Risk Factors Comparison 2025-02-27 to 2024-02-28 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 **Our Business and** the Development of Our Product Candidates 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, **including inability to demonstrate sufficient safety or efficacy, or** challenges associated with its regulatory ~~pathway~~ **approval** , **manufacturing** or **commercialization** ~~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 **for the treatment of Huntington' s disease** . In ~~December~~ **July** ~~2023~~ **2024** , we announced updated interim data from our ongoing Phase I / II clinical trials of AMT- 130, ~~including 30 months~~ **as summarized under " Business — Our Development** 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 **for Huntington' s Disease "** in **this Annual Report on Form 10 combination with perioperative immune suppression to evaluate near- K. These** ~~term safety, along with our plans to initiate regulatory interactions with the FDA and EMA to discuss the~~ interim data ~~and strategies~~ **follow notification from FDA in May 2024 that the agency granted RMAT designation** for ~~ongoing development of~~ AMT- 130 **based on AMT- 130' s potential to address the major unmet medical need among patients with Huntington' s disease. In addition, in December 2024, following our initial Type B meeting, we announced that we had reached agreement with FDA on key elements of an Accelerated Approval pathway for AMT- 130. In correspondence leading up to and following the Type B meeting, FDA agreed that data from the ongoing Phase I / II studies of AMT- 130, compared to a natural history external control, may serve as the primary basis for a BLA submission under FDA' s Accelerated Approval pathway. FDA also agreed that cUHDRS may be used as an intermediate clinical endpoint and that reductions in NfL measured in CSF may serve as supportive evidence of therapeutic benefit in the application for accelerated approval** . There are numerous factors that could impede or otherwise negatively impact our further development of AMT- 130, including, but not limited to, **potential** patient safety issues ~~,~~ **;** our failure to demonstrate sufficient clinical efficacy or durability of response data to warrant further development **or accelerated approval by FDA** , ~~delays in~~ **EMA or any other regulatory authority;** our ability to ~~enroll~~ **achieve alignment with FDA and other regulatory authorities on the primary statistical analysis plan and CMC requirements to support registration and the timing of such regulatory alignment; the results from future interim data readouts from our Phase I / II trial, including the three- year follow- up data from treated** patients **and safety and tolerability data from the third cohort; any requirement** ~~or~~ **for a Phase III confirmatory study; the timing and resources associated with our planned marketing applications; our ability to successfully commercialize AMT- 130 should we choose to do so without a partner;** challenges with ~~regulatory authorities~~ **potential development or commercial partners, should we choose to pursue further development or commercialization of AMT- 130 with a partner; and our ability to fund the further development and commercialization of the AMT- 130 program** . Any one or combination of these factors could force us to halt or discontinue the ongoing clinical trials of AMT- 130 **or related commercialization efforts** . Certain of these risk factors are heightened in the context of drug development for rare diseases like Huntington' s disease **and novel investigational products like gene therapies** 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. **Notwithstanding alignment** ~~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 **key elements of** ~~our novel gene therapy technology, we are unable predict how regulatory authorities will interpret our data or whether they~~ **the accelerated** ~~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 **pathway** ~~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 the 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. If we were required to, or if we chose to, discontinue development of AMT- 130 or any other **current or** future product candidates, or if any of them were to fail to receive regulatory approval or achieve sufficient market

acceptance, we could be prevented from or significantly delayed in achieving profitability and our business would be adversely affected. 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 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. **In June 2024, we announced that the FDA granted Regenerative Medicine Advanced Therapy (" RMAT ") designation for AMT- 130 based on the potential of AMT- 130 to address the major unmet medical need among patients with Huntington' s disease. Following our initial Type B meeting with the FDA, we announced in December 2024 that we had reached agreement with FDA on key elements of an accelerated approval pathway for AMT- 130 and have initiated BLA readiness activities based on this regulatory alignment.** We are also advancing three other product candidates ~~into~~ **through Phase I / II** clinical development – AMT- 260 for the treatment of **mTLE** ~~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 our voluntary postponement and comprehensive safety investigation into suspected unexpected serious adverse reactions in three patients. A failure of one or more clinical trials can occur at any stage and for a variety of 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 **an insufficient** study period for assessing the effectiveness of the product candidate ~~insufficient in length to assess potential clinical development~~ ; ● failures or delays in reaching agreement 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 clinical research organizations (" CROs ") and clinical trial sites; ● failures or delays in ~~patient~~ **identifying and** recruiting ~~into~~ **patients in our** clinical **studies** ~~trials or in the addition of new investigators~~ ; ● delays in receiving regulatory authorization to conduct 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, our chosen bases for comparison as it relates to **measurements of** clinical efficacy, our interpretation **and statistical analyses** of data **collected** 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; ● 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~~ **failing to** meet the necessary quality requirements; ● unanticipated clinical trial costs or insufficient funding, including paying substantial application user fees; ● 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 **third- party** ~~manufacturing~~ **manufacturers or their** ~~facility~~ **facilities** or ~~process~~ **processes** ; 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~~ **our** product candidates in humans. Such trials ~~and~~ **,** regulatory review and approval take many years. **Our** ~~It is impossible to predict when or if any of our~~ clinical trials ~~will~~ **may never yield results that** demonstrate that **our** 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 **efficacy or** 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, safety warnings, labeling statements or contraindications; ● be subject to changes in the way our products 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 other challenges; or ● experience **reputational** 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 **that we may not have sufficient resources to conduct or** for which we may not be able to meet the regulatory authorities' standards. Our ability to recruit patients for our clinical trials is 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~~ **our** clinical ~~trial~~ **trials** , which may delay or impede our planned trials **and development timelines** . In addition, we or any of our collaborators may not be able to ~~locate~~ **identify** and enroll ~~enough~~ **sufficient** eligible patients to participate in these trials as required by the FDA, the EMA or ~~similar~~ **other** 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 **several of** 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~~ **trial** eligibility ~~in some~~ **for certain** 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~~ **Patients** may **also** be reluctant to enroll in **clinical trials for** gene therapy ~~trials~~ **candidates** where ~~there are~~ other therapeutic alternatives **are** available **due** ~~or that may become available for various reasons, including, but not limited to,~~ uncertainty about the safety or effectiveness ~~of a new therapeutic such as a~~ gene ~~therapy~~ **therapies** and the possibility that treatment with ~~a~~ **one** gene therapy ~~therapeutic~~ could preclude future gene therapy treatments due to the formation of antibodies following and in response to the treatment **, or other unknown factors associated with novel therapeutics** . ~~Any~~ **Our** inability to successfully initiate or complete preclinical and clinical ~~development~~ **studies** could result in additional costs to us or impair our ability to receive marketing approval, to generate revenues from product sales or **from reaching certain development milestones, or** obtain regulatory **approval** ~~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 predictive of long- term efficacy in late- stage clinical trials, and our progress in trials for one product candidate may not be predictive of progress in trials for other product candidates. 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 **interim** results from ~~early~~ **our ongoing Phase I / II** clinical trials of AMT- 130, our product candidate targeting Huntington' s disease, may not be predictive of the results of **future interim analyses or** 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 **or how the results from our clinical trials are analyzed** , whether as a result of regulatory feedback or changes in clinical trial procedures and protocols, may also impact ~~their~~ -- **the** ~~performance in~~ **results of** subsequent **analyses or** 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 the results are not reproducible or if our products show diminishing activity over time, our product candidates may not receive approval from the FDA, EMA or comparable regulatory authorities **, or may have conditional approvals revoked** . Data obtained from preclinical and clinical activities ~~are~~ **may be** subject to varying interpretations **and analyses** , which may delay, limit, or prevent regulatory approval. In addition, we may encounter regulatory delays or rejections ~~because of many factors~~ **due to shifting political priorities** , ~~including~~ **resulting changes in regulatory agencies or other** 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. ~~Interim~~ **Additionally, we are currently conducting and may in the future conduct clinical trials that utilize an " open- label " trial design. An " open- label " clinical trial is one where both the patient and investigator know whether the patient is receiving the investigational therapeutic candidate (as opposed to an existing approved drug or placebo). Open- label trials typically test only the investigational therapeutic**

candidate and sometimes may do so at different dose levels. ~~or~~ **For** ~~preliminary~~ **example, our ongoing Phase I / II clinical trial of AMT- 130 is designed as an open- label trial following a 12- month core study period during which certain patients received a sham surgical procedure. Certain of these patients crossed over to treatment with AMT- 130 and are now subject to long- term, unblinded follow- up monitoring for a period of five years. Open- label trials are subject to various limitations that may bias the interpretation of the data. Open- label trials may be subject to a " patient bias " where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. In addition, open- label trials may be subject to an " investigator bias " where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. Accordingly, the results from our open- label trials, including early indications of potential efficacy, may not be predictive of future clinical trial results. Early evidence of slowing of disease progression in our AMT- 130 clinical trial may not be predictive of continued evidence of potential efficacy as we continue to collect follow- up** data from ~~studies~~ **patients enrolled in the trial. Interim or preliminary results from** ~~or~~ **our clinical** trials ~~announced or published from time to time~~ may change as more data become available ~~and~~ **, as such data** are subject to **regulatory** audit and verification procedures ~~that~~ **, and regulatory review, which** could result in material changes in the final ~~data~~ **results and conclusions** . From time to time, we publicly disclose interim ~~or~~ **,** preliminary **or other** data from preclinical studies and clinical trials, which are based on a preliminary **and sometimes post hoc** analysis of **such** ~~then- available~~ data ~~,~~ **. With respect to interim** and **preliminary data,** 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 **regulatory** 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~~ **July** ~~2023~~ **2024** , we announced updated interim data from our ongoing Phase I / II clinical ~~trial~~ **trials** of AMT- 130, along with our expectation that we will present additional clinical updates with respect to AMT- 130 in the future. **As part of the July 2024 update, we announced a statistically significant, dose- dependent, slowing in disease progression for high- dose patients dosed with AMT- 130, as measured by cUHDRS, as well as a statistically significant reduction of NfL in CSF. Such measures of statistical significance were based on a post- hoc analysis of data from patients treated with AMT- 130 compared to a propensity score- weighted external control cohort.** Interim data from **our** clinical trials **, including the AMT- 130 trial, and our analyses of** that **data** ~~we may complete~~ are subject to the risk that one or more of ~~the clinical outcomes~~ **our interim conclusions** may materially change as ~~patient enrollment continues and~~ more patient data become available **and as regulatory interactions focused on statistical analysis of the clinical data progress, among other factors** . Significant differences between interim data and ~~final~~ **subsequent** data could ~~seriously harm~~ **change the nature of our conclusions with respect to the safety and efficacy of our product candidates, which could adversely impact** our business. **We have and may in the future disclose interim results based on post- hoc analyses, the pooling of data from multiple studies, or using statistical assessments or comparisons, including comparisons to historical controls, which regulatory authorities may not agree with. The FDA may find that calculations of statistical significance using nominal p- values are not sufficiently reliable or subject to certain statistical limitations and, as a result, determine that our preliminary results are insufficient evidence of clinical efficacy. Accordingly,** ~~Third~~ **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 **negatively** impact the value of the particular program, ~~the approvability~~ **its prospects** ~~or~~ **for approval and** ~~commercialization of the particular product candidate or~~ **our business** ~~product and our company in general~~ . **In December** ~~For example, we plan to initiate regulatory interactions in the first half of~~ 2024 ~~to discuss the U. S.~~ **, following our initial Type B meeting, we announced that we had reached agreement with FDA on key elements of** ~~and~~ **an** ~~European~~ **accelerated approval pathway for AMT- 130, including that** data from ~~our~~ **the** ongoing Phase I / II **studies** ~~clinical trial~~ of AMT- 130 ~~and potential strategies~~ **, compared to a natural history external control, may serve as the primary basis** for ~~ongoing~~ **a BLA submission under FDA' s Accelerated Approval pathway. FDA also agreed that cUHDRS may be used as an intermediate clinical endpoint and that reductions in NfL measured in CSF may serve as supportive evidence of therapeutic benefit in the application for accelerated approval. Notwithstanding alignment with the agency on these elements, we may fail to continue to demonstrate clinical efficacy or durability of response data to warrant further** development ~~of AMT- 130. These~~ **or accelerated approval by FDA, EMA or any other** regulatory ~~authorities~~ **authority** ~~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~~ **may be top- line results** 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 **public** ~~disclosure~~ **disclosures** . Any information we determine not to disclose may ultimately be deemed significant by ~~you or~~ others with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate or our business. If the 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, and commercialize, product candidates may be harmed,

which could seriously harm our business **. Data analyses conducted on a post- hoc basis and using external, historical controls may not be accepted as a basis for regulatory approval. We have in the past and may in the future undertake certain analyses to further understand the data and potential reasons for the study results, including retrospective, post- hoc, and subgroup analyses. Because these analyses are not pre- planned and studies may not be adequately designed for these analyses, they may not be a reliable nor an acceptable basis for regulatory approval. For example, in conjunction with our July 2024 interim data update for AMT- 130, we conducted a post- hoc analysis of clinical outcomes for the 21 treated patients at 24 months compared to an expanded, propensity- weighted external control consisting of 154 patients. Among other conclusions in this interim update, we reported, based on this analysis, a statistically significant, dose- dependent, slowing in disease progression measured by cUHDRS observed through 24 months in patients receiving the high dose of AMT- 130. We also reported a statistically significant reduction of CSF NfL observed in patients treated with AMT- 130. Some of our favorable statistical data from these trials also are based on nominal p- values. Nominal p- values are subject to certain limitations, and because of these limitations, regulatory authorities may give less weight to nominal p- values, compared to standard p- values. As such, we anticipate proposing to the FDA a pre- specified statistical analysis to support a potential BLA submission. An unfavorable view of our proposed statistical analyses by regulatory authorities could negatively impact our ability to obtain, or the timing of, regulatory approval, which would have a material adverse effect on our revenue and adversely impact our business and financial results** . 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 **CSF** 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. **We seek** ~~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~~ **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 **for which commercialization has been exclusively out- licensed to CSL Behring** , we may not be ~~able to~~ **successful in** ~~identify~~ **identifying** or ~~develop~~ **developing additional** ~~product~~ **products** ~~candidates~~ that are safe and effective. Even if we are successful in continuing to build our pipeline, the potential **new** product candidates that we identify may not be suitable for **or may fail in** 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 **programs and** product candidates, including the decisions stemming from our ~~Reorganization~~ **prior restructuring efforts** , may not lead to the development of any viable commercial product and may divert resources away from ~~better~~ **other value- driving** opportunities ~~. 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 significant harm to our business, results of operations and financial position and materially adversely affect our share price. **We** ~~Our business development strategy depends on our ability to obtain rights to key technologies through in- licenses and support the development of our product pipeline through out- licenses, and those efforts~~ may not be successful **in obtaining rights from external parties to new product candidates and key technologies, or in securing partnerships to support the development or commercialization of our product candidates** . We may expand our product pipeline from time to time through strategic transactions that involve in- licensing the rights to key technologies, including those related to gene delivery, genes, and gene cassettes. For example, in July 2021, we acquired uniQure France (formerly Corlieve Therapeutics SAS) and its lead program, now known as AMT- 260, to treat refractory MTLE. AMT- 260 is being developed based on exclusive licenses to

certain patents uniQure France obtained from two French research institutions ~~that continue to collaborate with us~~. uniQure France also obtained an exclusive license from Regenxbio, Inc. to use AAV9 in connection with the delivery of any sequence that affects the expression of the GRIK2 gene in humans. Notwithstanding **prior** efforts to expand our product pipeline, the cost of drug development is high as is the rate of failure in the drug development process. In order to fund the development of ~~some of~~ our existing product candidates **, including the costs associated with submitting a BLA for AMT- 130 and related commercial planning and readiness activities**, we may seek to out- license some of our product candidates or technologies to other pharmaceutical or biotechnology companies or other third parties **to** ~~. The aim of such out- licensing would be~~ generate non- dilutive funds in the form of up- front or milestone payments or royalties. Such decisions will be taken on a case- by- case basis, as the opportunity arises or is required. The future success of our business will depend in significant part on our business development efforts with respect to existing and future product candidates, including our ability to in- license or otherwise acquire the rights to additional product candidates or technologies, particularly through our collaborations with academic research institutions, and our ability to out- license product candidates and technologies for which collaboration with external parties forms a part of our business strategy **or is necessary to cover certain development costs**. However, we may be unable to in- license or acquire the rights to any such product candidates or technologies from third parties on acceptable terms or at all. The in- licensing and acquisition of gene therapy technologies is a competitive area, and many more established companies are also pursuing strategies to license or acquire product candidates or technologies that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources ~~and greater~~ **or superior** clinical development and commercialization capabilities. In addition, companies that perceive us to be competitors may be unwilling to license rights to us. Furthermore, we may be unable to identify suitable product candidates or technologies within our areas of focus. If we are unable to successfully obtain rights to suitable product candidates or technologies, our business, financial condition, and prospects could suffer. Similarly, there is no guarantee that we will generate product candidates that are suitable for out **-** licensing or attractive to potential collaborators, and even if we do, there is no guarantee that we will be successful in identifying potential licensees and successfully negotiating such collaborations on agreeable terms if and when required. Any failure with respect to our business development efforts may materially affect our ability to finance our business and support the development of our product pipeline. Negative public opinion and increased regulatory scrutiny of gene therapy and genetic research may damage **the** public perception of our product candidates or adversely affect our ability to conduct our business or obtain marketing approvals for our product candidates. Gene therapy remains a novel technology. Our technology utilizes vectors derived from viruses, which may be perceived as unsafe or may result in unforeseen adverse events. Public perception may be influenced by claims that gene therapies are unsafe, and gene therapies may not ultimately gain the acceptance of the public or the medical community. The risk of cancer remains a concern for gene therapy, and we cannot guarantee that patients treated in any of our planned or future clinical studies will not develop cancer **or experience other adverse events** as a result of being treated with our product candidates. In addition, there is the potential risk of delayed adverse events following exposure to gene therapy products due to persistent biological activity of the genetic material or other components of products used to carry the genetic material. Public and medical community adoption of any of our gene therapies will 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 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 prescribing treatments that involve the use of our products 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 of gene therapies or negative public opinion may 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 patients ~~have~~ experienced serious adverse events during our clinical trials of AMT- 060 (HEMGENIX ®), etranacogene dezaparvovec (AMT- 061), and AMT- 130. However, adverse events in our clinical trials or those conducted by third parties (even if not ultimately attributable to our product candidates), and the resulting publicity, could result in delay, a hold or termination of our clinical trials, increased governmental regulation, unfavorable public perception, failure of the medical community to accept and prescribe gene therapy treatments, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates. If any of these events should occur, it may have a material adverse effect on our business, financial condition, and results of operations. 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 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 diseases.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, ~~Roche~~ **Prilenia Therapeutics,CombiGene,Caritas Therapeutics,Alnylam** ,Wave Life Sciences, **Bayer AG** ~~Alnylam Pharmaceuticals,Regeneron and Skyhawk Therapeutics~~ (**AskBio** ~~for Huntington' s disease~~), ~~Neurona and Combigene (for TLE),Biogen,Ionis,Neurimmune,Regeneron,Alnylum Pharmaceuticals and Voyager Therapeutics (for ALS) and~~ Amicus ~~Therapeutics,Sanofi,Takeda,Chiesi,Idorsia,Sangamo~~ Therapeutics,4D Molecular Therapeutics, ~~Skyline Pharmaceuticals and~~ **Sanofi,Idorsia,Amicus,Spark,Takeda,Chiesi,** CANbridge **,Abeona,Annexon,Vico,Alexion** (**AZ** ~~for Fabry disease~~) **,Neurona,Combigene,NeuExcell,EpiBlok,Biogen,ionis,Eisai and Lexeo** .Our commercial opportunity ~~and / or the receipt of royalties from the sale of any approved products (should we chose to commercialize our products with a commercial partner)~~ 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** ~~our prior restructuring efforts~~ 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.** Certain of our product candidates may require medical devices for product administration and / or diagnostics, resulting in our product candidates being deemed combination products or otherwise being dependent upon additional regulatory approvals. This may result in the need to comply with additional regulatory requirements. If we are unable to meet these regulatory requirements, we may be delayed or not be able to obtain product approval. Certain of our product candidates require medical devices for administration, such as AMT- 130 and AMT- 260, each of which requires a stereotactic, magnetic resonance imaging guided catheter. Other of our product candidates may also require the use of a companion diagnostic device to confirm the presence of specific genetic or other biomarkers. In addition, certain of our product candidates, including AMT- 130 and AMT- 260, may require the use of immunosuppressive agents to reduce the inflammatory responses associated with administration. It is possible that our product candidates would be deemed to be combination products, potentially necessitating compliance with the FDA' s investigational device regulations, separate marketing application submissions for the medical device component, a demonstration that our product candidates are safe and effective when used in combination with the medical devices, cross- labeling with the medical device, and compliance with certain of the FDA' s device regulations. If we are not able to comply with the FDA' s device regulations, if we are not able to effectively partner with the applicable medical device manufacturers, if we or any partners are not able to obtain any required FDA clearances or approvals of the applicable medical devices, or if we are not able to demonstrate that our product candidates are safe and efficacious when used with the applicable medical devices, we may be delayed in or may never obtain FDA approval for our product candidates, which would materially harm our business. Moreover, certain of our delivery modalities, such as direct delivery of product candidates to the brain, may require significant time and physician ability and skill. If physicians are not able to effectively deliver our product candidates to the applicable site of action or if delivery modalities are too difficult, or if there is reluctance to administer immunosuppressive agents that are outside of the standard of care to treat immune responses from the administration of our therapies, we may never be able to obtain approval for our product candidates, may be delayed in obtaining approval, or, following approval, physicians may not adopt our product candidates, any of which may materially harm our business. Risks Related to ~~Our Manufacturing Our manufacturing facilities are subject to significant government regulations and approvals. If we fail to comply with these regulations or maintain these approvals, our business could be materially harmed. With the exception of AMT- 260 and AMT- 162, we produce our gene therapies at our Lexington Facility using a proprietary baculovirus expression vector system. Our Lexington Facility, where we manufacture HEMGENIX ®, is subject to ongoing regulation and periodic inspection by the FDA, EU member state, and other regulatory bodies to ensure compliance with cGMP and other requirements. Any failure to follow and document our adherence to such cGMP regulations or other regulatory requirements may lead to significant delays in the availability of products for commercial sale or clinical study, may result in the termination of or a hold on a clinical study, or may delay or prevent filing or approval of marketing applications for our products. Failure to comply with applicable regulations could also result in the FDA, EU member state, or other applicable authorities taking various actions, including: ● levying fines and other civil penalties; ● imposing consent decrees or injunctions; ● requiring us to suspend or put on hold one or more of our clinical trials; ● suspending or withdrawing regulatory approvals; ● delaying or refusing to approve pending applications or supplements to approved applications; ● requiring us to suspend manufacturing activities or product sales, imports or exports; ● requiring us to communicate with physicians and other~~

customers about concerns related to actual or potential safety, efficacy, and other issues involving our products; ● mandating or recommending product recalls or seizing products; ● imposing operating restrictions; or ● seeking criminal prosecutions, among other outcomes. Poor control of production processes can also lead to the introduction of adventitious agents or other contaminants, or to inadvertent changes in the properties or stability of a product candidate that may not be detectable in final product testing and that could have an adverse effect on clinical studies, or patient safety or efficacy. Moreover, if our manufacturing facility is not able to meet regulatory requirements, we may need to implement costly and time- consuming remedial actions. Any of the foregoing could materially harm our business, financial condition, and results of operations. Moreover, if we are not able to manufacture a sufficient amount of our product candidates for clinical studies or eventual commercialization, or if we are unable to manufacture sufficient supply of HEMGENIX ® consistent with our manufacturing and supply obligations to CSL Behring, our development programs and commercial prospects will be harmed. If we cannot produce an adequate amount of our drug substance and product in compliance with the applicable regulatory requirements, we may need to contract with a third party to do so, in which case third party manufacturers may not be available to us on favorable terms or at all. The addition of a new manufacturer may also require FDA, EMA, EU, and other regulatory authority approvals, which we may not be able to obtain. Gene therapies are complex, expensive and difficult to manufacture. We could experience capacity, production or technology transfer challenges that could result in delays in our development or commercialization schedules or otherwise adversely affect our business. Our proprietary manufacturing process leveraging insect cells and baculoviruses to produce to AAV- based gene therapies is highly complex and is regularly subject to variation or production difficulties. Issues with any of our manufacturing processes, even minor deviations from our standard processes, could result in insufficient yield, product deficiencies or manufacturing failures that result in adverse patient reactions, lot failures, insufficient inventory, product recalls and product liability claims. Additionally, we may not be able to scale up some or all our manufacturing processes as necessary and on our desired timelines to meet the demands of our clinical product pipeline, which may result in delays in regulatory approvals, inability to produce sufficient amounts of clinical or commercial product, or otherwise adversely affect our business. Factors common to the manufacturing process associated with most biologics and drugs could also cause production interruptions for us, including, without limitation, raw materials shortages and other supply chain challenges, raw material failures, limited control over pricing of raw materials, growth media failures, equipment malfunctions, costs associated with servicing real property lease and other contractual obligations, facility contamination, labor problems, natural disasters, disruption in utility services, public health crises, terrorist activities, war or cases of force majeure and acts of God that are beyond our control. We also may encounter problems in hiring and retaining the experienced and specialized personnel needed to operate our manufacturing facilities, processes and testing, which could result in delays in our production or difficulties in maintaining compliance with applicable regulatory requirements. We manufacture HEMGENIX ® at our Lexington Facility which is optimized to meet our commercial manufacturing and supply obligations pursuant to the CSL Behring collaboration. This optimization and dedicated capacity for HEMGENIX ® could limit our ability to manufacture other product candidates or components thereof to support our development programs or those of third parties. The manufacturing of HEMGENIX ® pursuant to our obligations under the CSL Behring Collaboration is expensive and requires the dedication of significant company resources. In September 2022, CSL Behring notified us of its intent to transfer manufacturing technology in the coming years related to HEMGENIX ® to a third- party contract manufacturer to be designated by CSL Behring in the future. Until CSL Behring identifies and designates a new manufacturer capable of supporting the commercial requirements of HEMGENIX ®, we will continue to incur significant costs associated with our manufacturing and supply obligations. Following such transfer, we may experience challenges in adapting our Lexington Facility to meet the manufacturing and supply needs for products other than HEMGENIX ® as a result of excess capacity or our ability to adapt to new processes, among other challenges. Any problems or limitations with respect to our manufacturing processes or facilities, including our existing commercial supply and manufacturing obligations to CSL Behring, could make us a less attractive collaborator for academic research institutions and other parties, which could limit our access to additional attractive development programs or sources of capital, result in delays in our clinical development or marketing schedules and materially harm our business. We currently rely and expect to continue to rely on third parties to conduct product manufacturing for certain of our product candidates, and these third parties may not perform satisfactorily. We currently rely, and expect to continue to rely, on third parties for the production of some of our preclinical study and planned clinical trial materials and, therefore, we can control only certain aspects of their activities. The facilities used by us and our contract manufacturers to manufacture certain of our product candidates must be reviewed by the FDA pursuant to inspections that will be conducted after we submit a BLA to the FDA. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with the cGMP for the manufacture of our products and product candidates that are not manufactured in house. If we or our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or other regulatory bodies, we will not be able to obtain and / or maintain regulatory approval for our products manufactured by third parties. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative third- party manufacturers, which may not be available and which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. Our use of viruses, chemicals and other potentially hazardous materials requires us to comply with regulatory requirements and exposes us to significant potential liabilities. Our development and manufacturing processes involve the use of viruses, chemicals, other potentially hazardous materials and produce waste products. Accordingly, we are subject to national, federal, state, and local laws and regulations in the U. S. and the Netherlands governing the use, manufacture, distribution, storage, handling, treatment, and disposal of these materials. In addition to ensuring the safe handling of these materials, we are subject to increased

~~safeguards and security measures for many of these agents, including controlling access and screening of entities and personnel who have access to them, and establishing a comprehensive national database of registered entities. In the event of an accident or failure to comply with environmental, occupational health and safety and export control laws and regulations, we could be held liable for damages that result, and any such liability could exceed our assets and resources, and could result in material harm to our business, financial condition, and results of operations. Our resources might be adversely affected if we are unable to validate our manufacturing processes and methods or develop new processes and methods to meet our product supply needs and obligations. The manufacture of our AAV gene therapies is complex and requires significant expertise. Even with the relevant experience and expertise, manufacturers of gene therapy products often encounter difficulties in production, particularly in scaling out and validating initial production and ensuring that the product meets required specifications. These problems include difficulties with production costs and yields, quality control, including stability and potency of the product, quality assurance testing, operator error, shortages of qualified personnel, as well as compliance with strictly enforced federal, state, and foreign regulations. In the past, we have manufactured certain batches of product candidates intended for nonclinical, clinical and process validation purposes that have not met all our pre- specified quality parameters. To meet our expected future production needs and our regulatory filing timelines for gene therapy product candidates, we will need to complete the validation of our manufacturing processes and methods for each program, and we may need to develop and validate new or larger scale manufacturing processes and methods. If we are unable to consistently manufacture our gene therapy product candidates or any approved products in accordance with our pre- specified quality parameters and applicable regulatory standards, it could adversely impact our ability to validate our manufacturing processes and methods, to meet our production needs, to file a BLA or other regulatory submissions, to develop our other proprietary programs, to conserve our cash, or to receive financial payments pursuant to our agreements with third parties. Risks Related to~~ Regulatory Approval of Our Products

We cannot predict when or if we will obtain marketing approval to commercialize our product candidates. The development and commercialization of our product candidates, including their design, testing, manufacture, safety, efficacy, purity, recordkeeping, labeling, storage, approval, advertising, promotion, sale, and distribution, are subject to comprehensive regulation by the FDA and other regulatory agencies in the U. S., the EMA, and other regulatory agencies of the member states of the European Union, and similar regulatory authorities in other jurisdictions. Failure to obtain marketing approval for a product candidate in a specific jurisdiction will prevent us from commercializing the product candidate in that jurisdiction and our ability to generate revenue will be materially impaired. The process of obtaining marketing approval for our product candidates in the U. S., the European Union, and other countries is expensive and may take many years, if approval is obtained at all. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, **reductions in staffing or other personnel limitations within a regulatory agency,** or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application **. Due to the recent change in presidential administration in the U. S., we face substantial uncertainty regarding potential regulatory developments that may adversely affect our business, including those related to potential decreases in spending in the federal government, potential staffing reductions, or any other potential constraints on the FDA' s ability to engage in routine oversight and product review activities or its ability to exercise regulatory authority** . 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 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 complete their 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 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 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, which **are and** will ~~likely~~ be applicable to our product candidates ~~prior to our obtaining regulatory approval in the U. S. or the EU~~ . 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 changes relating to gene therapy development. By example, FDA issued a number of 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. **Under proposed** ~~Moreover, the European Commission conducted a public consultation in early 2013 on the application of~~ EU legislation ~~that governs~~ **, there is also a suggested amendment in relation to** advanced therapy medicinal products ~~, including gene therapy~~ **to the effect that hospital pharmacies would be afforded greater flexibility to prepare** ~~products~~ **product** ~~, which could result in changes in the data we need to submit to the EMA~~ for **dispensing on** ~~our product candidates to gain regulatory approval or change~~ the ~~requirements~~ **basis of the estimated**

prescriptions within that hospital for ~~tracking, handling and distribution of~~ the **following 7** ~~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 --~~ **days rather than** , ~~require additional resources~~ **as at present** , ~~and ultimately result~~ in ~~rejection~~ **response to individual prescriptions** . 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~~ **leverage** certain specialized **regulatory** pathways **and designations, such as the FDA' s accelerated approval pathway and RMAT designation,** to develop our product candidates or to seek **licensure. Even if one or more of our product candidates receives such a designation or is permitted to pursue such a pathway, we may be unable to obtain and maintain the benefits associated with such designations and pathways. In May 2024 the FDA granted RMAT designation for AMT- 130 based on AMT- 130' s potential to address the major unmet medical need among patients with Huntington' s disease. The designation followed the FDA' s review of interim Phase I / II clinical data for AMT- 130 and was based on an analysis comparing 24- month clinical data from the AMT- 130 trials to a non- concurrent criteria- matched natural history cohort. In December 2024, following our initial Type B meeting which was scheduled on the basis of our RMAT designation for AMT- 130, we announced that we had reached agreement with FDA on key elements of an accelerated approval pathway for AMT- 130, as described under " Business — Recent Product Candidate Developments " in this Annual Report on Form 10- K. In the future, we may seek additional product designations intended to facilitate the development or** regulatory **review or** approval **process** ~~. We may not qualify~~ for ~~these pathways, or~~ **our product candidates,** such **as** ~~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~~ fast- track 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. An RMAT designation is designed to accelerate approval for regenerative advanced therapies. Priority review designation is intended to accelerate the FDA marketing application review timeframe for 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 **(in the case of AMT- 130)** , or breakthrough therapies, or granted access to the PRIME scheme, **more frequent** 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 **(other than AMT- 130)** 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. Biologics studied for their safety and effectiveness in treating serious or life- threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may **also** receive accelerated approval by the FDA, meaning the agency may approve the product candidate based upon a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. ~~Even if we do qualify~~ **As part of our alignment with FDA in December 2024 on the accelerated approval pathway for AMT- 130, the agency agreed that cUHDRS may be used as an intermediate clinical endpoint and that reductions in NfL measured in CSF may serve as supportive evidence of therapeutic benefit in the application** for accelerated approval **. There is no guarantee that we would be able to obtain accelerated approval as FDA may disagree with our interim endpoint or may find that such endpoint is not met following subsequent clinical data. These designations and accelerated approval pathways may not lead to a faster development or regulatory review or approval process and may not increase the likelihood that our product candidates**

will receive marketing approval. Even though we have aligned with the FDA on elements of the accelerated approval pathway for AMT- 130, we may not ultimately be successful in obtaining marketing approval for AMT- 130 , 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, which could result in the FDA withdrawing our product from the market. In recent years, the accelerated approval pathway has come under significant FDA and public scrutiny **and it is unclear how the incoming Trump Administration in the U. S. will address regulations related to accelerated approval pathways, if at all** . Accordingly, it is uncertain whether the FDA may be more conservative in granting accelerated approval or, if granted, more apt to withdraw approval if clinical benefit is not confirmed. There is no guarantee that regulatory interactions with FDA or comparable foreign authorities will result in our ability to avail ourselves of any specialized approval pathways for our product candidates. 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 **, AMT- 191 and AMT- 162** 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 **for a number of reasons, including, but not limited to** 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. 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 criteria with respect to orphan products are evolving, especially in 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 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 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 **. It is also possible that periods of regulatory exclusivity may change. By example, the EU has proposed exclusivity changes, in the form of draft legislation, that would effectively shorten the periods of EU orphan market exclusivity and data exclusivity** . 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 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. **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 ~~access~~ **afford** treatment with our products and our ~~potential~~ 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.Moreover,payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives.For example,the Center for Medicare & Medicaid Innovation at the Centers for Medicare & Medicaid Services **(" CMS ")** may develop new payment and delivery models,such as bundled payment models ~~in the future.Currently,if a drug product is reimbursed by Medicare or Medicaid,pricing and rebate programs must comply with,as applicable,the Medicare Prescription Drug,Improvement,and Modernization Act of 2003 as well as the Medicaid rebate requirements of the Omnibus Budget Reconciliation Act of 1990 (" OBRA "),the Veterans Health Care Act of 1992,Deficit Reduction Act of 2005,and the Patient Protection and Affordable Care Act,each as amended~~ .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 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 ~~high- Medicare spend~~ 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 and 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 adopted in the future,any of which could limit ~~coverage and / or~~ 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 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- 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 on our product pricing.Furthermore,there has been 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 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 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 product candidates.The relatively small market size for orphan indications and the potential for long- term therapeutic benefit from a single administration present challenges ~~for~~ **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** 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, 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 **, and frequently does,** require that this confirmatory trial be commenced prior to FDA granting a product accelerated approval. ~~An~~ **If FDA requires that a confirmatory study be underway prior to BLA approval, this could delay any planned BLA submissions and FDA marketing approvals. Moreover, 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 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 our product candidates will depend on the successful development and eventual commercialization of our product candidates **, whether we choose to pursue further development or commercialization our product candidates alone or with a partner** . ~~The~~ **If we are** ~~success~~ **successful in obtaining marketing approval from applicable regulatory authorities for AMT- 130 or any** of **our other product candidates, our ability to generate revenues from** our product candidates will depend on **our success in** ~~many factors, including~~ : ● **actual** ~~successful completion of preclinical studies and clinical trials, and other work required by regulators; ●~~ receipt and maintenance of marketing approvals from applicable regulatory authorities; ● **launch of commercial sales of** ~~obtaining and maintaining patent and trade secret protection and non- patent, exclusivities for~~ our ~~product~~ **products** ~~candidates~~ **, if approved, whether alone or in collaboration with others** ; ● maintaining regulatory approvals ~~using our~~ **, including** manufacturing ~~facility in Lexington, Massachusetts~~ **approvals for our third- party manufacturing sites** ; ● **complying** ~~launch and commercialization of our products, if approved, whether alone or in collaboration~~ with ~~others~~ **any applicable post- approval commitments and requirements, and maintaining a continued acceptable overall safety profile** ; ● 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 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 healthcare coverage and adequate reimbursement of our 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 **; and ● obtaining and maintaining patent and trade secret protection and non- patent, exclusivities for our product candidates** . Even if our product candidates are approved, they may be subject to limitations that make commercialization difficult **, and we may experience these difficulties regardless of whether we choose to commercialize our product candidates alone or with a partner** . 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 (“ 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 .-Any approved gene therapy we seek to ~~commercialize~~ **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 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 **.** . 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 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. For example, 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 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..... 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~~ **product candidates designed to treat** 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. 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 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 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. We face substantial competition, and others..... or necessary for, our programs. Risks Related to **Manufacturing and** Our Dependence on Third Parties **The Lexington Transaction may not yield the benefits that we expect and may result in additional risks to our business, including those related to Genezen' s ability to manufacture HEMGENIX in accordance with regulatory requirements and to meet CSL Behring' s supply requirements for commercial product. In connection with the closing of the Lexington Transaction in July 2024, we and Genezen entered into certain additional agreements, including a commercial supply agreement pursuant to which Genezen will manufacture and supply our requirements of HEMGENIX ® pursuant to our manufacturing and supply obligations to CSL Behring, and development and other manufacturing services agreement pursuant to which Genezen will manufacture, supply and provide certain development services to support the requirements of our investigational gene therapy programs and for other discretionary services related to the manufacture of HEMGEMIX ®, along with other customary agreements. As a component of our broader efforts to focus our business and reduce operating expenses, the**

Lexington Transaction is expected to reduce our cash burn as a result of a reduction in facility and personnel- related costs, among others. The Lexington Transaction may not ultimately reduce our operating expenses as we expect. In addition, we may be exposed to additional costs and risks related to or as a result of the Lexington Transaction, including, without limitation additional expenses associated with outsourcing certain manufacturing and development services, as well as our contractual obligations and minimum financial commitments to Genezen under the CSA and the DMSA, supply- related risks related Genezen' s ability and capacity to satisfy our continued obligations to CSL Behring and the supply requirements of our other product candidates, including the CMC and supply- related requirements for our BLA submission for AMT- 130, contractual default under our agreements with Genezen or with CSL Behring, and other third- party risks relative to our partnership with Genezen. The occurrence of any of the foregoing or any other risks as a result of or related to the Lexington Transaction could considerably harm our business and impact our financial condition and results of operations. Gene therapies are complex, expensive and difficult to manufacture. Genezen or any third- party manufacturer that we engage could experience capacity, production or technology transfer challenges that could result in delays in our development or commercialization schedules or otherwise adversely affect our business. Our proprietary manufacturing processes leveraging insect cells and baculoviruses to produce AAV- based gene therapies are highly complex and regularly subject to variation or production difficulties. Issues with any of our manufacturing processes, even minor deviations from our standard processes, could result in insufficient yield, product deficiencies or manufacturing or supply failures that could result in adverse patient reactions, lot failures, insufficient inventory, product recalls and product liability claims. Additionally, we and our third- party manufacturers, including Genezen, may not be able to scale up some or all our manufacturing processes as necessary and on our desired timelines to meet the demands of our clinical product pipeline and regulatory timelines, which may result in delays in regulatory approvals, inability to produce sufficient amounts of clinical or commercial product, or otherwise adversely affect our business. Factors common to the manufacturing process associated with most biologics and drugs could also cause production interruptions for us or our third- party manufacturers, including, without limitation, raw materials shortages and other supply chain challenges, raw material failures, limited control over pricing of raw materials, growth media failures, equipment malfunctions, costs associated with servicing real property lease and other contractual obligations, facility contamination, labor problems, natural disasters, disruption in utility services, public health crises, terrorist activities, war or cases of force majeure and other events beyond our control. We or our third- party manufacturers also may encounter problems in hiring and retaining the experienced and specialized personnel needed to evaluate and supervise manufacturing and quality operations and, in the case of our contract manufacturers, operate manufacturing facilities, processes and testing, which could result in delays in our production or difficulties in maintaining compliance with applicable regulatory requirements. Genezen may experience the same personnel- related challenges resulting in the same delays and compliance issues. Prior to the Lexington Transaction, we manufactured HEMGENIX ® at the Lexington Facility, which is optimized to meet HEMGENIX ® product specifications and the commercial manufacturing and supply obligations under our collaboration with CSL Behring. Following the Lexington Transaction, Genezen is responsible for the manufacturing and supply of HEMGENIX ® at the Lexington Facility, though we remain contractually obligated to CSL Behring consistent with the terms of our development and commercial supply agreement with CSL Behring. While uniQure has priority and preferential status with Genezen, Genezen may not have sufficient capacity to support our other development programs or those of its other customers, which may negatively impact our business and ability to advance development goals unrelated to HEMGENIX ® and our obligations to CSL Behring. The manufacturing of HEMGENIX ® pursuant to our obligations under the CSL Behring Agreement is expensive and requires the dedication of significant resources, notwithstanding the Lexington Transaction and our subcontracting to Genezen. In September 2022, CSL Behring notified us of its intent to transfer manufacturing technology related to HEMGENIX ® to a third- party contract manufacturer designated by CSL Behring. Until CSL Behring completes the transfer of manufacturing technology to this new manufacturer, and until such manufacturer is able to demonstrate that it is capable of supporting the commercial requirements of HEMGENIX ® sufficient for regulatory approval, we will continue to incur significant costs associated with the manufacturing and supply of HEMGENIX ® through our contractual relationship with Genezen. Should Genezen encounter a manufacturing issues or if Genezen is unable to provide a sufficient supply of HEMGENIX ® consistent with agreed- upon forecasting mechanisms, we may be unable to fulfil our contractual commitments to CSL Behring and may, thus, face contractual liabilities. Following the Lexington Transaction, Genezen may experience challenges in adapting the Lexington Facility to meet the manufacturing and supply needs for products other than HEMGENIX ® as a result of capacity and resource constraints, or its inability to adapt to new manufacturing processes, among other challenges. Any problems or limitations with respect to our manufacturing processes or facilities, including the existing commercial supply and manufacturing obligations to CSL Behring, could make us a less attractive collaborator for academic research institutions and other parties, which could limit our access to additional attractive development programs or sources of capital, result in delays in our clinical development or marketing schedules and materially harm our business. The manufacturing of our products and product candidates is subject to significant government regulations and approvals. We currently rely and expect to continue to rely on third parties to manufacture our product candidates, and these third parties may not perform satisfactorily or may fail to comply with these regulations or maintain these approvals. The manufacturing of our products and product candidates is subject to significant government regulation. We currently rely, and expect to continue to rely, on third parties for the production of our preclinical study and planned clinical trial materials and, therefore, we can control only certain aspects of their activities. Following the Lexington Transaction, we rely on Genezen for the production of HEMGENIX ® and will have preferential access to the Lexington Facility for the

production of materials related to AMT- 130 and AMT- 191 programs under separately negotiated development and supply arrangements. The facilities used by Genezen and our other contract manufacturers are subject to FDA inspections, including after we submit a BLA. We are completely dependent on Genezen and our other contract manufacturers to execute on our manufacturing processes for HEMGENIX ® and other product candidates and for compliance with cGMP requirements. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or other regulatory bodies, we will not be able to obtain and / or maintain regulatory approval for our products manufactured by third parties. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative third- party manufacturers, which may not be available and which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. With the exception of AMT- 260 and AMT- 162 and prior to the Lexington Transaction, we produced our gene therapies at the Lexington Facility using our proprietary manufacturing processes. The Lexington Facility is and will continue to be subject to ongoing regulation and periodic inspection by the FDA, EU member state, and other regulatory bodies to ensure compliance with cGMP and other requirements. Any failure to follow and document our adherence to such cGMP regulations or other regulatory requirements may lead to significant delays in the availability of products for commercial sale or clinical study, may result in the termination of or a hold on a clinical study, or may delay or prevent filing or approval of marketing applications for our products. Failure to comply with applicable regulations could also result in the FDA, EU member state, or other applicable authorities taking various actions, including: ● taking enforcement actions or levying fines and other civil penalties; ● imposing consent decrees or injunctions; ● requiring us to suspend or put on hold one or more of our clinical trials, or conduct new or additional trials; ● suspending or withdrawing regulatory approvals; ● delaying or refusing to approve pending applications or supplements to approved applications; ● requiring us to suspend manufacturing activities or product sales, imports or exports; ● requiring us to communicate with physicians and other customers about concerns related to actual or potential safety, efficacy, and other issues involving our products; ● mandating or recommending product recalls or seizing products; ● imposing operating restrictions; or ● seeking criminal prosecutions, among other outcomes. Poor control of production processes can also lead to the introduction of adventitious agents or other contaminants, or to inadvertent changes in the properties or stability of a product candidate that may not be detectable in final product testing and that could have an adverse effect on clinical studies, or patient safety or efficacy. Moreover, if the Lexington Facility or the manufacturing facilities of any third- party manufacturer we may engage is not able to meet regulatory requirements, we or they may need to implement costly and time-consuming remedial actions. Any of the foregoing could materially harm our business, financial condition, and results of operations. Moreover, if we, Genezen or our other third- party manufacturers are not able to manufacture a sufficient amount of our product candidates for clinical studies or eventual commercialization, or if Genezen is unable to satisfy our manufacturing and supply obligations to CSL Behring, our development programs and commercial prospects will be harmed. If Genezen cannot produce an adequate amount of our drug substance and product in compliance with the applicable regulatory requirements, we may need to contract with another third party to do so, and there is no guarantee that such third- party manufacturers will be available to us and able to manufacture on favorable terms or at all. The addition of a new manufacturer may also require FDA, EMA, EU, and other regulatory authority approvals, which we may not be able to obtain. Our use of viruses, chemicals and other potentially hazardous materials requires us and our contract manufacturers to comply with regulatory requirements and exposes us to significant potential liabilities. Our development and manufacturing processes and those of our third- party contract manufacturers involve the use of viruses, chemicals, other potentially hazardous materials and produce waste products. Accordingly, we and our third-party manufacturers are subject to national, federal, state, and local laws and regulations in the U. S. and Europe governing the use, manufacture, distribution, storage, handling, treatment, and disposal of these materials. In addition to ensuring the safe handling of these materials, these laws and regulations impose increased safeguards and security measures for many of these agents, including controlling access and screening of entities and personnel who have access to them, and establishing a comprehensive national database of registered entities. In the event of an accident or failure to comply with environmental, occupational health and safety and export control laws and regulations, we or our third-party contract manufacturers could be held liable for damages that result, and any such liability could exceed our assets and resources, and could result in material harm to our business, financial condition, and results of operations. Our business may be adversely affected if we or third- party manufacturers are unable to validate our manufacturing processes and methods or develop new processes and methods to meet our product supply needs and obligations. The manufacture of our AAV gene therapies is complex and requires significant expertise. Even with the relevant experience and expertise, manufacturers of gene therapy products often encounter difficulties in production, particularly in scaling out and validating initial production and ensuring that the product meets required specifications. These problems include difficulties with production costs and yields, quality control, including stability and potency of the product, quality assurance testing, instances of operator error, shortages of qualified personnel, as well as compliance with strictly enforced federal, state, and foreign regulations. In the past and prior to the Lexington Transaction, we have manufactured certain batches of product candidates intended for nonclinical, clinical and process validation purposes that have not met all our pre- specified quality parameters. To meet our expected future production needs and our regulatory filing timelines for gene therapy product candidates, Genezen will need to complete the validation of our manufacturing processes and methods for each program, and we may need to develop and validate new or larger scale

manufacturing processes and methods to meet our needs. If Genezen or any other third- party manufacturer we engage is unable to consistently manufacture our gene therapy product candidates or any approved products in accordance with our pre- specified quality parameters and applicable regulatory standards, it could adversely impact our ability to validate our manufacturing processes and methods, to meet our production needs, to timely file a BLA or other regulatory submissions, to develop our other proprietary programs, to conserve our cash, or to receive financial payments pursuant to our agreements with 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 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, **manufacture materials for** 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 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 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 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 **business development strategy or existing** 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 **research,** 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~~ **from** 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 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 **different** forms of intellectual property, including in- licensed and **fully or co-** owned patents **and patent applications** to protect our intellectual property. Our success depends in large part on our ability to obtain and maintain this protection in the U. S., the European Union, and other countries **or regions** , 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, **may not** prevent competitors from competing with us or otherwise provide us with any competitive advantage. ~~The~~ **At least some of the** patents we own ~~currently~~ are ~~and~~ **or** 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 patent cases in ~~each of Canada, the United Kingdom,~~ the Netherlands **, the EU** and the U. S. pertaining to licensed rights of etranacogene dezaparvovec was assumed by CSL Behring ~~on~~ **in** 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 **Behring** ' s successful commercialization of HEMGENIX ® and, in turn, could negatively impact our financial position. 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. 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~~ **jurisdictions** 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~~ **jurisdictions** 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 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~~ **share** 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 **confidential or** 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 **protections** ~~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 Pricing and Reimbursement We and our commercial..... harm our business. Risks Related to Our Financial Position and Need for Additional Capital We had net losses in the years ended December 31, **2024 and**

2023 ~~and 2022~~ , have incurred significant losses in previous years and expect to incur losses ~~during~~ **in** the **future,** ~~current and over the next several years~~ and may never achieve or maintain profitability. We had a net loss of $ ~~308~~ **239** . ~~5~~ **6** million in the year ended December 31, ~~2023~~ **2024** , and ~~a net loss of~~ $ ~~126~~ **308** . ~~8~~ **5** million in the year ended December 31, ~~2022~~ **2023** . ~~We incurred~~ **Other than** a gain ~~of 329. 6 million~~ in **the** year ended December 31, 2021 ~~; however~~ , **which** ~~such gain~~ was primarily attributable to one- time license revenue from CSL Behring **we** ~~. We~~ have incurred significant losses **throughout our operating history** ~~in the years prior to 2021~~ . As of December 31, ~~2023~~ **2024** , we had an accumulated deficit of $ ~~890~~ **1, 130** . ~~4~~ **0** million. **We** ~~In the past, we~~ have financed our operations **to date** 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 ~~2024~~ **2025** ~~and into the second quarter of 2027~~ primarily from our existing ~~cash, cash equivalents, and~~ cash resources. We have devoted substantially all our financial resources and efforts to **date to** research and development **of our products and product candidates** , including **the conduct of** preclinical studies and clinical trials **and related manufacturing requirements** . ~~We expect to~~ **Even if we succeed in receiving marketing approval for and commercialize AMT- 130 or other of our product candidates, we will** continue to incur ~~significant expenses~~ **substantial research** and ~~losses over~~ **development and** ~~the~~ **other** ~~next several years~~ **expenditures to develop and market additional potential products for the foreseeable future** , and our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that we will continue to incur net losses for the foreseeable future as we: ● ~~continue to fund~~ **incur costs associated with late- stage development of** AMT- 130 **as well as** ~~in its ongoing clinical trials and advance our other~~ -- **the** ~~product candidates into~~ **preparation of commercialization of AMT- 130; ● continue to fund the** clinical development **of our** ~~;~~ ~~● incur the~~ **other** ~~costs associated with the manufacturing of preclinical, clinical and commercial supplies of our~~ product candidates; ● **incur the costs associated with the manufacturing of preclinical, clinical and commercial supplies of our product candidates through our partnership with Genezen and other third- party manufacturers; ●** seek regulatory ~~approvals~~ **approval for AMT- 130 and** for any **other** product candidates ~~that successfully complete clinical trials~~ **; ● hire and retain personnel to support our business; ● enhance our operational, financial and management information systems and personnel** ; ● maintain, expand and protect our intellectual property portfolio; ~~● hire additional personnel to support our business; ● enhance our operational, financial and management information systems and personnel;~~ and ● incur legal, accounting and other expenses operating as a public company. **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 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. **We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business or otherwise increase the size of our future net losses.** Our failure to **generate** ~~become and remain profitable would depress the~~ value ~~of~~ **for** our **shareholders** ~~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 need to raise additional funding in order to advance the development of our product candidates **and support the commercial launch of AMT- 130** , 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 ongoing activities and we will need to obtain substantial additional funding ~~in order~~ to ~~fund~~ **support** the development of our product pipeline and ~~support our~~ continuing operations. ~~In~~ **On January 7, 2025, we entered into an underwriting agreement Leerink Partners LLC, Stifel, Nicolaus & Company, Incorporated and Guggenheim Securities, LLC., as representatives of the several underwriters named therein, in connection with the issuance and sale of 4, 411, 764 or our ordinary shares at a public offering price of $ 17. 00 per share, less underwriting discounts and commissions, pursuant to a shelf registration statement on Form S- 3 and accompanying prospectus (Registration No. 333- 284168), which became effective upon filing on January 7, 2025, and a prospectus supplement thereunder. The offering closed on January 10, 2025, and we net proceeds of approximately $ 70. 1 million, after deducting underwriting discounts and fees. We received an** ~~addition~~ **additional $ 10. 6 million in net proceeds upon the underwriters' exercise of their option to purchase additional ordinary shares at the public offering price in February 2025. Based on our current operating plan** , **research and development plans and our timing expectations related to the progress of our programs, and following the January 2025 public offering,** we **believe that our existing cash and cash equivalents and investment securities will be sufficient to fund our operations through the second half of 2027. We** have based our **current** ~~estimate~~ **estimates** 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 ~~2023~~ **2024** Amended Facility with Hercules 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, 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 **or successfully pursue strategic partnerships where necessary** , 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..... increased borrowing costs in the future Our business development **and** ~~strategy~~ **strategic initiatives, including divestitures such as the Lexington Transaction, acquisitions, partnerships, collaborations or other transactions,** may not ~~produce~~ **achieve** ~~the~~ **their intended benefits** ~~cash flows expected~~ or ~~could~~ **goals and may** result in additional ~~costs and challenges~~ **risks to our business** . ~~In~~ **We have recently and historically pursued various strategic initiatives, transactions and business arrangements, including the July 2024 Lexington Transaction and the** July 2021 **acquisition of** ~~, we acquired~~ uniQure France and its lead program **(** ~~, now known as~~ AMT- 260 **). We** ~~, targeting refractory MTLE, and~~ may, from time to time, enter into strategic transactions consistent with our business development **and financial** objectives. ~~Any acquisition or~~ **Implementing these and other** strategic **initiatives has included, and may in the future include, divestitures, acquisitions, asset purchases, partnerships, collaborations, joint ventures and other investments. Certain of these** ~~transaction~~ **transactions and arrangements have been and may in the future be material to us both from a strategic and financial perspective. These initiatives, whether successful or not, have been, and may continue to be, complex, time- consuming and expensive, may divert management' s attention, and** could expose us to ~~unknown liabilities~~ **operational challenges** and **potential inefficiencies. We may miscalculate the** risks , and we may incur additional costs..... other laws and regulations. The costs associated with ~~an alleged or~~ **our** ~~actual violation of any of~~ **strategic initiatives at the time** ~~the~~ **they are made** ~~foregoing could be substantial and could cause irreparable harm to our~~ **or may not** ~~reputation or otherwise~~ have **the resources** ~~a material adverse effect on our~~ **or ability** ~~business, financial condition, and results of operations. We are subject~~ to **access all** ~~laws governing data protection in~~ the **relevant** ~~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 **to evaluate them properly, including with regard to the research and development- related risks, manufacturing and compliance issues, or the outcome of ongoing legal** and other personal and private information. They often..... and EU member states governing the processing **proceedings** ~~of personal data, impose strict obligations and restrictions on the ability to collect, use, analyze and transfer personal information, including health data from clinical trials and adverse event reporting~~ . GDPR obligations applicable to us may include..... the corporate group in question. (There are similar caps in GBP under the..... information technology systems and infrastructure, there can be no assurance that **we will be able to achieve all of our intended goals with respect to** such ~~measures will prevent service interruptions~~ **strategies within the anticipated timeframes, if at all,** or ~~security breaches that~~ **fully realize the expected benefits of any such transactions or arrangements. Divestitures (including the Lexington Transaction), product rationalizations or asset sales** could ~~adversely affect~~ **result in asset impairments, or reductions to the size or scope of** our business ~~and the further development and commercialization of~~ **, our market share in particular markets** ~~our~~ **or our opportunities and ability to compete with respect to certain markets, therapeutic areas or** ~~product products and product candidates could~~ **. We may not** be **successful** ~~delayed. See Part I, Item 1C, Cybersecurity,~~ in **separating divested** ~~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, may impose additional costs on our business~~ **businesses** ~~and 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~~ **or assets** ~~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 **negatively impact our ongoing and future operations. For example, the Lexington Transaction may** result in ~~increases in taxes~~ **continued financial and operational exposure related to the divested assets or businesses , through guarantees or other financial arrangements, indemnification obligations, continued manufacturing and supply and transition services obligations to the divested businesses, or potential litigation. In addition, we may also not be able to realize the intended or anticipated benefits from such** ~~transportation ----~~ **transactions , such as realizing the anticipated** ~~costs~~ **cost savings, maintaining employee morale** and ~~utilities~~ **retaining key management and other employees to operate our retained business, or may be unable to realize the intended or expected goals, outlooks, synergies or operating efficiencies with respect to such transactions. The overall execution of our strategic initiatives may result in material unanticipated problems, expenses, liabilities, competitive responses, operational inefficiencies, adverse tax consequences, impairment or restructuring charges, loss of important third- party relationships, difficulty attracting and retaining qualified employees, and diversion of management' s and / or employee' s attention** , among other ~~expenses~~ **potential adverse consequences** . ~~Moreover~~ **In addition** , **we** ~~natural disasters and extreme weather conditions~~ may ~~impact the productivity of~~ **have to terminate a strategic alliance, agreement** ~~our~~ **or** ~~facilities~~ **arrangement** , ~~the ability of the patients in our~~ **or** ~~clinical trials to maintain compliance with trial protocols or~~ **our** ~~access clinical trial sites, the operation of our supply chain, or consumer buying patterns~~ **partners may be unable to fulfill their collaboration** . **Any** ~~The occurrence~~ of ~~any of these~~ -- **the** ~~events~~ **risks described above** could have a material adverse effect on our ~~business. ESG and sustainability initiatives continue to attract political and social attention have resulted in both existing and pending international agreements and national, regional, and local legislation, regulatory measures, reporting obligations and policy changes. There is increasing societal pressure in some of the 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 ESG matters 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 ESG and sustainability metrics. Such ratings are used by 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. 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~~ -- **reputation** ~~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 **, cash flows,** ~~. Risks Related to Employee Matters and Managing Our Growth Our future success depends on our~~ ability to **pay dividends** ~~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~~ **and /** ~~extended period because of the limited number of individuals in our~~ - **or** ~~industry with the breadth and depth of skills and experience required to successfully develop gene therapy products. 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~~ **share price** unable to continue to attract and retain..... persons, could materially damage our business . Actions that we have taken **or may take in the future** 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~~ **a restructuring of our business** to reprioritize our portfolio of development candidates, conserve financial resources and better align our workforce with current business needs. **In June 2024, we announced the sale of the Lexington Facility and related manufacturing assets in conjunction with our broader efforts to reduce operating expenses and cash burn. In addition, in August 2024, we announced the outcome of our strategic review intended to conserve capital, streamline operations and ensure sufficient cash resources to advance multiple clinical- stage programs through potentially meaningful milestones. This restructuring, inclusive of the sale of our Lexington facility and associated employee transitions to Genezen, involved the elimination of approximately 65 % of our global workforce, or approximately 300 roles across the company.** We may encounter challenges in the execution of these **and any future restructuring** efforts, and these challenges could impact our financial results. Although we believe that these actions will **streamline operations and** reduce ~~operating~~ costs, we cannot guarantee that ~~the~~ **these** ~~Reorganization~~ **restructuring efforts** will achieve or sustain the targeted benefits, or that the benefits, even if achieved, will be adequate to meet our long- term expectations **and the needs of our business** . As a result of ~~the~~ **these** ~~Reorganization~~ **restructuring efforts** , we will incur additional costs in the near term, including cash expenditures for employee ~~transition~~ **transitions** , notice ~~period~~ **periods** and severance payments, **costs associated with** employee ~~benefits~~ - **benefit** ~~,~~ **programs** and related **restructuring** facilitation **and transaction** costs. Additional risks associated with the continuing impact of ~~the~~ **these** ~~Reorganization~~ **restructuring efforts** 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 **regulatory or** 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. **unable to continue to attract** and ~~retaliation~~ **retain high quality personnel** , **our ability to pursue our business may be harmed** and ~~we~~ **our growth strategy** may ~~in the future~~ be **limited** ~~subject to additional claims of non- compliance with similar or other laws and regulations~~ .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 ~~. The~~ Risks Related to Our Ordinary Shares The **market** price of our ordinary shares has been and may in the future be volatile and fluctuate substantially. Our **ordinary** 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~~ **24** , ~~2024~~ **2025** the sale price of our ordinary shares ranged from a high of $ 82. 49 to a low of $ ~~4~~ **3** . ~~72~~ **73** . The closing price on February ~~23~~ **24** , ~~2024~~ **2025** ~~,~~ was $ ~~6~~ **11** . ~~32~~ **48** per ordinary share. In recent years, the stock market in general and the market for shares of ~~smaller~~ **biotechnology and** biopharmaceutical companies

in particular have experienced significant price and volume fluctuations that have often been unrelated or disproportionate to changes in the operating performance of 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~~ **competing** products or technologies; ● results of **our** clinical trials ~~of our product candidates~~ or those of our competitors; ● public perception and market reaction to our interim data from **our** clinical trials; ● public perception of gene ~~therapy~~ **therapies and companies developing gene therapies**; ● interactions with the FDA **and other regulatory authorities** on the design of our clinical trials ~~and~~ **,** regulatory endpoints **and accelerated approval pathways available to us**; ● regulatory delays and greater government regulation of potential products due to adverse events; ● regulatory ~~or~~ **,** legal **and political** 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 **, strategic transactions** and restructurings **; ● future issuances, sales, resales or repurchases or anticipated issuances, sales, resales or repurchases, of our ordinary shares, including due to the expiration of contractual lock- up agreements**; ● 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~~ **technologies**; ● actual or anticipated changes in estimates as to financial results, development timelines **; ● failure to meet expectations of investors** 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; ● general economic, industry and market conditions; and ● the **realization of any of** ~~other~~ -- **the** factors described in this " Risk Factors " section. Following periods of such **market** volatility ~~in the market price of a company' s securities~~, securities class ~~action~~ **actions have** ~~litigation has often~~ been brought against ~~that company~~ **companies experiencing such volatility in the price of their securities**. Because of the potential volatility of our ~~stock~~ **ordinary share** 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 ~~26~~ **25** . ~~6~~ **2** % of our issued ~~shares~~ **share capital** ~~(including such shares to be issued in relation to exercisable options to purchase ordinary shares) as of December 31, 2023~~. As a result, if these shareholders were to choose to act together, they may be able, as a practical matter, to ~~control~~ **influence** many matters submitted to our shareholders for approval, as well as our management and affairs. For example, these ~~persons~~ **shareholders**, if they choose to act together, could ~~control~~ **influence** 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 **. 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 a public limited liability 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. Under Dutch law, our board members are required to act in the long- term interest of the company, considering the interests of shareholders, employees, and other stakeholders. This governance approach differs from that of some U. S. jurisdictions, where directors may focus primarily on maximizing shareholder value. As a result, decisions made by our board may be different than those that would be taken by a company organized under the law of some U. S. jurisdictions. 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, such as the public offering of our ordinary shares completed in January 2025. Our shareholders' reluctance to approve further issuances of ordinary shares could adversely affect our ability to raise capital and fund development programs and continued operations. Dutch corporate governance laws evolve over time, and future changes may impact the governance structure and shareholder rights applicable to Dutch public limited companies whose securities are traded in the United States or otherwise adversely affect the rights of investors. For more information on relevant provisions of Dutch corporate law and of our articles of association, see the description of our capital stock included in Exhibit 4. 1 and our articles of association filed as Exhibit 3. 1 to this Annual Report on Form 10- K**. Provisions of our articles of association or Dutch corporate law might deter acquisition bids for us that might **otherwise** be considered favorable and ~~prevent or frustrate any attempt~~ **could make it more difficult** to replace our board **, ensuring continuity and stability in corporate governance in line with Dutch law and case law requirements. t**. 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 dismissed or ~~suspected~~ **suspended** at a general meeting of shareholders by a two- thirds majority of votes cast representing more than half of our outstanding ordinary shares; ● a provision that our executive directors may only

be appointed upon binding nomination of the 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~~ **Furthermore** , ~~according to~~ **in accordance with** Dutch corporate law, **shareholders with the right to propose agenda items for the general meeting** ~~our~~ **or request the convening of a general meeting must first engage in consultation with the** board ~~can~~ **. If exercising such rights may result in a change in our strategy (for example, through the dismissal of one or more directors), the board must be given the opportunity to** invoke a **reasonable period to respond to the shareholders' intentions. If invoked, the board must use such response period for further deliberation and constructive consultation with the concerned shareholder (s) and thereafter report on this consultation and the exploration of alternatives to the general meeting. The response period may be invoked only once for any given general meeting and shall not apply in respect of a matter for which a response period or a statutory** cooling- off period **(as discussed below) has been previously invoked. 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~~ **Shareholders representing at least 3 % of our issued share capital may request the Enterprise Chamber (Ondernemingskamer) for early termination of the** cooling- off period ~~, our general meeting~~ **. The Enterprise Chamber must rule in favor** of **the request if the** shareholders **can demonstrate that (i) our board of directors, in light of the circumstances at hand when the cooling- off period was invoked, could not reasonably have concluded that the relevant proposal or hostile offer constituted a material conflict with the interests of our company and its business, or (ii) our board of directors cannot reasonably believe that a continuation of the cooling- off period** would **contribute** ~~not be able~~ to ~~dismiss, suspend~~ **careful policy- making;** or ~~appoint directors~~ (**iii** ~~or amend the provisions in our articles of association dealing with those matters~~) ~~except at the~~ **other** ~~proposal~~ **defensive measures, having the same purpose, nature, and scope as the cooling-** ~~of~~ **off** ~~our board~~ **period, have been activated during the cooling- off period** . 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 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 **, which is uncertain** . ~~If we fail~~ **We have not paid any dividends since our incorporation. Even if future operations lead** to ~~maintain~~ **significant levels of distributable profits, we currently expect those earnings, if any, will be reinvested in our business and that dividends will not be paid until we have** an ~~effective system of internal controls~~ **established revenue stream to support paying dividends. In addition** , ~~we~~ **payment of future cash dividends** may be **made only if** ~~unable to accurately report our results of operations or~~ **our** ~~prevent fraud~~ **shareholders' (deficit) / equity exceeds the sum of** ~~or~~ **our** ~~fail~~ **paid- in and called- up share capital plus the reserves required** to ~~meet~~ **be maintained by Dutch law** ~~our~~ **or by our articles** ~~reporting obligations, and investor confidence and the market price~~ of **association. Accordingly, shareholders cannot rely on dividend income from** our ordinary shares ~~may be materially~~ and **any returns** ~~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 **investment** ~~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 **will likely depend entirely upon any** ~~. 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 **appreciation in the price of our ordinary shares** . 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 consequences to U. S. holders. **We believe that we were** ~~A corporation organized outside the U. S. generally will be classified as~~ a passive foreign investment company (" PFIC ") for **the 2024 taxable year. 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 ~~,~~ **during which** a **U. S. holder holds ordinary shares, certain adverse U. S. federal income tax consequences may apply to such U. S. holders and a such** 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. **A** ~~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, **in order** to make **certain of** 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 **ordinary** shares, the possible implications to them of ~~us~~ **our** being treated as a PFIC (including the availability of applicable ~~election~~ **elections** , **and** whether making any such election would be advisable in their particular circumstances) as well as the **U. S.** federal, state, local and foreign tax considerations applicable to such holders in connection with the purchase, ownership ~~,~~ and disposition of our **ordinary** 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 organized and existing under the laws of the Netherlands. ~~Some of~~ **Accordingly, under Dutch private international law,** the **rights** ~~members of our board~~ and ~~senior management~~ **obligations of our shareholders vis- à- vis the company originating from Dutch corporate law and our articles of association, as well as the civil liability of our officers (functionarissen), including our directors and executive officers, are governed in certain respects by Dutch law. Certain of our executive officers** reside outside the **United States. Depending on the subject matter of the action brought against us and / or our officers, United States courts may lack jurisdiction over such persons. If a Dutch court has jurisdiction, that court will apply Dutch procedural law and Dutch private international law to determine applicable substantive law. Depending on the subject matter of the claim, a competent Dutch court may apply Dutch law rather than** U. S **. securities law** . 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. **Dutch courts typically do** ~~In addition, it is~~ not **apply U. S.** ~~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~~ **directly, but** ~~the~~ **they may consider** ~~U. S. brought in a court of competent jurisdiction in the~~ **them** ~~Netherlands~~ **if a claim is refiled under Dutch legal principles (such as under general tort law (onrechtmatige daad)** . The U. S. and the Netherlands currently do not have a treaty providing for the ~~reciprocal~~ **automatic** recognition and enforcement of judgments, other than arbitration awards, in civil and commercial matters. ~~Consequently~~ **In addition, both the Hague Convention on Choice of Court Agreements (2005) and the Hague Judgments Convention (2019) have entered into force for the Netherlands but have not entered into force for the United States. As a result** , 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~~ **enforced** 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 **Dutch** ~~principles of~~ public policy ~~of the Netherlands~~ **(ordre public)** . 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 **exceed** ~~they are necessary to compensate~~ actual **compensation** ~~losses or damages~~ . ~~Enforcement and recognition~~ **Recognition and enforcement** of **foreign** judgments ~~of U. S. courts in the Netherlands~~ are solely governed by the ~~provisions of the~~ Dutch Civil Procedure Code **(Wetboek van Burgerlijke Rechtsvordering)** . 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 **not obligated to, and do not, comply with all best practice provisions of the Dutch Corporate Governance Code. We are subject to the Dutch Corporate Governance Code (the " DCGC "). The DCGC contains principles and best practice provisions on corporate governance that regulate relations between the board and the general meeting and matters in respect of financial reporting, auditors, disclosure, compliance and enforcement standards. The DCGC follows the principle of " comply or explain ". Accordingly, companies must disclose in their statutory annual reports whether they comply with the provisions of the DCGC. If** a ~~public~~ company **, subject to** ~~(naamloze vennootschap) organized under~~ the ~~laws of the Netherlands~~ **DCGC, does not comply with certain provisions, it must provide** ~~and~~ **an** ~~our corporate affairs~~ **explanation for such non- compliance. While we** are ~~governed by~~ **subject to the DCGC, we do not comply with all of its best practice provisions. This may affect** ~~our~~ **your** ~~articles of association~~ **rights as a shareholder** and ~~by~~ **you may not have** the ~~laws governing~~ **same level of protection as a shareholder in a Dutch company that fully** ~~companies incorporated in~~ **complies with the DCGC. General Risks Our future success depends on our ability to retain key executives, technical staff, and** ~~the~~ **other** ~~Netherlands~~ **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 ~~rights~~ **loss** of ~~our shareholders and~~ the ~~responsibilities~~ **services** of **any** ~~members~~ **member** 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~~ **our senior management** ~~interests as a shareholder, and our~~ **or** ~~directors may take actions that would be different than those~~ **the inability to hire** ~~that would be taken by a company organized under the law of some U. S. jurisdictions. In addition, in accordance with our~~ **or retain experienced management personnel** ~~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~~ **execute our**

business plan and ~~fund~~ **harm our operating results. We are highly dependent on hiring, training, retaining, and motivating key personnel to lead our research and** development **, clinical** ~~programs and continued~~ operations **, and manufacturing efforts . Although we have entered into employment agreements with our key personnel, each of them may terminate their employment subject to the notice provisions in such agreements. We do not maintain key person insurance for any of our senior management or employees.** ~~There~~ -- **The** ~~can~~ **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 ~~no assurance that Dutch law will not change in~~ **difficult and may take an extended period because of** the ~~future~~ **limited number of individuals in** ~~or~~ **our** ~~that it will serve~~ **industry with the breadth and depth of skills and experience required** to ~~protect investors~~ **successfully develop gene therapy products. The competition for qualified personnel** in **the pharmaceutical field is intense, and** ~~a similar fashion afforded under corporate law principles in the~~ **there is a limited pool** ~~U. S., which could adversely affect the rights~~ of ~~investors~~ **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** . We may be adversely affected by unstable market and economic conditions **and potential macroeconomic effects** , such as inflation, **new or increased tariffs and higher interest rates,** which may negatively impact our business, financial condition and ~~stock~~ **share** price. ~~Market~~ **Macroeconomic** conditions **beyond our control** such as **economic instability, changes in tax laws and regulations, including based on the recent U. S. presidential election, trade restrictions, additional tariffs, export controls,** inflation **, high interest rates** , volatile energy costs, geopolitical issues, ~~war~~ **armed hostilities, such as the ongoing conflicts between Russia and Ukraine and in the Middle East** , 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 **outside of the biotechnology sector** with ~~steadier~~ **more predictable investment** 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~~ **share** price or could require us to delay or abandon development or commercialization plans. 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. Our management is responsible for establishing and maintaining adequate internal control over financial reporting and disclosure controls. Internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with applicable accounting principles. 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 or disclosure controls, we could experience material misstatements in our financial statements and fail to meet our reporting obligations under the Exchange Act, which would likely cause investors to lose confidence in our reported financial information or disclosures. This could in turn limit our access to capital markets and our ability to fund our business, harm our results of operations, and could 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. Our internal computer systems, or those of our collaborators, third- party vendors, contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our business and 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 and hackers, malicious code, employee theft or misuse, sophisticated nation- state and nation- state- supported actors, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures, among other potential risks. The size and complexity of our information technology systems, and those of our collaborators, third- party vendors, contractors and consultants, and the large amounts of proprietary and confidential information stored on these 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 remote work policy may increase our vulnerability to such 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 patients involved in our clinical trials or our 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 and expose us to claims for damages, regulatory fines, penalties or litigation. 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 designed 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. If securities or industry analysts **do not publish,** 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~~ **ordinary** shares depends in part on the research and reports that securities or industry analysts publish about us or our business. **We do not control these analysts, or the content and opinions included in their reports.** If one or more of the analysts who cover us downgrades our ~~common~~ **ordinary** shares or publishes inaccurate or unfavorable research about our business, our **ordinary** share price ~~may~~ **could** 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~~ **share** 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~~ **along with expected regulatory** approval timelines for ~~commercial sales~~ **our product candidates** . ~~All these~~ **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 **share price may decline. Environmental sustainability and social initiatives that we undertake may impose additional costs on our business and expose us to new risks. Concern over the impact of climate change may result in new or additional legislative and regulatory requirements to reduce or mitigate its effects on the environment, which could result in increased expenses and expenditure of company resources as we seek to comply with such requirements. More broadly, there has been increasing public focus by shareholders, patients, activists, the media, governmental and non- governmental organizations and other constituencies on a variety of environmental, social and other sustainability matters, resulting in new and pending international agreements and national, regional, and local legislation, regulatory measures, public reporting obligations and potential policy changes across jurisdictions. We may experience pressure in some of the countries in which we operate to make commitments with respect to our greenhouse gas emissions as well as other sustainability- focused matters. 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, including new reporting requirements for businesses operating in the European Union, which may require the that we dedicate additional capital and personnel resources toward compliance with these measures. If we fail to comply with new laws, regulations or reporting requirements, our reputation and business could be harmed. Furthermore, increasing attention on environmental and sustainability matters 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. We cannot guarantee that any initiatives we adopt to respond to stakeholder expectations will have the desired effect. Moreover, initiatives that we adopt in some countries in which we operate may be viewed differently in other countries in which we operate. Any failure to meet the expectations of our investors, regulators,** stock ~~price may decline~~ **exchanges or other stakeholders with respect to sustainability matters could materially adversely affect our business, financial condition, and results of operations** . ~~79~~