ordinary shares** ; and ● a requirement that certain matters, including an amendment of our articles of association, may only be brought to our shareholders for a vote upon a proposal by **our board. Moreover, according to Dutch corporate law, our board can invoke a cooling- off period of up to 250 days in the event of an unsolicited takeover bid or certain shareholder activism. During a cooling- off period, our general meeting of shareholders would not be able to dismiss, suspend or appoint directors (or amend the provisions in our articles of association dealing with those matters) except at the proposal of** our board. We do not expect to pay dividends in the foreseeable future. We have not paid any dividends since our incorporation. Even if future operations lead to significant levels of distributable profits, we currently intend ~~that~~ **those** earnings, if any, will be reinvested in our business and that dividends will not be paid until we have an established revenue stream to support continuing dividends. Accordingly, shareholders cannot rely on dividend income from our ordinary shares and any returns on an investment in our ordinary shares will likely depend entirely upon any future appreciation in the price of our ordinary shares. If we fail to maintain an effective system of internal controls, we may be unable to accurately report our results of operations or prevent fraud or fail to meet our reporting obligations, and investor confidence and the market price of our ordinary shares may be materially and adversely affected. If we fail to maintain the adequacy of our internal control over financial reporting, we may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting. If we fail to maintain effective internal control over financial reporting, we could experience material misstatements in our financial statements and fail to meet our reporting obligations, which would likely cause investors to lose confidence in our reported financial information. This could in turn limit our access to capital markets, harm our results of operations, and lead to a decline in the trading price of our ordinary shares. Additionally, ineffective internal control over financial reporting could expose us to increased risk of fraud or misuse of corporate assets and subject us to potential delisting from The Nasdaq Global Select Market, regulatory investigations and civil or criminal sanctions. Our reporting and compliance obligations may place a significant strain on our management, operational and financial resources **,** and systems for the foreseeable future. ~~Risks for U. S. Holders~~ We have in the past qualified and in the future may qualify as a passive foreign investment company, which may result in adverse U. S. federal income tax ~~consequence~~ **consequences** to U. S. holders. **A corporation organized outside the U. S. generally** ~~Based on our average value of our gross assets, our cash and cash equivalents as well~~ **will be classified** ~~as the price of our shares we qualified~~ as a passive foreign investment company (" PFIC ") for U. S. federal income tax ~~for 2016 and 2022 but not for 2017 through 2021. A corporation organized outside the U. S. generally will be classified as a PFIC for U. S. federal income tax~~ purposes in any taxable year in which at least 75 % of its gross income is passive income or on average at least 50 % of the gross value of its assets is attributable to assets that produce passive income or are held to produce passive income. Passive income for this purpose generally includes dividends, interest, royalties, rents and gains from commodities and securities transactions. **Based on our average value of our gross assets, our cash and cash equivalents as well as the price of our ordinary shares, we expect to be classified as a PFIC for U. S. federal income tax for 2023.** Our status in any taxable year will depend on our assets and activities in each year, and because this is a factual determination made annually after the end of each taxable year, there can be no assurance that we will continue to qualify as a PFIC in future taxable years. The market value of our assets may be determined in large part by reference to the market price of our ordinary shares, which is likely to fluctuate, and may fluctuate considerably given that market prices of biotechnology companies have been especially volatile. If we were considered a PFIC for the current taxable year or any future taxable year, a U. S. holder would be required to file annual information returns for such year, whether the U. S. holder disposed of any ordinary shares or received any distributions in respect of ordinary shares during such year. In certain circumstances a U. S. holder may be able to make certain tax elections that would lessen the adverse impact of PFIC status; however, to make such elections the U. S. holder will usually have to have been provided information about the company by us, and we do not intend to provide such information. The U. S. federal income tax rules relating to PFICs are complex. U. S. holders are urged to consult their tax advisors with respect to the purchase, ownership and disposition of our shares, the possible implications to them of us being treated as a PFIC (including the availability of applicable election, whether making any such election would be advisable in their particular circumstances) as well as the federal, state, local and foreign tax considerations applicable to such holders in connection with the purchase, ownership, and disposition of our shares. Any U. S. or other foreign judgments may be difficult to enforce against us in the Netherlands. Although we report as a U. S. domestic filer for SEC reporting purposes, we are ~~incorporated~~ **organized and existing** under the laws of the Netherlands. Some of the members of our board and senior management reside outside the U. S. **In addition, a significant portion of our assets are located outside the U. S** . As a result, it may not be possible for shareholders to effect service of process within the U. S. upon such persons or to enforce judgments against them or us in U. S. courts, including judgments predicated upon the civil liability provisions of the federal securities laws of the U. S ~~.~~. In addition, it is not clear whether a Dutch court would impose civil liability on us or any of our Board members in an original action based solely upon the federal securities laws of the ~~United States~~ **U. S.** brought in a court of competent jurisdiction in the Netherlands. The U. S. and the Netherlands currently do not have a treaty providing for the reciprocal recognition and enforcement of judgments, other than arbitration awards, in civil and commercial matters. Consequently, a final judgment for payment given by a court in the U. S., whether or not predicated solely upon U. S. securities laws, would not automatically be recognized or enforceable in the Netherlands. To obtain a judgment which is enforceable in the Netherlands, the party in whose favor a final and conclusive judgment of the U. S. court has been rendered will be required to file its claim with a court of competent jurisdiction in the Netherlands. Such party may submit to the Dutch court the final judgment rendered by the U. S. court. If and to the extent that the Dutch court finds that the jurisdiction of the U. S. court has been based on grounds which are internationally acceptable and that proper legal procedures

have been observed, the Dutch court will, in principle, give binding effect to the judgment of the U. S. court, unless such judgment contravenes principles of public policy of the Netherlands. Dutch courts may deny the recognition and enforcement of punitive damages or other awards. Moreover, a Dutch court may reduce the amount of damages granted by a U. S. court and recognize damages only to the extent that they are necessary to compensate actual losses or damages. Enforcement and recognition of judgments of U. S. courts in the Netherlands are solely governed by the provisions of the Dutch Civil Procedure Code. Therefore U. S. shareholders may not be able to enforce against us or our board members or senior management who are residents of the Netherlands or countries other than the U. S. any judgments obtained in U. S. courts in civil and commercial matters, including judgments under the U. S. federal securities laws. The rights and responsibilities of our shareholders and directors are governed by Dutch law and differ in some important respects from the rights and responsibilities of shareholders under U. S. law. **We are** ~~Although we report as~~ a ~~U. S. domestic filer for SEC purposes,~~ **public company (naamloze vennootschap) organized under the laws of the Netherlands and** our corporate affairs are governed by our articles of association and by the laws governing companies incorporated in the Netherlands. The rights of our shareholders and the responsibilities of members of our board under Dutch law are different than under the laws of some U. S. jurisdictions. In the performance of their duties, our board members are required by Dutch law to consider the interests of uniQure, its shareholders, its employees, and other stakeholders and not only those of our shareholders (as would be required under the law of most U. S. jurisdictions). As a result of these considerations **, it is possible that some of these parties will have interests that are different from, or in addition to, your interests as a shareholder, and** our directors may take ~~action~~ **actions** that would be different than those that would be taken by a company organized under the law of some U. S. jurisdictions. ~~70~~ **In addition, in accordance with our articles of association, approval of our shareholders is required before our board of directors can authorize the issuance of our ordinary shares in an equity financing. Our shareholders' reluctance to approve such further issuances of ordinary shares could adversely affect our ability to raise capital and fund development programs and continued operations. There can be no assurance that Dutch law will not change in the future or that it will serve to protect investors in a similar fashion afforded under corporate law principles in the U. S., which could adversely affect the rights of investors. We may be adversely affected by unstable market and economic conditions, such as inflation, which may negatively impact our business, financial condition and stock price. Market conditions such as inflation, volatile energy costs, geopolitical issues, war, unstable global credit markets and financial conditions could lead to periods of significant economic instability, diminished liquidity and credit availability, diminished expectations for the global economy and expectations of slower global economic growth going forward. Our business and operations may be adversely affected by such instability, including any such inflationary fluctuations, economic downturns, volatile business environments and continued unstable or unpredictable economic and market conditions. Inflation in particular has the potential to adversely affect our liquidity, business, financial condition, and results of operations by increasing our overall cost structure. The existence of inflation in the economy has resulted in, and may continue to result in, higher interest rates and capital costs, shipping costs, supply shortages, increased costs of labor, weakening exchange rates and other similar effects. As a result of inflation, we have experienced, and may continue to experience, cost increases across our business. Although we may take measures to mitigate the impact of this inflation, if these measures are not effective our business, financial condition, results of operations and liquidity could be materially adversely affected. Even if such measures are effective, there could be a difference between the timing of when these beneficial actions impact our results of operations and when cost inflation is incurred. Any such volatility and disruptions may have adverse consequences on us or the third parties on whom we rely. If economic and market conditions deteriorate or do not improve, it may make any future financing efforts more difficult to complete, more costly and more dilutive to our shareholders. Additionally, due to our volatile industry and industry- wide declining stock values, investors may seek to pursue non- biotech investments with steadier returns. Failure to secure any necessary financing in a timely manner or on favorable terms could have a material adverse effect on our operations, financial condition or stock price or could require us to delay or abandon development or commercialization plans. If securities or industry analysts cease to publish or publish inaccurate or unfavorable research about our business, our share price and trading volume could decline. The trading market for our common shares depends in part on the research and reports that securities or industry analysts publish about us or our business. If one or more of the analysts who cover us downgrades our common shares or publishes inaccurate or unfavorable research about our business, our share price may decline. If one or more of these analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our shares could decrease, which might cause our share price and trading volume to decline. If we do not achieve our projected development and financial goals in the timeframes we announce and expect, the commercialization of our product candidates may be delayed and, as a result, our stock price may decline. We estimate the timing of the accomplishment of various scientific, clinical, regulatory, and other product development goals, along with financial and other business- related milestones. From time to time, we publicly announce the expected timing of some of these milestones along with guidance as to our cash runway. These milestones may include the commencement or completion of scientific studies, clinical trials, the submission of regulatory filings and interactions with regulatory authorities, and approval timelines for commercial sales. All these milestones are based on a variety of assumptions that may prove to be untrue. The timing of our actual achievement of these milestones can vary dramatically compared to our estimates, in many cases for reasons beyond our control. If we do not meet these milestones, including those that are publicly announced, the development and commercialization of our products may be delayed, our business could suffer reputational harm and, as a result, our stock price may decline.**