Risk Factors Comparison 2025-02-12 to 2024-02-14 Form: 10-K

Legend: **New Text** ~~Removed Text~~ Unchanged Text Moved Text Section

Risks Related to Our Business We are substantially dependent on revenue from our products. Our revenue depends upon continued sales of our products as well as the financial rights we have in our anti- CD20 therapeutic programs. A significant portion of our revenue is concentrated on sales of our products in increasingly competitive markets. Any of the following negative developments relating to any of our products or any of our anti- CD20 therapeutic programs may adversely affect our revenue and results of operations or could cause a decline in our stock price: • the introduction, greater acceptance or more favorable reimbursement of competing products, including new originator therapies, generics, prodrugs and biosimilars of existing products and products approved under abbreviated regulatory pathways; • safety or efficacy issues; • limitations and additional pressures on product pricing or price increases, including those relating to inflation and those resulting from governmental or regulatory requirements, including those relating to any future potential drug price negotiation under the IRA; increased competition, including from generic or biosimilar versions of our products; or changes in, or implementation of, reimbursement policies and practices of payors and other third- parties; • adverse legal, administrative, geopolitical events, regulatory or legislative developments; or • our ability to maintain a positive reputation among patients, healthcare providers and others, which may be impacted by our pricing and reimbursement decisions. LEQEMBI **is** ~~and SKYCLARYS are~~ in the early stages of commercial launch in the U. S **. and certain international markets and SKYCLARYS is in the early stages of commercial launch in the U. S. and certain European markets** . In addition to risks associated with new product launches and the other factors described in these Risk Factors, Biogen' s and Eisai' s ability to successfully commercialize LEQEMBI and our ability to successfully commercialize SKYCLARYS may be adversely affected due to: • Eisai' s ability to obtain and maintain adequate reimbursement for LEQEMBI; • the effectiveness of Eisai' s and Biogen' s commercial strategy for marketing LEQEMBI; • requirements such as participation in a registry and the use of imaging or other diagnostics for LEQEMBI; • our ability to obtain approval in other markets; • the approval of other new products for the same or similar indications; • Eisai' s and Biogen' s ability to maintain a positive reputation among patients, healthcare providers and others in the Alzheimer' s disease community, which may be impacted by pricing and reimbursement decisions relating to LEQEMBI, which are made by Eisai **and / or third parties** ; • Biogen' s ability to obtain and maintain adequate reimbursement for SKYCLARYS; and • the effectiveness of Biogen' s commercial strategy for marketing SKYCLARYS. Our long- term success depends upon the successful development of new products and additional indications for our existing products. Our long- term success will depend upon the successful development of new products from our research and development activities or our licenses or acquisitions from third ~~-~~parties, as well as additional indications for our existing products. Product development is very expensive and involves a high degree of uncertainty and risk and may not be successful. Only a small number of research and development programs result in the commercialization of a product. It is difficult to predict the success and the time and cost of product development of novel approaches for the treatment of diseases. The development of novel approaches for the treatment of diseases, including development efforts in new modalities such as those based on the antisense oligonucleotide platform and gene therapy, ~~may present~~ **presents** additional challenges and risks, including obtaining approval from regulatory authorities that have limited experience with the development of such therapies. For example, we are currently seeking approval of ~~SKYCLARYS~~ **LEQEMBI** in Europe **and the approval of a subcutaneous formulation of LEQEMBI in the U. S.** and any delays or challenges ~~regarding its approval in Europe~~ may ~~adversely~~ impact our ability to realize the anticipated benefits from **LEQEMBI** ~~the Reata acquisition~~ . Clinical trial data are subject to differing interpretations and even if we view data as sufficient to support the safety, effectiveness and / or approval of an investigational therapy, regulatory authorities may disagree and may require additional data, limit the scope of the approval or deny approval altogether. Furthermore, the approval of a product candidate by one regulatory agency does not mean that other regulatory agencies will also approve such product candidate. Success in preclinical work or early- stage clinical trials does not ensure that later stage or larger scale clinical trials will be successful. Clinical trials may indicate that our product candidates lack efficacy, have harmful side effects, result in unexpected adverse events or raise other concerns that may significantly reduce or delay the likelihood of regulatory approval. This may result in terminated programs, significant restrictions on use and safety warnings in an approved label, adverse placement within the treatment paradigm or significant reduction in the commercial potential of the product candidate. Even if we could successfully develop new products or indications, we may make a strategic decision to discontinue development of a product candidate or indication if, for example, we believe commercialization will be difficult relative to the standard of care or we prioritize other opportunities in our pipeline. **Additionally,** ~~Sales~~ **sales** of new products or products with additional indications may not meet investor expectations. If we fail to compete effectively, our business and market position would suffer. The biopharmaceutical industry and the markets in which we operate are intensely competitive. We compete in the marketing and sale of our products, the development of new products and processes, the acquisition of rights to new products with commercial potential and the hiring and retention of personnel. We compete with biotechnology and pharmaceutical companies that have a greater number of products on the market and in the product pipeline, substantially greater financial, marketing, research and development and other resources and other technological or competitive advantages. Our products continue to face increasing competition from the introduction of new originator therapies, generics, prodrugs and biosimilars of existing products and products approved under abbreviated regulatory pathways. Some of these products are likely to be sold at substantially lower prices than our branded products. The introduction of such products as well as other lower- priced competing products has reduced, and may in the future, significantly reduce both the price that we are able to charge for our products and the volume of

products we sell, which will negatively impact our revenue. For instance, demand and price for TECFIDERA declined significantly as a result of multiple TECFIDERA generic entrants entering the U. S. market in 2020. In addition, in some markets, when a generic or biosimilar version of one of our products is commercialized, it **has in the past and** may **in the future** be automatically substituted for our product and significantly reduce our revenue in a short period of time. Our ability to compete, maintain and grow our business may also be adversely affected due to a number of factors, including: • the introduction of other products, including products that may be more efficacious, safer, less expensive or more convenient alternatives to our products, including our own products and products of our collaborators; • the off- label use by physicians of therapies indicated for other conditions to treat patients; • patient dynamics, including the size of the patient population and our ability to identify, attract and maintain new and current patients to our therapies; • the reluctance of physicians to prescribe, and patients to use, our products without additional data on the efficacy and safety of such products; • damage to physician and patient confidence in any of our products, generic or biosimilars of our products or any other product from the same class as one of our products, or to our sales and reputation as a result of label changes, pricing and reimbursement decisions or adverse experiences or events that may occur with patients treated with our products or generic or biosimilars of our products; • inability to obtain and maintain appropriate pricing and adequate reimbursement for our products compared to our competitors in key markets; or • our ability to obtain and maintain patent, data or market exclusivity for our products. Our business may be adversely affected if we do not successfully execute or realize the anticipated benefits of our strategic and growth initiatives. The successful execution of our strategic and growth initiatives ~~may depend~~ **depends** upon internal development projects, commercial initiatives and external opportunities, which may include the acquisition and in- licensing of products, technologies, companies, the entry into strategic alliances and collaborations or our Fit for Growth program, as well as our ability to execute on ~~previously- announced~~ **strategic decisions and** initiatives ~~such as the exploration of strategic options for our biosimilars business~~ . While we believe we have a number of promising programs in our pipeline, failure or delay of internal development projects to advance or difficulties in executing on our commercial initiatives could impact our current and future growth, resulting in additional reliance on external development opportunities for growth. Supporting the further development of our existing products and potential new products in our pipeline will require significant capital expenditures and management resources, including investments in research and development, sales and marketing, manufacturing capabilities and other areas of our business. We have made, and may continue to make, significant operating and capital expenditures for potential new products prior to regulatory approval with no assurance that such investment will be recouped, which may adversely affect our financial condition, business and operations. The availability of high quality, fairly valued external product development is limited and the opportunity for their acquisition is highly competitive. As such, we are not certain that we will be able to identify suitable candidates for acquisition or if we will be able to reach agreement to make any such acquisition if suitable candidates are identified. We may fail to initiate or complete transactions for many reasons, including failure to obtain regulatory or other approvals as well as a result of disputes or litigation. Furthermore, we may not be able to achieve the full strategic and financial benefits expected to result from transactions **or strategic decisions, such as the decision to retain the biosimilars business** , or the benefits may be delayed or not occur at all. We may also face additional costs or liabilities in completed transactions that were not contemplated prior to completion. Any failure in the execution of a transaction, in the integration of an acquired asset or business or in achieving expected synergies could result in slower growth, higher than expected costs, the recording of asset impairment charges and other actions which could adversely affect our business, financial condition and results of operations. For example, we recently acquired Reata and **HI- Bio and** are in the process of integrating Reata **and HI- Bio** into our Company. The ultimate success of our ~~acquisition~~ **acquisitions** of Reata **and HI- Bio** and our ability to realize the anticipated benefits from the ~~acquisition~~ **acquisitions** , including **future performance of** the SKYCLARYS **product and further development of the felzartamab** product and anticipated synergies, depends on, among other things, how effective we are in integrating the Biogen ~~and~~ **,** Reata **and HI- Bio** operations. We face risks associated with our Fit for Growth program that may impair our ability to achieve anticipated savings and operational efficiencies or that may otherwise harm our business. These risks include delays in implementation of cost optimization actions, loss of workforce capabilities, higher than anticipated separation expenses, litigation and the failure to meet financial and operational targets. In addition, the calculation of the anticipated cost savings and other benefits resulting from our Fit for Growth program are subject to many estimates and assumptions. These estimates and assumptions are subject to significant business, economic, competitive and other uncertainties and contingencies, many of which are beyond our control. ~~if~~ **If** these estimates and assumptions are incorrect or if we experience delays or unforeseen events, our business and financial results could be adversely affected. Sales of our products depend, to a significant extent, on adequate coverage, pricing and reimbursement from third- party payors, which are subject to increasing and intense pressure from political, social, competitive and other sources. Our inability to obtain and maintain adequate coverage, or a reduction in pricing or reimbursement, could have an adverse effect on our business, reputation, revenue and results of operations. Sales of our products depend, to a significant extent, on adequate coverage, pricing and reimbursement from third- party payors. When a new pharmaceutical product is approved, the availability of government and private reimbursement for that product, diagnosis of the condition it treats and the cost to administer it may be uncertain, as is the pricing and amount for which that product will be reimbursed. Pricing and reimbursement for our products may be adversely affected by a number of factors, including: • changes in, and implementation of, federal, state or foreign government regulations or private third- party payors' reimbursement policies; • pressure by employers on private health insurance plans to reduce costs; • consolidation and increasing assertiveness of payors seeking price discounts or rebates in connection with the placement of our products on their formularies and, in some cases, the imposition of restrictions on access or coverage of particular drugs or pricing determined based on perceived value; • our ability to receive reimbursement for our products or our ability to receive comparable reimbursement to that of competing products; and • our value- based contracting program pursuant to which we aim to tie the pricing of our products to their clinical values by either aligning price to patient outcomes or adjusting price for

patients who discontinue therapy for any reason, including efficacy or tolerability concerns. Our ability to set the price for our products varies significantly from country to country and, as a result, so can the price of our products. Governments may use a variety of cost- containment measures to control the cost of products, including price cuts, mandatory rebates, value- based pricing and reference pricing (i. e., referencing prices in other countries and using those reference prices to set a price). Drug prices are under significant scrutiny in the markets in which our products are prescribed; for example the IRA has certain provisions related to drug pricing **, including the ability for the U. S. government to set prices for certain drugs in Medicare** . We expect drug pricing and other health care costs to continue to be subject to intense political and societal pressures on a global basis. Certain countries set prices by reference to the prices in other countries where our products are marketed. Our inability to obtain and maintain adequate prices in a particular country may not only limit the revenue from our products within that country but may also adversely affect our ability to secure acceptable prices in existing and potential new markets, which may limit market growth and result in reductions in revenue. This may create the opportunity for third- party cross- border trade or influence our decision to sell or not to sell a product, thus adversely affecting our geographic expansion plans and revenue. Additionally, in certain jurisdictions governmental health agencies may adjust, retroactively and / or prospectively, reimbursement rates for our products. Reimbursement for our products by governments, including the timing of any reimbursements, may also be affected by budgetary or political constraints, particularly in challenging economic environments. Government agencies often do not set their own budgets and therefore, have limited control over the amount of money they can spend. In addition, these agencies experience political pressure that may dictate the manner in which they spend money. There can be no assurance that the economic, budgeting or political issues will not worsen and adversely impact sales or reimbursements of our products. Competition from current and future competitors may negatively impact our ability to maintain pricing and our market share. New products marketed by our competitors could cause our revenue to decrease due to potential price reductions and lower sales volumes. Additionally, the introduction of generic or biosimilar versions of our products, follow- on products, prodrugs or products approved under abbreviated regulatory pathways may significantly reduce the price that we are able to charge for our products and the volume of products we sell. Many payors continue to adopt benefit plan changes that shift a greater portion of prescription costs to patients, including more limited benefit plan designs, higher patient co- pay or co- insurance obligations and limitations on patients' use of commercial manufacturer co- pay payment assistance programs (including through co- pay accumulator adjustment or maximization programs). Significant consolidation in the health insurance industry has resulted in a few large insurers and pharmacy benefit managers exerting greater pressure in pricing and usage negotiations with drug manufacturers, significantly increasing discounts and rebates required of manufacturers and limiting patient access and usage. Further consolidation among insurers, pharmacy benefit managers and other payors would increase the negotiating leverage such entities have over us and other drug manufacturers. Additional discounts, rebates, coverage or plan changes, restrictions or exclusions as described above could have a material adverse effect on sales of our affected products. Our failure to obtain or maintain adequate coverage, pricing or reimbursement for our products could have an adverse effect on our business, reputation, revenue and results of operations. We depend on relationships with collaborators and other third- parties for revenue, and for the development, regulatory approval, commercialization and marketing of certain of our products and product candidates, which are outside of our full control **, and if these relationships fail, our business may be adversely affected** . We rely on a number of collaborative and other third- party relationships for revenue and the development, regulatory approval, commercialization and marketing of certain of our products and product candidates. We also outsource certain aspects of our regulatory affairs and clinical development relating to our products and product candidates to third- parties. Reliance on third- parties subjects us to a number of risks, including: • we may be unable to control the resources our collaborators or third- parties devote to our programs, products or product candidates, which may affect our ability to achieve development goals or milestones; • disputes may arise under an agreement, including with respect to the achievement and payment of milestones, payment of development or commercial costs, ownership of rights to technology developed, and the underlying agreement may fail to provide us with significant protection or may fail to be effectively enforced if the collaborators or third- parties fail to perform; • the interests of our collaborators or third- parties may not always be aligned with our interests, and such parties may not **protect and enforce any intellectual property rights or** pursue regulatory approvals or market a product in the same manner or to the same extent that we would, which could adversely affect our revenue, or may adopt tax strategies that could have an adverse effect on our business, results of operations or financial condition; • third- party relationships require the parties to cooperate, and failure to do so effectively could adversely affect product sales or the clinical development or regulatory approvals of product candidates under joint control, could result in termination of the research, development or commercialization of product candidates or could result in litigation or arbitration; • any failure on the part of our collaborators or third- parties to comply with applicable laws, including tax laws, regulatory requirements and / or applicable contractual obligations or to fulfill any responsibilities they may have to protect and enforce any intellectual property rights underlying our products could have an adverse effect on our revenue or reputation as well as involve us in possible legal proceedings; and • any improper conduct or actions on the part of our collaborators or third- parties could subject us to civil or criminal investigations and monetary and injunctive penalties, require management attention, impact the accuracy and timing of our financial reporting and / or adversely impact our ability to conduct business, our operating results and our reputation. Given these risks, there is considerable uncertainty regarding the success of our current and future collaborative efforts. If these efforts fail, our product development or commercialization of new products could be delayed, revenue from products could decline and / or we may not realize the anticipated benefits of these arrangements. Our results of operations may be adversely affected by current and potential future healthcare reforms. In the U. S., federal and state legislatures, health agencies and third- party payors continue to focus on containing the cost of health care. Legislative and regulatory proposals, enactments to reform health care insurance programs (including those contained in the IRA) and increasing pressure from social sources could significantly influence the manner in which our products are prescribed, purchased and reimbursed. For example, provisions of the PPACA

have resulted in changes in the way health care is paid for by both governmental and private insurers, including increased rebates owed by manufacturers under the Medicaid Drug Rebate Program, annual fees and taxes on manufacturers of certain branded prescription drugs, the requirement that manufacturers participate in a discount program for certain outpatient drugs under Medicare Part D and ~~the expansion of the number of hospitals eligible for discounts~~ under Section 340B of the Public Health Service Act **and similar state legislation** . These changes have had and are expected to continue to have a significant impact on our business. We may face uncertainties as a result of efforts to repeal, substantially modify or invalidate some or all of the provisions of the PPACA. There is no assurance that the PPACA, as currently enacted or as amended in the future, will not adversely affect our business and financial results, and we cannot predict how future federal or state legislative or administrative changes relating to healthcare reform will affect our business. There is substantial public attention on the costs of prescription drugs and we expect drug pricing and other health care costs to continue to be subject to intense political and societal pressures on a global basis. In addition, there have been (including elements of the IRA), and are expected to continue to be, legislative proposals to address prescription drug pricing. **We face uncertainties regarding potential healthcare reforms** ~~Some of these proposals could have significant effects on our business~~ , ~~including~~ **governmental policy** ~~an~~ **and prioritization,** ~~executive order issued in September 2020 to test a " most favored nation " model for Part B and Part D drugs that tie reimbursement rates to international drug pricing metrics. These actions~~ and the uncertainty about the future of the PPACA and healthcare laws may put downward pressure on pharmaceutical pricing and increase our regulatory burdens and operating costs. There is also significant economic pressure on state budgets, that may result in states increasingly seeking to achieve budget savings through mechanisms that limit coverage or payment for our drugs. In recent years, some states have considered legislation and ballot initiatives that would control the prices of drugs, including laws to allow importation of pharmaceutical products from lower cost jurisdictions outside the U. S. and laws intended to impose price controls on state drug purchases. State Medicaid programs are requesting manufacturers to pay supplemental rebates and requiring prior authorization by the state program for use of any drug for which supplemental rebates are not being paid. Government efforts to reduce Medicaid expense may lead to increased use of managed care organizations by Medicaid programs. This may result in managed care organizations influencing prescription decisions for a larger segment of the population and a corresponding limitation on prices and reimbursement for our products. In the E. U. and some other international markets, the government provides health care at low cost to consumers and regulates pharmaceutical prices, patient eligibility or reimbursement levels to control costs for the government- sponsored health care system. Many countries have announced or implemented measures, and may in the future implement new or additional measures, to reduce health care costs to limit the overall level of government expenditures. These measures vary by country and may include, among other things, patient access restrictions, suspensions on price increases, prospective and possible retroactive price reductions and other recoupments and increased mandatory discounts or rebates, recoveries of past price increases and greater importation of drugs from lower- cost countries. These measures have negatively impacted our revenue and may continue to adversely affect our revenue and results of operations in the future. Our success in commercializing biosimilars is subject to risks and uncertainties inherent in the development, manufacture and commercialization of biosimilars. If we are unsuccessful in such activities, our business may be adversely affected. The development, manufacture and commercialization of biosimilar products require specialized expertise and are very costly and subject to complex regulation. Our success in commercializing biosimilars is subject to a number of risks, including: • Reliance on Third- Parties. We are dependent, in part, on the efforts of collaboration partners and other third- parties over whom we have limited or no control in the development and manufacturing of biosimilars products. For example, a recently **completed** ~~announced potential~~ acquisition of a contract development and manufacturing organization by a third party **may impact its operational, strategic or financial risk** . If these third- parties fail to perform successfully, or reduce their third party manufacturing production, our biosimilar product development or commercialization of biosimilar products could be delayed, revenue from biosimilar products could decline and / or we may not realize the anticipated benefits of these arrangements; • **Competitive Challenges. Biosimilar products face significant competition, including from innovator products and biosimilar products offered by other companies that may receive greater acceptance or more favorable reimbursement. Local tendering processes may restrict biosimilar products from being marketed and sold in some jurisdictions. The number of competitors in a jurisdiction, the timing of approval and the ability to market biosimilar products successfully in a timely and cost- effective manner are additional factors that may impact our success in this business area; •** Regulatory Compliance. Biosimilar products may face regulatory hurdles or delays due to the evolving and uncertain regulatory and commercial pathway of biosimilars products in certain jurisdictions; • Ability to Provide Adequate Supply. Manufacturing biosimilars is complex. If we encounter any **persistent** manufacturing or supply chain difficulties we may be unable to meet demand. We are dependent on a third- party for the manufacture of our biosimilar products and such third- party may not perform its obligations in a timely and cost- effective manner or in compliance with applicable regulations and may be unable or unwilling to increase production capacity commensurate with demand for our existing or future biosimilar products **. For example, one of our contract manufacturers for IMRALDI and BENEPALI was acquired by a third party in December 2024, which may have an impact on our biosimilars business** ; • Intellectual Property and Regulatory Challenges. Biosimilar products may face extensive intellectual property clearances and infringement litigation, injunctions or regulatory challenges, which could prevent the commercial launch of a product or delay it for many years or result in imposition of monetary damages, penalties or other civil sanctions and damage our reputation; **and** • Failure to Gain Market and Patient Acceptance. Market success of biosimilar products will be adversely affected if patients, physicians and / or payors do not accept biosimilar products as safe and efficacious products offering a more competitive price or other benefit over existing therapies ~~; and • Competitive Challenges. Biosimilar products face significant competition, including from innovator products and biosimilar products offered by other companies that may receive greater acceptance or more favorable reimbursement. Local tendering processes may restrict biosimilar products from being marketed and sold in some jurisdictions. The number of competitors in a jurisdiction, the~~

~~timing of approval and the ability to market biosimilar products successfully in a timely and cost- effective manner are additional factors that may impact our success in this business area. The decision to explore strategic options related to our biosimilars business could adversely affect our operations related to our biosimilars business~~ . Risks Related to Intellectual Property If we are unable to obtain and maintain adequate protection for our data, intellectual property and other proprietary rights, our business may be harmed. Our success, including our long- term viability and growth, depends, in part, on our ability to obtain and defend patent and other intellectual property rights, including certain regulatory forms of exclusivity, that are important to the commercialization of our products and product candidates. Patent protection and / or regulatory exclusivity in the U. S. and other important markets remains uncertain and depends, in part, upon decisions of the patent offices, courts, administrative bodies and lawmakers in these countries. We may fail to obtain, defend or preserve patent and other intellectual property rights, including certain regulatory forms of exclusivity, or the protection we obtain may not be of sufficient breadth and degree to protect our commercial interests in all countries where we conduct business, which could result in financial, business or reputational harm to us or could cause a decline or volatility in our stock price. In addition, settlements of such proceedings often result in reducing the period of exclusivity and other protections, resulting in a reduction in revenue from affected products. In many markets, including the U. S., manufacturers may be allowed to rely on the safety and efficacy data of the innovator' s product and do not need to conduct clinical trials before marketing a competing version of a product after there is no longer patent or regulatory exclusivity. In such cases, manufacturers often charge significantly lower prices and a major portion of the company' s revenue may be reduced in a short period of time. In addition, manufacturers of generics and biosimilars may choose to launch or attempt to launch their products before the expiration of our patent or other intellectual property protections. Furthermore, our products may be determined to infringe patents or other intellectual property rights held by third- parties. Legal proceedings, administrative challenges or other types of proceedings are and may in the future be necessary to determine the validity, scope or non- infringement of certain patent rights claimed by third- parties to be pertinent to the manufacture, use or sale of our products. Legal proceedings may also be necessary to determine the rights, obligations and payments claimed during and after the expiration of intellectual property license agreements we have entered with third parties. Such proceedings are unpredictable and are often protracted and expensive. Negative outcomes of such proceedings could hinder or prevent us from manufacturing and marketing our products, require us to seek a license for the infringed product or technology or result in the assessment of significant monetary damages against us that may exceed amounts, if any, accrued in our financial statements. A failure to obtain necessary licenses for an infringed product or technology could prevent us from manufacturing or selling our products. Furthermore, payments under any licenses that we are able to obtain could reduce our profits from the covered products and services. Any of these circumstances could result in financial, business or reputational harm to us or could cause a decline or volatility in our stock price. Risks Related to Development, Clinical Testing and Regulation of Our Products and Product Candidates Successful preclinical work or early stage clinical trials does not ensure success in later stage trials, regulatory approval or commercial viability of a product. Positive results in a clinical trial **have in the past and** may not **in the future** be replicated in subsequent or confirmatory trials. Additionally, success in preclinical work or early stage clinical trials does not ensure that later stage or larger scale clinical trials will be successful or that regulatory approval will be obtained. Even if later stage clinical trials are successful, regulatory authorities may delay or decline approval of our product candidates. Regulatory authorities may disagree with our view of the data, require additional studies, disagree with our trial design or endpoints or not approve adequate reimbursement. Regulatory authorities may also fail to approve the facilities or processes used to manufacture a product candidate, our dosing or delivery methods or companion devices. Regulatory authorities **have in the past and** may **in the future** grant marketing approval that is more restricted than anticipated, including limiting indications to narrow patient populations and the imposition of safety monitoring, educational requirements, requiring confirmatory trials and risk evaluation and mitigation strategies. The occurrence of any of these events could result in significant costs and expense, have an adverse effect on our business, financial condition and results of operations and / or cause our stock price to decline or experience periods of volatility. Clinical trials and the development of biopharmaceutical products is a lengthy and complex process. If we fail to adequately manage our clinical activities, our clinical trials or potential regulatory approvals may be delayed or denied. Conducting clinical trials is a complex, time- consuming and expensive process. Our ability to complete clinical trials in a timely fashion depends on a number of key factors, including protocol design, regulatory and institutional review board approval, patient enrollment rates and compliance with current Good Clinical Practices. If we or our third- party clinical trial providers or third- party CROs do not successfully carry out these clinical activities, our clinical trials or the potential regulatory approval of a product candidate may be delayed or denied. We have opened clinical trial sites and are enrolling patients in a number of countries where our experience is limited. In most cases, we use the services of third- parties to carry out our clinical trial related activities and rely on such parties to accurately report their results. Our reliance on third- parties for these activities may impact our ability to control the timing, conduct, expense and quality of our clinical trials. One CRO has responsibility for a substantial portion of our activities and reporting related to our clinical trials and if such CRO does not adequately perform, many of our trials may be affected, including adversely affecting our expenses associated with such trials. We may need to replace our CROs, which may result in the delay of the affected trials or otherwise adversely affect our efforts to obtain regulatory approvals and commercialize our product candidates. Adverse safety events or restrictions on use and safety warnings for our products can negatively affect our business, product sales and stock price. Adverse safety events involving our marketed products, generic or biosimilar versions of our marketed products or products from the same class as one of our products may have a negative impact on our business. Discovery of safety issues with our products could create product liability and could cause additional regulatory scrutiny and requirements for additional labeling or safety monitoring, withdrawal of products from the market and / or the imposition of fines or criminal penalties. Adverse safety events may also damage physician, patient and / or investor confidence in our products and our reputation. Any of these could result in adverse impacts on our results of operations. Regulatory authorities are making greater amounts of stand- alone safety information

directly available to the public through periodic safety update reports, patient registries and other reporting requirements. The reporting of adverse safety events involving our products or products similar to ours and public rumors about such events may increase claims against us and may also cause our product sales to decline or our stock price to experience periods of volatility. Restrictions on use or safety warnings that may be required to be included in the label of our products may significantly reduce expected revenue for those products and require significant expense and **divert** management time. Risks Related to Our Operations A breakdown or breach of our information systems could subject us to liability or interrupt the operation of our business. We are increasingly dependent upon information systems and data to operate our business. Changes in how we operate have caused us to modify our business practices in ways that heighten this dependence, including changing the requirement that most of our office- based employees in the U. S. and our other key markets work from the office, with many of our employees now working in hybrid or full- remote positions. As a result, we are increasingly dependent upon our information systems to operate our business and our ability to effectively manage our business depends on the security, reliability and adequacy of our information systems and data, which includes use of cloud technologies, including Software as a Service (SaaS), Platform as a Service (PaaS) and Infrastructure as a Service (IaaS). Breakdowns, invasions, corruptions, destructions and / or breaches, which ~~impact~~ may include **impacts such as** , but not limited to, comprising the capacity, reliability or security of our information systems or those of our business partners, including our cloud ~~tech nologies~~ **technologies** , and / or unauthorized access to our data and information could subject us to significant liability, negatively impact our business operations, and / or require replacement of technology and / or sizeable ransom payments. Our information systems, including our cloud technologies, continue to increase in multitude and complexity, increasing our vulnerability when breakdowns, malicious intrusions and random attacks occur. Data privacy or security breaches also pose a risk that sensitive data, including intellectual property, trade secrets or personal information belonging to us, patients, customers or other business partners, may be exposed to unauthorized persons or to the public. Cybersecurity threats and incidents are increasing in their frequency, sophistication and intensity, and are becoming increasingly difficult to detect, particularly when they impact vendors, customers or suppliers, and other companies in our supply chain. Cybersecurity threats and incidents are often carried out by motivated, well- resourced, skilled and persistent actors, including nation states, organized crime groups, " hacktivists " and may include or target employees or contractors acting with careless or malicious intent. Recent developments in the threat landscape include use of **adversarial** AI **techniques** and machine learning, as well as an increased number of cyber extortion attacks, with higher financial ransom demand amounts and increasing sophistication and variety of ransomware techniques and methodology. Geopolitical instability, including that related to Russia' s invasion of Ukraine or the conflict in the Middle East, may increase the risk of cybersecurity threats. Cybersecurity threats or incidents may include deployment of harmful malware and key loggers, ransomware, a denial- of- service attack, a malicious website, the use of social engineering and other means to affect the confidentiality, integrity and availability of our information systems and data. Cybersecurity threats and incidents also include manufacturing, hardware or software supply chain attacks, which could cause a delay in the manufacturing of products or products produced for contract manufacturing or lead to a data privacy or security breach. Our key business partners face similar risks and any security breach of their systems could adversely affect our security posture. In addition, our increased use of cloud technologies heightens these and other operational risks, and any failure by cloud or other technology service providers to adequately safeguard their systems and prevent cyber- attacks could disrupt our operations and result in misappropriation, corruption or loss of confidential or propriety information. While we continue to build and improve our systems and infrastructure, including our business continuity plans, there can be no assurance that our efforts will prevent cybersecurity threats or incidents in our systems and any such incidents could materially adversely affect our business and operations and / or result in the loss of critical or sensitive information, which could result in material financial, legal, operational or reputational harm to us, loss of competitive advantage or loss of consumer confidence. Our liability insurance may not be sufficient in type or amount to cover us against claims related to security breaches, cyber- attacks and other related breaches. Regulations continue to change as regulators worldwide consider new rules. For example, the SEC has adopted additional disclosure rules regarding cyber security risk management, strategy, governance and incident reporting by public companies. These new regulations or other regulations being considered in Europe and around the world may impact the manner in which we operate. Regulators ~~are imposing~~ **currently impose** new data privacy and security requirements, including ~~new and greater~~ monetary fines for privacy violations. For example, the E. U.' s General Data Protection Regulation established regulations regarding the handling of personal data, and provides an enforcement authority and imposes large penalties for noncompliance. ~~New~~ U. S. data privacy and security laws, such as the CCPA, and others that may be passed, similarly introduce requirements with respect to personal information, and non- compliance with the CCPA may result in liability through private actions (subject to statutorily defined damages in the event of certain data breaches) and enforcement. Failure to comply with these current and future laws, policies, industry standards or legal obligations or any security incident resulting in the unauthorized access to, or acquisition, release or transfer of personal information may result in governmental enforcement actions, litigation, fines and penalties or adverse publicity and could cause our customers to lose trust in us, which could have a material adverse effect on our business and results of operations. **The increasing use of AI- based software presents new risks and challenges and could adversely affect our business and reputation. The use of AI- based software is increasingly being used in the biopharmaceutical industry, including by us, such as for research, marketing, manufacturing and commercialization, and we expect to use technology that uses AI in the future. As with many developing technologies, AI- based software presents risks and challenges. For example, algorithms may be flawed; data sets may be insufficient, of poor quality or contain biased information; and inappropriate or controversial data practices could impair results. If the analyses that AI- based software assist in producing are deficient or inaccurate, we could be subjected to competitive harm, potential legal liability and brand or reputational harm. Use of AI- based software may also lead to cybersecurity risks or the release of confidential proprietary information, including personal data, which may impact our ability to realize the benefit of our intellectual property or violate our internal**

policies, data protection laws or contractual requirements. The use of AI- based software may also result in unauthorized access of personal data or the intellectual property of third parties. Since the use of AI is subject to new or evolving laws and regulations, compliance may impose operational costs and limit our ability to use AI- based software, and failure to comply may result in potential government actions, litigation, fines, penalties or adverse publicity. Manufacturing issues could substantially increase our costs, limit supply of our products and / or reduce our revenue. The process of manufacturing our products is complex, highly regulated and subject to numerous risks, including: • Risks of Reliance on Third- Parties and Single Source Providers. We rely on third- party suppliers and manufacturers for many aspects of our manufacturing process for our products and product candidates. In some cases, due to the unique manner in which our products are manufactured, we rely on single source providers of raw materials and manufacturing supplies. These third- parties are independent entities subject to their own unique operational **, strategic** and financial risks that are outside of our control. For example, a recently **completed** ~~announced potential~~ acquisition of a contract development and manufacturing organization by a third party **may impact its operational, strategic or financial risk** . These third- parties may not perform their obligations in a timely and cost- effective manner or in compliance with applicable regulations, and they may be unable or unwilling to increase production capacity commensurate with demand for our existing or future products. Finding alternative providers could take a significant amount of time and involve significant expense due to the specialized nature of the services and the need to obtain regulatory approval of any significant changes to our suppliers or manufacturing methods. We cannot be certain that we could reach agreement with alternative providers or that the FDA or other regulatory authorities would approve our use of such alternatives. • Global Bulk Supply Risks. We rely on our manufacturing facilities for the production of drug substance for our large molecule products and product candidates. Our global bulk supply of these products and product candidates depends on the uninterrupted and efficient operation of these facilities, which could be adversely affected by equipment failures, labor or raw material shortages, geopolitical instability, public health epidemics, natural disasters, **adverse weather events,** power failures, cyber- attacks and many other factors. • Risks Relating to Compliance with current GMP (cGMP). We and our third- party providers are ~~generally~~ required to maintain compliance with cGMP and other stringent requirements **, as applicable,** and are subject to inspections by the FDA and other regulatory authorities to confirm compliance. Any delay, interruption or other issues that arise in the manufacture, fill- finish, packaging or storage of our products as a result of a failure of our facilities or operations or those of third- parties to receive regulatory approval or pass any regulatory agency inspection could significantly impair our ability to develop and commercialize our products. Significant noncompliance could also result in the imposition of monetary penalties or other civil or criminal sanctions and damage our reputation. • Risk of Product Loss. The manufacturing process for our products is extremely susceptible to product loss due to contamination, oxidation, equipment failure or improper installation or operation of equipment or vendor or operator error. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects and other supply disruptions. If microbial, viral or other contaminations are discovered in our products or manufacturing facilities, we may need to close our manufacturing facilities for an extended period of time to investigate and remediate the contaminant. Any adverse developments affecting our manufacturing operations or the operations of our third- party suppliers and manufacturers may result in shipment delays, inventory shortages, lot failures, product withdrawals or recalls or other interruptions in the commercial supply of our products. Furthermore, factors such as geopolitical events, global health outbreaks, **adverse** weather events, labor or raw material shortages **, imposition of tariffs or trade restrictions** and other supply chain disruptions could result in difficulties and delays in manufacturing our products, which could have an adverse impact on our results in operations or result in product shortages. We may also have to take inventory write- offs and incur other charges and expense for products that fail to meet specifications, undertake costly remediation efforts or seek more costly manufacturing alternatives. Such developments could increase our manufacturing costs, cause us to lose revenue or market share as patients and physicians turn to competing therapeutics, diminish our profitability or damage our reputation. In addition, although we have business continuity plans to reduce the potential for manufacturing disruptions or delays and reduce the severity of a disruptive event, there is no guarantee that these plans will be adequate, which could adversely affect our business and operations. Management, personnel and other organizational changes may disrupt our operations, and we may have difficulty retaining personnel or attracting and retaining qualified replacements on a timely basis for the management and other personnel who may leave the Company **, which could disrupt our business and adversely affect our operations** . Changes in management, other personnel and our overall retention rate may disrupt our business, and any such disruption could adversely affect our operations, programs, growth, financial condition or results of operations. New members of management may have different perspectives on programs and opportunities for our business, which may cause us to focus on new opportunities or reduce or change emphasis on our existing programs. Our success is dependent upon our ability to attract and retain qualified management and other personnel in a highly competitive environment. Qualified individuals are in high demand, and we may incur significant costs to attract or retain them. We may face difficulty in attracting and retaining talent for a number of reasons, including management changes, integration related to the Reata **and HI- Bio** ~~acquisition~~ **acquisitions** , the underperformance or discontinuation of one or more marketed, pre- clinical or clinical programs, recruitment by competitors or changes in the overall labor market. In addition, changes in our organizational structure or in our flexible working arrangements could impact employees' productivity and morale as well as our ability to attract, retain and motivate employees. We cannot ensure that we will be able to hire or retain the personnel necessary for our operations or that the loss of any personnel will not have a material impact on our financial condition and results of operations. If we fail to comply with the extensive legal and regulatory requirements affecting the health care industry, we could face increased costs, penalties and a loss of business. Our activities, and the activities of our collaborators, distributors and other third- party providers, are subject to extensive government regulation and oversight in the U. S. and in foreign jurisdictions, and are subject to change and evolving interpretations, which could require us to incur substantial costs associated with compliance or to alter one or more of our business practices. The FDA and comparable foreign agencies directly regulate many of our most critical business activities,

including the conduct of preclinical and clinical studies, product manufacturing, advertising and promotion, product distribution, adverse event reporting, product risk management and our compliance with good practice quality guidelines and regulations. Our interactions with physicians and other health care providers that prescribe or purchase our products are also subject to laws and government regulation designed to prevent fraud and abuse in the sale and use of products and place significant restrictions on the marketing practices of health care companies. Health care companies are facing heightened scrutiny of their relationships with health care providers and have been the target of lawsuits and investigations alleging violations of laws and government regulation, including claims asserting submission of incorrect pricing information, impermissible off- label promotion of pharmaceutical products, payments intended to influence the referral of health care business, submission of false claims for government reimbursement, antitrust violations or violations related to environmental matters. There is also enhanced scrutiny of company- sponsored patient assistance programs, including testing, insurance premium and co- pay assistance programs and donations to third- party charities that provide such assistance. The U. S. government has challenged some of our donations to third- party charities that provide patient assistance. If we, or our vendors or donation recipients, are found to fail to comply with relevant laws, regulations or government guidance in the operation of these or other patient assistance programs, we could be subject to significant fines or penalties. Risks relating to compliance with laws and regulations may be heightened as we continue to expand our global operations and enter new therapeutic areas with different patient populations, which may have different product distribution methods, marketing programs or patient assistance programs from those we currently utilize or support. Conditions and regulations governing the health care industry are subject to change, with possible retroactive effect, including: • new laws, regulations or judicial decisions, or new interpretations of existing laws, regulations or judicial decisions, related to health care availability, pricing or marketing practices, compliance with employment practices, method of delivery, payment for health care products and services, compliance with health information and data privacy and security laws and regulations, tracking and reporting payments and other transfers of value made to physicians and teaching hospitals, extensive anti- bribery and anti- corruption prohibitions, product serialization and labeling requirements and used product take- back requirements; • changes in the FDA and foreign regulatory approval processes **, staffing, resources** or perspectives that may delay or prevent the approval of new products and result in lost market opportunity; • government shutdowns or relocations may result in delays to the review and approval process, slowing the time necessary for new drug candidates to be reviewed and / or approved, which may adversely affect our business; • requirements that provide for increased transparency of clinical trial results and quality data, such as the EMA' s clinical transparency policy, which could impact our ability to protect trade secrets and competitively- sensitive information contained in approval applications or could be misinterpreted leading to reputational damage, misperception or legal action, which could harm our business; and • changes in FDA and foreign regulations that may require additional safety monitoring, labeling changes, restrictions on product distribution or use or other measures after the introduction of our products to market, which could increase our costs of doing business, adversely affect the future permitted uses of approved products or otherwise adversely affect the market for our products. **Additionally, conditions and regulations governing the health care industry in the U. S. are subject to greater risk of change and uncertainty as a result of changes in legislative and regulatory priorities and personnel.** Violations of governmental regulation may be punishable by criminal and civil sanctions, including fines and civil monetary penalties and exclusion from participation in government programs, including Medicare and Medicaid, as well as against executives overseeing our business. We could also be required to repay amounts we received from government payors or pay additional rebates and interest if we are found to have miscalculated the pricing information we submitted to the government. In addition, legal proceedings and investigations are inherently unpredictable, and large judgments or settlements sometimes occur. While we believe that we have appropriate compliance controls, policies and procedures in place to comply with the laws or regulations of the jurisdictions in which we operate, there is a risk that acts committed by our employees, agents, distributors, collaborators or third- party providers might violate such laws or regulations. Whether or not we have complied with the law, an investigation or litigation related to alleged unlawful conduct could increase our expense, damage our reputation, divert management time and attention and adversely affect our business. Our sales and operations are subject to the risks of doing business internationally. We are increasing our presence in international markets, subjecting us to many risks that could adversely affect our business and revenue. There is no guarantee that our efforts and strategies to expand sales in international markets will succeed. Emerging market countries may be especially vulnerable to periods of global and local political, legal, regulatory and financial instability and may have a higher incidence of corruption and fraudulent business practices. Certain countries may require local clinical trial data as part of the drug registration process in addition to global clinical trials, which can add to overall drug development and registration timelines. We may also be required to increase our reliance on third- party agents or distributors and unfamiliar operations and arrangements previously utilized by companies we collaborate with or acquire in emerging markets. Our sales and operations are subject to the risks of doing business internationally, including: • the impact of public health epidemics on the global economy and the delivery of healthcare treatments; • less favorable intellectual property or other applicable laws; • the inability to obtain necessary foreign regulatory approvals of products in a timely manner; • limitations and additional pressures on our ability to obtain and maintain product pricing, reimbursement or receive price increases, including those resulting from governmental or regulatory requirements; • increased cost of goods due to factors such as inflation and supply chain disruptions; • additional complexity in manufacturing **or conducting clinical research** internationally, including materials manufactured **in China or working with CROs** in China; • delays in clinical trials relating to geopolitical instability related to Russia' s invasion of Ukraine and the military conflict in the Middle East; • the inability to successfully complete subsequent or confirmatory clinical trials in countries where our experience is limited; • longer payment and reimbursement cycles and uncertainties regarding the collectability of accounts receivable; • fluctuations in foreign currency exchange rates that may adversely impact our revenue, net income and value of certain of our investments; • the imposition of governmental controls; • diverse data privacy and protection requirements; • increasingly complex standards for complying with foreign laws and regulations that may

differ substantially from country to country and may conflict with corresponding U. S. laws and regulations; • the ~~far- reaching~~ anti- bribery and anti- corruption legislation ~~in~~ **across** the **globe** ~~U. K.~~, including the U. K. Bribery Act 2010, and elsewhere and escalation of investigations and prosecutions pursuant to such laws; • compliance with complex import and export control laws; • changes in tax laws; and • the imposition of tariffs or embargoes and other trade restrictions. In addition, our international operations are subject to regulation under U. S. law. For example, the U. S. FCPA prohibits U. S. companies and their representatives from paying, offering to pay, promising to pay or authorizing the payment of anything of value to any foreign government official, government staff member, political party or political candidate for the purpose of obtaining or retaining business or to otherwise obtain favorable treatment or influence a person working in an official capacity. In many countries, the health care professionals we regularly interact with may meet the FCPA' s definition of a foreign government official. Failure to comply with domestic or foreign laws could result in various adverse consequences, including possible delay in approval or refusal to approve a product, recalls, seizures or withdrawal of an approved product from the market, disruption in the supply or availability of our products or suspension of export or import privileges, the imposition of civil or criminal sanctions, the prosecution of executives overseeing our international operations and damage to our reputation. Any significant impairment of our ability to sell products outside of the U. S. could adversely impact our business and financial results. In addition, while we believe that we have appropriate compliance controls, policies and procedures in place to comply with the FCPA, there is a risk that acts committed by our employees, agents, distributors, collaborators or third- party providers might violate the FCPA and we might be held responsible. If our employees, agents, distributors, collaborators or third- party providers are found to have engaged in such practices, we could suffer severe penalties and may be subject to other liabilities, which could negatively affect our business, operating results and financial condition. We built a large- scale biologics manufacturing facility and are building a gene therapy **, clinical packaging and other** manufacturing facility, which will result in the incurrence of significant investment with no assurance that such investment will be recouped. In order to support our future growth and drug development pipeline, we have expanded our large molecule production capacity by building a large- scale biologics manufacturing facility in Solothurn, Switzerland with no assurance that the additional capacity will be required or this investment will be recouped. Although the Solothurn facility was approved by the FDA for ~~ADUHELM and~~ LEQEMBI, there can be no assurance that the regulatory authorities will approve the Solothurn facility for the manufacturing of other products. Additionally, we are building a new gene therapy **, clinical packaging and other** manufacturing facility in RTP, North Carolina with no assurance that this investment will be fully utilized. If we are unable to fully utilize this gene therapy **, clinical packaging and other** manufacturing facility, charges from excess capacity may occur and would have a negative effect on our financial condition and results of operations. If we are unable to fully utilize our manufacturing facilities, our business may be harmed. Charges resulting from excess capacity may continue to occur and would have a negative effect on our financial condition and results of operations. The illegal distribution and sale by third- parties of counterfeit or unfit versions of our products or stolen products could have a negative impact on our reputation and business. Third- parties might illegally distribute and sell counterfeit or unfit versions of our products, which do not meet our rigorous manufacturing, distribution and testing standards. A patient who receives a counterfeit or unfit drug may be at risk for a number of dangerous health consequences. Our reputation and business could suffer harm as a result of counterfeit or unfit drugs sold under our brand name. Inventory that is stolen from warehouses, plants or while in- transit, and that is subsequently improperly stored and sold through unauthorized channels, could adversely impact patient safety, our reputation and our business. The increasing use of social media platforms ~~and artificial intelligence based software~~ presents new risks and challenges. Social media is increasingly being used to communicate about our products and the diseases our therapies are designed to treat. Social media practices in the biopharmaceutical industry continue to evolve and regulations relating to such use are not always clear and create uncertainty and risk of noncompliance with regulations applicable to our business. For example, patients may use social media channels to comment on the effectiveness of a product or to report an alleged adverse event. When such disclosures occur, there is a risk that we fail to monitor and comply with applicable adverse event reporting obligations or we may not be able to defend the company or the public' s legitimate interests in the face of the political and market pressures generated by social media due to restrictions on what we may say about our products. There is also a risk of inappropriate disclosure of sensitive information or negative or inaccurate posts or comments about us on social media. We may also encounter criticism on social media regarding our company, management, product candidates or products. The immediacy of social media precludes us from having real- time control over postings made regarding us via social media, whether matters of fact or opinion. Our reputation could be damaged by negative publicity or if adverse information concerning us is posted on social media platforms or similar mediums, which we may not be able to reverse. If any of these events were to occur or we otherwise fail to comply with applicable regulations, we could incur liability, face restrictive regulatory actions or incur other harm to our business. ~~Additionally, the use of AI based software is increasingly being used in the biopharmaceutical industry. Use of AI based software may lead to the release of confidential proprietary information which may impact our ability to realize the benefit of our intellectual property.~~ Risks Related to Holding Our Common Stock Our operating results are subject to significant fluctuations. Our quarterly revenue, expense and net income ~~(loss)~~ have fluctuated in the past and are likely to fluctuate significantly in the future due to the risks described in these Risk Factors as well as the timing of charges and expense that we may take. We have recorded, or may be required to record, charges that include: • the cost of restructurings or other initiatives to streamline our operations and reallocate resources; • the costs associated with decisions to terminate research and development programs; • impairments with respect to investments, fixed assets and long- lived assets, including IPR & D and other intangible assets; • inventory write- downs for failed quality specifications, charges for excess capacity, charges for excess or obsolete inventory and charges for inventory write- downs relating to product suspensions, expirations or recalls; • changes in the fair value of contingent consideration or our equity investments; • bad debt expense and increased bad debt reserves; • outcomes of litigation and other legal or administrative proceedings, regulatory matters and tax matters; • payments in connection with acquisitions, divestitures

and other business development activities and under license and collaboration agreements; • failure to meet certain contractual commitments; and • the impact of public health epidemics, on employees, the global economy and the delivery of healthcare treatments. Our revenue and certain assets and liabilities are also subject to foreign currency exchange rate fluctuations due to the global nature of our operations. Our efforts to mitigate the impact of fluctuating currency exchange rates may not be successful. As a result, currency fluctuations among our reporting currency, the U. S. dollar, and other currencies in which we do business will affect our operating results, often in unpredictable ways. Our net income may also fluctuate due to the impact of charges we may be required to take with respect to foreign currency hedge transactions. In particular, we may incur higher than expected charges from early termination of a hedge relationship. Our operating results during any one period do not necessarily suggest the anticipated results of future periods. Our investments in properties may not be fully realized. We own or lease real estate primarily consisting of buildings that contain research laboratories, office space and manufacturing operations. We may decide to consolidate or co- locate certain aspects of our business operations or dispose of one or more of our properties, some of which may be located in markets that are experiencing high vacancy rates and decreasing property values. If we determine that the fair value of any of our owned properties is lower than their book value, we may not realize the full investment in these properties and incur significant impairment charges or additional depreciation when the expected useful lives of certain assets have been shortened due to the anticipated closing of facilities. If we decide to fully or partially vacate a property, we may incur significant cost, including facility closing costs, employee separation and retention expense, lease termination fees, rent expense in excess of sublease income and impairment of leasehold improvements and accelerated depreciation of assets. Any of these events may have an adverse impact on our results of operations. We may not be able to access the capital and credit markets on **terms that are** favorable **to us** ~~terms,which could increase our financing costs~~ .We may seek access to the capital and credit markets to supplement our existing funds and cash generated from operations for working capital,capital expenditure and debt service requirements and other business initiatives.The capital and credit markets are experiencing,and have in the past experienced,extreme volatility and disruption,which leads to uncertainty and liquidity issues for both borrowers and investors.In the event of adverse market conditions,we may be unable to obtain capital or credit market financing on favorable terms which could significantly increase our financing costs.Changes in credit ratings issued by nationally recognized credit rating agencies could also adversely affect our cost of financing and the market price of our securities.Our indebtedness could adversely affect our business and limit our ability to plan for or respond to changes in our business.Our indebtedness,together with our significant contingent liabilities,including milestone and royalty payment obligations,could have important consequences to our business;for example,such obligations could:• increase our vulnerability to general adverse economic and industry conditions;• limit our ability to access capital markets and incur additional debt in the future;• require us to dedicate a substantial portion of our cash flow from operations to payments on our indebtedness,thereby reducing the availability of our cash flow for other purposes,including business development,research and development and mergers and acquisitions;and • limit our flexibility in planning for,or reacting to,changes in our business and the industry in which we operate,thereby placing us at a disadvantage compared to our competitors that have **less debt.** Our investment portfolio is subject to market, interest and credit risk that may reduce its value. We maintain a portfolio of marketable securities for investment of our cash as well as investments in equity securities of certain biotechnology companies. Changes in the value of our investment portfolio ~~could~~ **has in the past and may in the future** adversely affect our earnings. The value of our investments may decline due to, among other things, increases in interest rates, downgrades of the bonds and other securities in our portfolio, negative company- specific news, biotechnology market sentiment, instability in the global financial markets that reduces the liquidity of securities in our portfolio, declines in the value of collateral underlying the securities in our portfolio and other factors. Each of these events may cause us to record charges to reduce the carrying value of our investment portfolio or sell investments for less than our acquisition cost. Although we attempt to mitigate these risks through diversification of our investments and continuous monitoring of our portfolio' s overall risk profile, the value of our investments may nevertheless decline. There can be no assurance that we will ~~continue to~~ repurchase shares or that we will repurchase shares at favorable prices **, which may negatively affect our stock price** . From time to time our Board of Directors authorizes share repurchase programs. The amount and timing of share repurchases are subject to capital availability and our determination that share repurchases are in the best interest of our shareholders and are in compliance with all respective laws and our applicable agreements. Our ability to repurchase shares will depend upon, among other factors, our cash balances and potential future capital requirements for strategic transactions, our results of operations, our financial condition and other factors beyond our control that we may deem relevant. Additionally, the recently enacted IRA includes an excise tax on share repurchases, which will increase the cost of share repurchases. A reduction in repurchases under, or the completion of, our share repurchase programs could have a negative effect on our stock price. We can provide no assurance that we will repurchase shares at favorable prices, if at all. We may not be able to access..... our competitors that have less debt. Some of our collaboration agreements contain change in control provisions that may discourage a third- party from attempting to acquire us. Some of our collaboration agreements include change in control provisions that could reduce the potential acquisition price an acquirer is willing to pay or discourage a takeover attempt that could be viewed as beneficial to shareholders. Upon a change in control, some of these provisions could trigger reduced milestone, profit or royalty payments to us or give our collaboration partner rights to terminate our collaboration agreement, acquire operational control or force the purchase or sale of the programs that are the subject of the collaboration. General Risk Factors Our effective tax rate fluctuates, and we may incur obligations in tax jurisdictions in excess of accrued amounts **in our financial statements** . As a global biopharmaceutical company, we are subject to taxation in numerous countries, states and other jurisdictions. As a result, our effective tax rate is derived from a combination of applicable tax rates, including withholding taxes, in the various places that we operate. In preparing our financial statements, we estimate the amount of tax that will become payable in each of such places. Our effective tax rate may be different than experienced in the past or our current expectations due to many factors, including changes in the mix of our

profitability from country to country, the results of examinations and audits of our tax filings, adjustments to the value of our uncertain tax positions, interpretations by tax authorities or other bodies with jurisdiction, the result of tax cases, changes in accounting for income taxes and changes in tax laws **, especially in the U. S. and Switzerland,** and regulations **(including the Global Tax Deal Executive Order issued on January 20, 2025)** either prospectively or retrospectively and the effects of the ~~integration~~ **integrations** of Reata **and HI- Bio** . Our inability to secure or sustain acceptable arrangements with tax authorities and future changes in the tax laws, among other things, may result in tax obligations in excess of amounts accrued in our financial statements. The enactment of some or all of the recommendations set forth or that may be forthcoming in the OECD' s project on " Base Erosion and Profit Shifting " by tax authorities and economic blocs in the countries in which we operate, could unfavorably impact our effective tax rate. These initiatives focus on common international principles for the entitlement to taxation of global corporate profits and minimum global tax rates. Many countries have or are in the process of enacting legislation intended to implement the OECD GloBE Model Rules effective on January 1, 2024. The impact on the Company will depend on the timing of implementation, the exact nature of each country' s GloBE legislation, guidance and regulations **(including the Global Tax Deal Executive Order issued on January 20, 2025)** thereon and their application by tax authorities either prospectively or retrospectively. Our business involves environmental **and operational** risks, which include the cost of compliance and the risk of contamination or injury. Our business and the business of several of our strategic partners involve the controlled use of hazardous materials, chemicals, biologics and radioactive compounds **which make us subject to changing and evolving rules and interpretations, which could require us to incur substantial costs associated with compliance or to alter one or more of our business practices** . Although we believe that our safety procedures for handling and disposing of such materials comply with state, federal and foreign standards, there will always be the risk of accidental contamination or injury. If we were to become liable for an accident, or if we were to suffer an extended facility shutdown, we could incur significant costs, damages and penalties that could harm our business. Manufacturing of our products and product candidates also requires permits from government agencies for water supply and wastewater discharge. If we do not obtain appropriate permits, including permits for sufficient quantities of water and wastewater, we could incur significant costs and limits on our manufacturing volumes that could harm our business. Additionally, regulators ~~are considering~~ **have passed** new environmental disclosure rules. For example, the ~~SEC~~ **E. U., California** and **certain other countries we do business in have promulgated new climate disclosure rules that will generally require additional disclosure. Additionally,** other regulators are considering environmental disclosure rules **. These** ~~and California enacted~~ new **rules collectively** ~~environmental disclosure laws in October 2023 that~~ will **impose** ~~generally require~~ additional disclosure **requirements relating to** ~~and reporting by 2026. The new California laws, the Climate Corporate Data Accountability Act and the Climate- Related Financial Risk Act, each impose additional~~ climate- related **risks and emissions disclosures** ~~reporting requirements on large companies conducting business in the state of California~~ . We expect to be subject to these new laws **and regulations if or when they go into effect** , which **would** impose extensive reporting obligations about greenhouse gas emissions and climate- related financial risks. These recently enacted and proposed regulations may require us to incur compliance and disclosure costs and **will likely** require **substantial** management attention.