Risk Factors Comparison 2024-02-14 to 2023-02-09 Form: 10-K

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This report and other documents we file with the SEC contain forward- looking statements that are based on current expectations, estimates, forecasts and projections about us, our future performance, our business, our beliefs and our management' s assumptions. These statements are not guarantees of future performance and involve certain risks, uncertainties and assumptions that are difficult to predict. You should carefully consider the risks and uncertainties our business faces. The risks described below are not the only ones we face. Our business is also subject to the risks that affect many other companies, such as employment relations, general economic conditions, geopolitical events and international operations. Further, additional risks not currently known to us or that we currently believe are immaterial may in the future materially and adversely affect our business, operations, liquidity and stock price. SUMMARY Risks Related to Economic Conditions and Operating a Global Business..... in emerging markets. Risks Related to Government Regulations and Third- Party Policies • Our sales depend on coverage and reimbursement from government and commercial third- party payers, and pricing and reimbursement pressures have affected, and are likely to continue to affect, our profitability. • Guidelines and recommendations published by various organizations can reduce the use of our products. • ~~The~~ **We could be subject to additional tax liabilities, including from an adverse outcome in our ongoing tax dispute with the IRS and other tax examinations, enactment of the OECD minimum corporate tax rate agreement and the** adoption and interpretation of new tax legislation ~~or exposure to~~ **, and we anticipate** additional tax liabilities **from certain provisions of the 2017 Tax Act that will go into effect in 2026; such tax liabilities** could **adversely** affect our profitability **and results of operations** . • Our business may be affected by litigation and government investigations. Risks Related to Economic Conditions and Operating a Global Business **,Including During the COVID- 19 Pandemic** • **The COVID- 19 pandemic** ~~Our efforts to collaborate with or acquire other companies,products,or technology~~ ,and **the public and governmental effort** to ~~integrate~~ **mitigate against** the ~~operations~~ **spread** of ~~companies or~~ **the disease,have had,and are expected** to **continue to** ~~support the products or technology we~~ have ~~acquired~~ , **an adverse effect** ~~may not be successful~~ ,and may ~~result in unanticipated costs~~ **have a material adverse effect** , ~~delays~~ **on** ~~or~~ **our** ~~failures to realize the benefits~~ **clinical trials,operations,manufacturing,supply chains,distribution systems,product development,product sales,business and results** of **operations** ~~the transactions.• We may not be able to access the capital and credit markets on terms that are favorable to us,or at all~~ .• A breakdown of our information technology systems,cyberattack or information security breach could ~~significantly~~ compromise the confidentiality,integrity and availability of our information technology systems,network- connected control systems and / or our data,interrupt the operation of our business and / or affect our reputation.• Our sales and operations are subject to the risks of doing business internationally,including in emerging markets. **Risks Related to** Competition • Our products face substantial competition and our product candidates are also likely to face substantial competition. • Our intellectual property positions may be challenged, invalidated or circumvented, or we may fail to prevail in current and future intellectual property litigation. • We currently face competition from biosimilars and generics and expect to face increasing competition from biosimilars and generics in the future. • Concentration of sales at certain of our wholesaler distributors **,** and consolidation of private payers **, such as insurers, and PBMs has negatively affected, and** may **continue to** negatively affect **,** our business. Risks Related to Research and Development • We may not be able to develop commercial products despite significant investments in R & D. • We must conduct clinical trials in humans before we commercialize and sell any of our product candidates or existing products for new indications. • Our current products and products in development cannot be sold without regulatory approval. • Some of our products are used with drug delivery or companion diagnostic devices that have their own regulatory, manufacturing and other risks. • Some of our pharmaceutical pipeline and our commercial product sales rely on collaborations with third parties, which may adversely affect the development and sales of our products ~~. • Our efforts to collaborate with or acquire other companies, products, or technology, and to integrate the operations of companies or to support the products or technology we have acquired, may not be successful, and may result in unanticipated costs, delays or failures to realize the benefits of the transactions~~ . Risks Related to Operations • We perform a substantial majority of our commercial manufacturing activities at our facility in the U. S. territory of Puerto Rico and a substantial majority of our clinical manufacturing activities at our facility in Thousand Oaks, California; significant disruptions or production failures at these facilities could significantly impair our ability to supply our products or continue our clinical trials. • We rely on third- party suppliers for certain of our raw materials, medical devices and components. • Manufacturing difficulties, disruptions or delays could limit supply of our products and limit our product sales. • Our business and operations may be negatively affected by the failure, or perceived failure, of achieving our environmental, social and governance objectives. • The effects of global climate change and related natural disasters could negatively affect our business and operations. General Risk Factors • Global economic conditions may negatively affect us and may magnify certain risks that affect our business. • Our stock price is volatile. ~~•~~ **business and results of operations.** RISKS RELATED TO GOVERNMENT REGULATIONS AND THIRD- PARTY POLICIES Sales of our products depend on the availability and extent of coverage and reimbursement from third- party payers,including government healthcare programs and private insurance plans.Governments and private payers continue to pursue initiatives to manage drug utilization and contain costs.Further,pressures on healthcare budgets from the **pandemic,the** economic downturn and inflation continue and are likely to increase across the markets we serve.Payers are increasingly focused on costs,which have resulted,and are expected to continue to result,in lower reimbursement rates for our products or narrower populations for which payers will reimburse.Continued intense public scrutiny of the price of drugs and other healthcare costs,together with payer dynamics,have limited,and are likely to continue to limit,our

ability to set or adjust the price of our products based on their value,which can have a material adverse effect on our business.In the United States,particularly over the past few years,a number of legislative and regulatory proposals have been introduced and / or signed into law that attempt to lower drug prices.These include **legislation promulgated by** the IRA ~~legislation~~ that enables the U.S.government to set prices for certain drugs in Medicare,redesigns Medicare Part D benefits to shift a greater portion of the costs to manufacturers and enables the U.S.government to impose penalties if drug prices are increased at a rate faster than inflation.Additional proposals focused on drug pricing continue to be debated,and additional executive orders focused on drug pricing and competition are likely to be adopted and implemented in some form.Government actions or ballot initiatives at the state level also represent a highly active area of policymaking and experimentation,including pursuit of proposals that limit drug reimbursement under state run Medicaid programs based on reference prices or permitting importation of drugs from Canada.Such state policies may also eventually be adopted at the federal level.We are unable to predict which or how many policy,regulatory,administrative or legislative changes may ultimately be,or effectively estimate the consequences to our business if,enacted and implemented.However,to the extent that payer actions further decrease or modify the coverage or reimbursement available for our products,require that we pay increased rebates or shift other costs to us,limit or affect our decisions regarding the pricing of or otherwise reduce the use of our products,such actions could have a material adverse effect on our business and results of operations.— Changing U.S.federal coverage and reimbursement policies and practices have affected and are likely to continue to affect access to,pricing of and sales of our products A substantial portion of our U.S.business relies on reimbursement from federal government healthcare programs and commercial insurance plans regulated by federal and state governments.See Part I,Item 1.Business — Reimbursement.Our business has been and will continue to be affected by legislative actions changing U.S.federal reimbursement policy.For example,in **August** 2022,the IRA was enacted and includes provisions requiring that **:(1)** beginning in 2026,mandatory price setting be introduced in Medicare for certain drugs paid for under Parts B and D,whereby manufacturers must accept a price established by the government or face penalties on all U.S.sales (starting with ~~ten~~ **10** drugs in 2026,adding 15 in 2027 and 2028,and adding 20 in 2029 and subsequent years such that by 2031 approximately 100 drugs could be subject to such set prices) **;(2)** ~~.The Medicare price setting process began on August 29,2023 when CMS announced the first ten drugs for Medicare price setting,which includes ENBREL.Our wholly owned subsidiary,Immunex Corporation,which holds the rights to the ENBREL BLA,entered into an agreement with the U.S.government to participate in the price setting process and submitted the required data to CMS for ENBREL,including certain price,cost and patent data.The Medicare price setting process will conclude by August 1,2024,and by September 1,2024,CMS will publish prices that will be applicable to these ten drugs in the Medicare program beginning January 1,2026.Also under the IRA,~~ starting **in** ~~on January 1,~~ 2024,Medicare Part D ~~was~~ **be** redesigned to cap beneficiary out- of- pocket costs and,beginning January 1,2025,Federal reinsurance ~~will~~ be reduced in the catastrophic phase (resulting in a shift and increase of such costs to Part D plans and manufacturers,including by requiring manufacturer discounts on certain drugs) ~~.Further~~ **;and (3) beginning October 1** , **2022,manufacturers will owe** ~~the IRA created a mechanism for CMS to collect~~ rebates ~~from manufacturers~~ **on drugs reimbursed under Medicare Part D** if price increases outpace inflation ~~.Rebate obligations began to accrue October 1~~ , ~~2022 for Medicare Part D~~ and **beginning** January 1,2023 ~~for~~ **,will owe rebates on drugs reimbursed under** Medicare Part B ~~,but CMS has not yet issued invoices and has some discretion as to when it must bill manufacturers.We expect that several of our products will be subject to these inflation rebates,and several of our products have been on lists that are issued and updated on a quarterly basis by CMS under a related program under which Medicare beneficiaries are charged reduced coinsurance~~ if price increases ~~exceed~~ **outpace** inflation.The IRA' s drug pricing controls and Medicare redesign ~~are~~ **is** likely to have a material adverse effect on our sales **(particularly for our products that are more substantially reliant on Medicare reimbursement)** ,our business and our results of operations **.However** , ~~and such~~ **as the degree of** impact **from this legislation on our business** ~~is expected to increase through the end of the decade and will depend~~ **depends** on ~~factors including~~ **a number of implementation decisions,** the extent of ~~our portfolio~~ **the IRA** ' s **impact on** ~~exposure to Medicare reimbursement,the rate of inflation over time,the number of our products selected for mandatory price setting and the timing of market entry of generic or~~ **our** ~~biosimilar competition~~ **sales and,in turn,our business remains unclear** .Further,following the passage of the IRA,the environment remains dynamic ~~and U.S.policymakers continue to demonstrate interest in health care and drug pricing changes.For example~~ , ~~CMS issued a proposed Medicaid Drug Rebate Program rule that,if finalized,would require manufacturers to aggregate or " stack " all rebates,discounts,or other price concessions made to separate,unrelated entities across the pharmaceutical supply chain on a given unit of product to determine the " Best Price," a metric that is used to determine Medicaid rebates and 340B statutory rates.In early 2023,the HHS selected new healthcare payment and delivery models for testing,in response to an~~ **and in** October 2022 **,the Administration issued an** Executive Order on Lowering Prescription Drug Costs for Americans ~~,including the Accelerating Clinical Evidence Model,which could introduce new payment methods~~ that **calls** ~~reduce reimbursement~~ for **the HHS to issue a report within 90 days on Innovation Center models that would lower** ~~drugs~~ **drug** ~~approved under accelerated approval~~ **costs and promote access to innovative drug therapies for Medicare and Medicaid beneficiaries** . ~~That~~ **This** Executive Order ~~followed~~ **follows** a 2021 Executive Order **that included a timeline** designed to increase competition in the healthcare sector,including by calling for the FDA to develop prescription drug importation programs and the FTC to apply greater scrutiny of anticompetitive activity ~~and .~~ ~~responses~~ **Responses** to ~~which~~ **this order,** ~~include~~ **including by** ~~actions from~~ the HHS ~~(~~ **,** which released a report with drug pricing proposals that seek to promote competition ~~)~~ **,** and ~~from~~ **by** the USPTO ~~(~~ **,** which has taken steps to strengthen coordination with the FDA to address impediments to generic drug and biosimilar competition ~~)~~ . ~~Other~~ CMS policy changes and demonstration projects to test new care,delivery and payment models can also significantly affect how drugs,including our products,are covered and reimbursed.In **September** ~~the fourth quarter of~~ 2021,HHS released a plan to address drug pricing that included potential future mandatory models that link payment for prescription drugs and biologics to certain factors,including the overall cost of care. ~~In March 2023,the Administration released its budget plan for fiscal year 2024 that included proposals~~

to expand the number of drugs subject to mandatory Medicare price setting under the IRA,imposing such price setting activity earlier,and extending to commercial health insurance the requirement that drug manufacturers pay rebates if price increases outpace inflation.While those proposed expansions of the IRA' s drug pricing controls have not been enacted,the proposals demonstrate that this area continues to be a focus of the Administration. We also face risks related to the reporting of pricing data that affects reimbursement of and discounts provided for our products.U.S.government price reporting regulations are complex and may require biopharmaceutical manufacturers to update certain previously submitted data.If our submitted pricing data are incorrect,we may become subject to substantial fines and penalties or other government enforcement actions,which could have a material adverse effect on our business and results of operations.In addition,as a result of restating previously reported price data,we may be required to pay additional rebates and provide additional discounts.— Changing reimbursement and pricing actions in various states have negatively affected and may continue to negatively affect access to and have affected and may continue to affect sales of our products At the state level,government actions or ballot initiatives can also affect how our products are covered and reimbursed and / or create additional pressure on our pricing decisions.Existing and proposed state pricing laws have added complexity to the pricing of drugs and may already be affecting industry pricing decisions.A number of states have adopted,and many other states are considering,drug importation programs and **or** other pricing actions,including proposals designed to require biopharmaceutical manufacturers to report to the state proprietary pricing information or provide advance notice of certain price increases. **For example,a California law requires biopharmaceutical manufacturers to notify health insurers and government health plans at least 60 days before scheduled prescription drug price increases that exceed certain thresholds.Similar laws exist in Oregon and Washington.Additional proposals directed at Medicaid seek to penalize manufacturers for pricing drugs above a certain threshold or limit spending on biopharmaceutical products.** States are also enacting laws referencing the IRA and seeking to regulate **change the way** the **they pay for** 340B Drug Pricing Program.For example,following the passage of the IRA,bills have been proposed in multiple states that would apply the drug **drugs** price caps set **for patients covered** by HHS for Medicare to drug prices in an individual state **programs** . **New York has** For Medicaid patients,states have established a Medicaid drug spending cap **,** (New York) and **Massachusetts** implemented a new review and supplemental rebate negotiation process (Massachusetts) . Seven **Six** states (Colorado,Maine,New Hampshire,Maryland ,Minnesota ,Oregon and Washington) have enacted laws that establish **Prescription Drug Affordability Boards (** PDABs **)** to **study drug prices and** identify drugs that pose affordability challenges,and four such **in three** states **(Colorado,Maryland and Washington)** include authority for the state PDAB to set upper payment limits on certain drugs for in **–** state **regulated plans** patients,payers and providers . **Other** So far in 2024,no fewer than 11 states **may consider implementing similar policies and** have pending PDAB legislation.States with enacted PDAB laws **.Additionally** are in various phases of implementation , with Colorado ' s PDAB being the furthest along.In August 2023 , **Florida,Maine,New Hampshire,New Mexico** the Colorado PDAB announced the first five drugs to undergo an **and Vermont** affordability review,one of which is ENBREL.If the PDAB process determines that ENBREL is unaffordable,ENBREL could be subject to an upper payment limit as early as Q4 2024.Louisiana and Arkansas have enacted laws with mandates on manufacturers participating in 340B ,and **several other** thus far in 2024,no fewer than 15 states have **proposed** similar legislation pending.These bills vary , but include provisions on restricting a manufacturer' s ability to **direct implement importation of** drugs in 340B channels,recognizing 340B contract pharmacies and a prohibition on requiring the inclusion of 340B claims modifiers.Further,in Genesis Health Care,Inc.v.Becerra,the U.S.District Court for the District of South Carolina issued an order in November 2023 that enjoins the Health Resources and Services Administration from **Canada** enforcing its more restrictive interpretation of what is considered a patient under the 340B program,to the potential benefit of healthcare systems seeking to expand the application of 340B discounts . **The** Additionally,on January 5,2024,the FDA authorized **has met with representatives from Colorado,** Florida to move forward with its importation program proposal.Colorado ,Maine **and** ,New Hampshire,New Mexico **to discuss those** ,Texas and Vermont have also enacted state **states ' proposed** importation laws **programs** ,and some have submitted **the FDA may be working towards approving such** plans for approval to the FDA .Other states could adopt similar approaches or could pursue different policy changes in a continuing effort to reduce their costs.Ultimately,as with U.S.federal government actions,existing or future state government actions or ballot initiatives may also have a material adverse effect on our product sales,business and results of operations.— U.S.commercial payer actions have affected and may continue to affect access to and sales of our products Payers,including healthcare insurers,PBMs,integrated healthcare delivery systems (vertically- integrated organizations built from consolidations of healthcare insurers and PBMs) and group purchasing organizations,increasingly seek ways to reduce their costs.With increasing frequency,payers are adopting benefit plan changes that shift a greater proportion of drug costs to patients.Such measures include more limited benefit plan designs,high deductible plans,higher patient co- pay or coinsurance obligations and more significant limitations on patients' use of manufacturer commercial co- pay assistance programs.Further,government regulation of payers may affect these trends.For example,CMS finalized a policy for plan years starting on or after January 1,2021 that has caused commercial payers to more widely adopt co- pay accumulator adjustment programs.While the U.S.District Court for the District of Columbia struck down this policy in September 2023 and further clarified in December 2023 that its ruling had the effect of reinstating the co- pay accumulator adjustment policy from 2020,CMS and HHS have signaled that they do not intend to enforce certain restrictions from the 2020 policy that would reduce the adoption of co- pay accumulator adjustment programs.Payers,including PBMs,have sought,and continue to seek,price discounts or rebates in connection with the placement of our products on their formularies or those they manage,and to also impose restrictions on access to or usage of our products (such as Step Therapy),require that patients receive the payer' s prior authorization before covering the product,and / or chosen to exclude certain indications for which our products are approved.For example,some payers require physicians to demonstrate or document that the patients for whom Repatha has been prescribed meet their utilization criteria,and these requirements have served to limit and may continue to limit patient access to Repatha treatment.In

an effort to reduce barriers to access,we reduced the net price of Repatha by providing greater discounts and rebates to payers (including PBMs that administer Medicare Part D prescription drug plans),and in response to a very high percentage of Medicare patients abandoning their Repatha prescriptions rather than paying their co- pay,we introduced a set of new National Drug Codes to make Repatha available at a lower list price.However,affordability of patient out- of- pocket co- pay cost has limited and may continue to limit patient use.Further,despite these net and list price reductions,some payers have restricted,and may continue to restrict,patient access and may seek further discounts or rebates or take other actions,such as changing formulary coverage for Repatha,that could reduce our sales of Repatha.These factors have limited,and may continue to limit,patient affordability and use,negatively affecting Repatha sales.Further,significant consolidation in the health insurance industry has resulted in a few large insurers and PBMs,which places greater pressure on pricing and usage negotiations with biopharmaceutical manufacturers,significantly increasing discount and rebate requirements and limiting patient access and usage.For example,in the United States,as of the beginning of ~~2024~~ **2023** ,the top five integrated health plans and PBMs controlled about 92 % of all pharmacy prescriptions.This high degree of consolidation among insurers ~~,~~ **and** PBMs and other payers,including **through** integrated healthcare delivery systems and / or with specialty or mail- order pharmacies and pharmacy retailers,has increased the negotiating leverage such entities have over us and other biopharmaceutical manufacturers and has resulted in greater price discounts,rebates and service fees realized by those payers from our business.Each of CVS,Express Scripts and United Health Group (among the top five integrated health plans and PBMs), **each** have Rebate Management Organizations that further increase their leverage to negotiate deeper discounts.Ultimately,additional discounts,rebates,fees,coverage changes,plan changes,restrictions or exclusions imposed by these commercial payers could have a material adverse effect on our product sales,business and results of operations.Policy reforms advanced by Congress or the Administration that refine the role of PBMs in the U.S.marketplace could have downstream implications or consequences for our business and how we interact with these entities.For example, ~~in~~ **on** June **7,** 2022,the FTC launched an inquiry into the business practices of PBMs **,** and ~~subsequently expanded the investigation to the three~~ -- **the** ~~rebate management organizations owned by the three largest PBMs.In addition,multiple Congressional Committees are investigating PBM practices and have also proposed legislation that could increase transparency and reporting of these practices and / or impact rebates and service fees.The~~ results of such inquiry could have an effect on manufacturer interactions with PBMs,resulting in changes to access for certain medicines.See **our —** Concentration of sales at certain of our wholesaler distributors ~~,~~ and consolidation of private payers ~~,such as insurers,and PBMs has negatively affected,and~~ may ~~continue to~~ negatively affect ~~,~~ our business.Our business is also affected by policies implemented by private healthcare entities that process Medicare claims,including Medicare Administrative Contractors.For example,in the second quarter of 2022,several Medicare Administrative Contractors issued notice **,in contravention of TEZSPIRE' s FDA approved labeling,** that TEZSPIRE would be added to their " self- administered drug " exclusion lists.Although the Medicare Administrative Contractors subsequently removed TEZSPIRE from their exclusion lists,these exclusions,if reintroduced and / or implemented,would result in Medicare beneficiaries with severe asthma losing access to TEZSPIRE coverage under Medicare Part B and potentially also under Medicare Advantage.— Government and commercial payer actions outside the United States have affected and will continue to affect access to and sales of our products Outside the United States,we expect countries will also continue to take actions to reduce their drug expenditures ~~and to reduce intellectual property protections~~ .See Part I,Item 1.Business — Reimbursement.Pressures to decrease drug expenditures may **further** intensify as ~~governments take actions to address budgets strained by high inflation,expenditures to respond to~~ the COVID- 19 pandemic **has strained government budgets** and ~~weak~~ **as** economic conditions **continue to worsen in certain regions** ,including in Europe where **high inflation and** the ~~effects of~~ **energy crisis relating to** the Russia – Ukraine conflict ~~have~~ **are** ~~challenged~~ **challenging** the economies in that region ~~.Further,the EU is currently undergoing a review and possible revision of its pharmaceutical legislation that,while full implementation is not expected before 2027,could lead to proposals that will reduce intellectual property protection for new products (including potentially shortening the duration of regulatory data exclusivity and orphan drug exclusivity protections),as well as change the reimbursement and regulatory landscape~~ .International reference pricing has been widely used by many countries outside the United States to control costs based on an external benchmark of a product' s price in other countries.International reference pricing policies can change quickly and frequently and may not reflect differences in the burden of disease,indications,market structures or affordability differences across countries or regions.Other expenditure control practices,including but not limited to the use of revenue clawbacks,rebates and **percentage** caps on ~~product sales~~ **price increases** ,are used in various foreign jurisdictions as well.In addition,countries may refuse to reimburse or may restrict the reimbursed population for a product when their national health technology assessments do not consider a medicine to demonstrate sufficient clinical benefit beyond existing therapies or to meet certain cost effectiveness thresholds.For example,despite the EMA' s approval of Repatha for the treatment of patients with established atherosclerotic disease,prior to 2020,the reimbursement of Repatha in France was limited to a narrower patient population (such as those with homozygous familial hypercholesterolemia (HoFH)) following a national health technology assessment.Many countries decide on reimbursement between potentially competing products through national or regional tenders that often result in one product receiving most or all of the sales in that country or region.Failure to obtain coverage and reimbursement for our products,a deterioration in their existing coverage and reimbursement or a decline in the timeliness or certainty of payment by payers to ~~hospitals~~ **physicians** and other providers has negatively affected,and may further negatively affect,the ability or willingness of healthcare providers to prescribe our products for their patients and otherwise negatively affect the use of our products or the prices we realize for them.Such changes have had,and could in the future have,a material adverse effect on our product sales,business and results of operations.Government agencies promulgate regulations and guidelines directly applicable to us and to our products.Professional societies,practice management groups,insurance carriers,physicians' groups,private health and science foundations and organizations involved in various diseases also publish guidelines and recommendations to healthcare providers,administrators and payers,as well as patient

communities.Recommendations by government agencies or other groups and organizations may relate to such matters as usage,dosage,route of administration and use of related therapies.In addition,a growing number of organizations are providing assessments of the value and pricing of biopharmaceutical products,and even organizations whose guidelines have historically been focused on clinical matters have begun to incorporate analyses of the cost effectiveness of various treatments into their treatment guidelines and recommendations.Value assessments may come from private organizations that publish their findings and offer recommendations relating to the products' reimbursement by government and private payers.Some companies and payers have announced pricing and payment decisions based in part on the assessments of private organizations.In addition,government health technology assessment organizations in many countries make reimbursement recommendations to payers in their jurisdictions based on the clinical effectiveness,cost- effectiveness and service effects of new,emerging and existing medicines and treatments.Such health technology assessment organizations have recommended,and may in the future recommend,reimbursement for certain of our products for a narrower indication than was approved by applicable regulatory agencies or may recommend against reimbursement entirely.See Our sales depend on coverage and reimbursement from government and commercial third- party payers,and pricing and reimbursement pressures have affected,and are likely to continue to affect,our profitability. ~~The EU has adopted regulations,effective beginning in January 2025,that are intended to increase cooperation among EU member states and harmonize various procedures and standards at the EU level in assessing health technologies and in support of joint clinical assessments of health technologies and medicines.These and other such~~ **Such** recommendations or guidelines may affect our reputation,and any recommendations or guidelines that result in decreased use,dosage or reimbursement of our products could have a material adverse effect on our product sales,business and results of operations.In addition,the perception by the investment community or stockholders that such recommendations or guidelines will result in decreased use and dosage of our products could adversely affect the market price of our common stock.We are subject to income and other taxes in the United States and other jurisdictions in which we do business.As a result,our provision for income taxes is derived from a combination of applicable tax rates in the various places we operate.Significant judgment is required for determining our provision for income tax.One or more of our legal entities file income tax returns in the U.S.federal jurisdiction,various U.S.state jurisdictions and **certain** foreign jurisdictions.Our income tax returns are routinely examined by tax authorities in those jurisdictions.Significant disputes can and have arisen with tax authorities involving issues regarding the timing and amount of deductions,the use of tax credits and allocations of income and expenses among various tax jurisdictions because of differing interpretations of tax laws,regulations and relevant facts,and such tax authorities (including the IRS) are becoming more aggressive in their audits and are particularly focused on such matters.In 2017,we received an RAR and a modified RAR from the IRS for the years 2010 – 2012,proposing significant adjustments that primarily relate to the allocation of profits between certain of our entities in the United States and the U.S.territory of Puerto Rico.We disagreed with the proposed adjustments and calculations and pursued resolution with the IRS administrative appeals office but were unable to reach resolution.In July 2021,we filed a petition in the U.S.Tax Court to contest two duplicate Statutory Notices of Deficiency (Notices) for the years 2010 – 2012 that we received in May and July 2021 which seek to increase our U.S.taxable income for the years 2010 – 2012.In 2020,we received an RAR and a modified RAR from the IRS for the years 2013 – 2015,also proposing significant adjustments that primarily relate to the allocation of profits between certain of our entities in the United States and the U.S.territory of Puerto Rico similar to those proposed for the years 2010 – 2012.We disagreed with the proposed adjustments and calculations and pursued resolution with the IRS appeals office but were unable to reach resolution.In July 2022,we filed a petition in the U.S.Tax Court to contest a Notice for the years 2013 – 2015 that we previously reported receiving in April 2022 that seeks to increase our U.S.taxable income for the years 2013 – 2015 and asserts penalties.We firmly believe that the IRS positions set forth in the 2010 – 2012 and 2013 – 2015 Notices are without merit.We are contesting the 2010 – 2012 and 2013 – 2015 Notices through the judicial process.The cases were consolidated on December 19,2022.We are currently also under examination by the IRS for the years 2016 – 2018 with respect to issues similar to those for the 2010 through 2015 period.In addition,we are under examination by a number of state and foreign tax jurisdictions.Final resolution of these complex tax matters is not likely within the next 12 months.We continue to believe our accrual for income tax liabilities is appropriate based on past experience,interpretations of tax law,application of the tax law to our facts and judgments about potential actions by tax authorities;however,due to the complexity of the provision for income taxes and uncertain resolution of these matters,the ultimate outcome of any tax matters may result in payments substantially greater than amounts accrued and could have a material adverse effect on the results of our operations.See Part II,Item 7.Management' s Discussion and Analysis of Financial Condition and Results of Operations — Results of Operations,Income Taxes,and Part IV — Note ~~7~~ **6** ,Income taxes,to the Consolidated Financial Statements.Our provision for income taxes and results of operations in the future could be adversely affected by changes to our operating structure,changes in the mix of income and expenses in countries with differing tax rates,changes in the valuation of deferred tax assets and liabilities and changes in applicable tax laws,regulations or administrative interpretations thereof.The 2017 Tax Act is complex and a large volume of regulations and guidance has been issued and could be subject to different interpretations.We could face audit challenges to our application of the 2017 Tax Act. ~~As previously reported~~ **In addition,there are several upcoming provisions in the 2017 Tax Act,including increases in the tax rates on foreign earnings and export income scheduled to take effect at the end of 2025,that could result in an increase in our effective tax rate.The Administration and Congress continue to discuss changes to existing tax law that could substantially increase the taxes we pay in the United States.Further** ,the OECD reached an agreement to align countries on a minimum corporate tax rate and an expansion of the taxing rights of market countries. **Some** ~~Effective January 1,2024,select~~ individual countries,including ~~the~~ **those in the** ~~United Kingdom and~~ EU ~~member countries~~ ,have ~~enacted~~ **proposed legislation to implement** the global minimum tax agreement **.In other countries such as the United States,however,the implementation of the OECD agreement remains highly uncertain.If enacted,either by all OECD participants or unilaterally by individual countries,the agreement could result in tax increases or double taxation that**

could affect our United States or foreign tax liabilities.Changes to existing tax law in the United States,the U.S.territory of Puerto Rico or other jurisdictions,including the changes and potential changes discussed above,could result in tax increases where we do business and could have a material adverse effect on the results of our operations.We and certain of our subsidiaries are involved in legal proceedings.See Part IV — Note 19,Contingencies and commitments,to the Consolidated Financial Statements.Civil and criminal litigation is inherently unpredictable,and the outcome can result in costly verdicts,fines and penalties,exclusion from federal healthcare programs and / or injunctive relief that affect how we operate our business.Defense of litigation claims can be expensive,time consuming and distracting,and it is possible that we could incur judgments or enter into settlements of claims for monetary damages or change the way we operate our business,which could have a material adverse effect on our product sales,business and results of operations.In addition,product liability is a major risk in testing and marketing biotechnology and pharmaceutical products.We may face substantial product liability exposure in human clinical trials and for products we sell after regulatory approval.Product liability claims,regardless of their merits,could be costly and divert management' s attention and could adversely affect our reputation and the demand for our products.We and certain of our subsidiaries have previously been named as defendants in product liability actions for certain of our products.We are also involved in government investigations that arise in the ordinary course of our business.In recent years,there has been a trend of increasing government investigations and litigations against companies operating in our industry,both in the United States and around the world.See Our sales depend on coverage and reimbursement from government and commercial third- party payers,and pricing and reimbursement pressures have affected,and are likely to continue to affect,our profitability.Our business activities outside of the United States are subject to the FCPA and similar antibribery or anticorruption laws,regulations or rules of other countries in which we operate,including the U.K.Bribery Act.We cannot ensure that all our employees,agents,contractors,vendors,licensees,partners or collaborators will comply with all applicable laws and regulations.On April 25,2019,we entered into a settlement agreement with the DOJ and the OIG of the HHS to settle certain allegations relating to our support of independent charitable organizations that provide patients with financial assistance to access their medicines.As a result,we entered into a corporate integrity agreement with the OIG that requires us to maintain a corporate compliance program and to undertake a set of defined corporate integrity obligations for a period of five years.While we expect to fully comply with all of our obligations under the corporate integrity agreement,failure to do so could result in substantial penalties and potential exclusion from government healthcare programs.We may also see new government investigations of or actions against us citing novel theories of recovery.For example,prosecutors are placing greater scrutiny on patient support programs,including commercial copay assistance programs,and further enforcement actions and investigations regarding such programs could limit our ability to provide co- pay assistance to commercial patients.Greater scrutiny has also been placed on sponsorships,speaker programs and other arrangements where healthcare professionals receive remuneration,travel or other value to participate in certain events,and further enforcement actions could limit our ability to participate in such arrangements.Any of these results could have a material adverse effect on our We may ~~not~~ **face substantial product liability exposure in human clinical trials and for products we sell after regulatory approval. Product liability claims, regardless of their merits, could** be ~~able~~ costly and divert management' s attention and could adversely affect our reputation and the demand for our products.We and certain of our subsidiaries have previously been named as defendants in product liability actions for certain of our products.We are also involved in government investigations that arise in the ordinary course of our business.In recent years,there has been a trend of increasing government investigations and litigations against companies operating in our industry,both in the United States and around the world.See Our sales depend on coverage and reimbursement from government and commercial third- party payers,and pricing and reimbursement pressures have affected,and are likely to continue to affect,our profitability.Our business activities outside of the United States are subject to the FCPA and similar antibribery or anticorruption laws,regulations or rules of other countries in which we operate,including the U.K.Bribery Act.We cannot ensure that all our employees,agents,contractors,vendors,licensees,partners or collaborators will comply with all applicable laws and regulations.On April 25,2019,we entered into a settlement agreement with the DOJ and the OIG of the HHS to settle certain allegations relating to our support of independent charitable organizations that provide patients with financial assistance to access ~~the~~ **their** ~~capital~~ **medicines. As a result, we entered into a corporate integrity agreement with the OIG that requires us to maintain a corporate compliance program** and ~~credit markets~~ **to undertake a set of defined corporate integrity obligations through April 2024. While we expect to fully comply with all of our obligations under the corporate integrity agreement, failure to do so could result in substantial penalties and potential exclusion from government healthcare programs. We may also see new government investigations of or actions against us citing novel theories of recovery. For example, prosecutors are placing greater scrutiny** on **patient support programs** ~~terms that are favorable to us~~ **, including commercial copay assistance programs, and further enforcement actions and investigations regarding such programs could limit** ~~or~~ **our** ~~at all~~ **ability to provide co- pay assistance to commercial patients. Greater scrutiny has also been placed on sponsorships, speaker programs and other arrangements where healthcare professionals receive remuneration, travel or other value to participate in certain events, and further enforcement actions could limit our ability to participate in such arrangements. Any of these results could have a material adverse effect on our business and results of operations** . RISKS RELATED TO ECONOMIC CONDITIONS AND OPERATING A GLOBAL BUSINESS **We seek innovation through significant investment** ~~, INCLUDING DURING THE COVID- 19 PANDEMIC The novel coronavirus identified~~ in **both internal** ~~late 2019, SARS- CoV- 2, which causes the disease known as COVID- 19, is an ongoing global pandemic that has resulted in public and governmental efforts to contain or slow the spread of the disease, including widespread shelter- in- place orders, social distancing interventions, quarantines, travel restrictions and various forms of operational shutdowns. The COVID- 19 pandemic and the resulting measures implemented in response to the pandemic are~~

adversely affecting, and are expected to continue to adversely affect, our business (including our R & D , clinical trials, operations, manufacturing, supply chains, distribution systems, product development and sales **external transactions, including collaborations, partnerships, alliances, licenses, joint ventures, mergers and acquisitions (collectively, acquisition activity). Acquisition** activities **may**), the business activities of our suppliers, customers, third- party payers and our patients. See Our current products and products in development cannot be sold without **subject to regulatory approvals or other requirements that are not within our control. Antitrust scrutiny by regulatory agencies and changes to** regulatory approval **process** ; see also We must conduct clinical trials in humans before we commercialize **the U. S.** and sell any of **foreign jurisdictions may cause approvals to take longer than anticipated to obtain, not be obtained at all,** our **or** product candidates or existing products for new indications. Due to the pandemic and these measures and their effects, we have experienced, and expect to continue -- **contain** to experience **burdensome conditions** , unpredictable reductions in demand **which may jeopardize, delay** for **or** certain of our products, exacerbated by COVID- 19 surges resulting in repeated shutdowns and / or disruptions in certain geographies. Federal, state and local, and international governmental policies and initiatives designed to reduce the transmission **anticipated benefits** of **acquisitions to us and could impede** COVID- 19 also have resulted in the cancellation **execution of** or **our** delay of diagnostic, elective, specialty and **business strategy. There can be no assurance that such regulatory or** other **approvals will be obtained or that all closing conditions required in connection** procedures and appointments to avoid non- essential patient exposure to medical environments and potential infection with **our acquisition activities** COVID- 19 and to focus limited resources and personnel capacity toward the treatment of COVID- 19. For example, an NPR / Harvard poll in 2021 found that, with hospitals crowded from COVID- 19, one in five U. S. households had to delay care for serious illnesses. These measures and challenges will **be satisfied** likely continue to varying degrees and have significantly reduced patient access to, and administration of, certain of our **or waived** drugs. For example , **which could result** Prolia requires administration by a healthcare provider in doctors' offices or **us being unable to complete** other -- **the** healthcare settings that **planned acquisition activities. Acquisition activities** are **complex, time consuming** affected by COVID- 19. The U. S. label for Prolia instructs healthcare professionals who discontinue Prolia to transition the patient to an **and expensive** alternative antiresorptive, including oral treatments that do not require administration by a healthcare provider. Further, as a result of COVID- 19, oncology patients, in consultation with their doctors, may be selecting therapies that are less immunosuppressive or therapies that do not require administration in a hospital setting, potentially adversely affecting sales of certain of our products. Also, new patients have been, and are expected to continue to be, less likely to be diagnosed and / or to start therapeutics during the pandemic, and these effects, together with the lower treatment rates during the pandemic, have had, and are expected to continue to have, a cumulative negative effect on the commercial performance of our business. The decrease in diagnoses over the course of the pandemic has suppressed the volume of new patients starting treatment, which we expect to continue to impact our business. As COVID- 19 infection rates ebb and flow, we anticipate there could be periodic backlogs of patients seeking appointments with physicians relating to a variety of medical conditions, and as a result, patients seeking treatment with certain of our products may have to navigate lower provider capacity, and this lower provider capacity could have a continued adverse effect on our sales. Further, the effects of the COVID- 19 pandemic may result in **unanticipated costs** long- term shifts in preferences among healthcare professionals and patients toward treatments that do not require administration by healthcare professionals or visits to medical facilities. As the pandemic continues , **delays** and if conditions worsen or if the duration of the pandemic extends significantly, we expect to experience additional adverse effects on our **or other** development, operational and commercial activities, customer purchases and our **or financial problems related** collections of accounts receivable. It remains uncertain the degree to which **integrating** these -- **the acquired company** adverse effects would impact our future operational and **business** commercial activities, customer purchases and our collections as conditions begin to improve. There was a resurgence in COVID- 19 infections in numerous jurisdictions in 2022, resulting in the reinstatement of stricter restrictions and shutdowns in a number of jurisdictions, including in the United States, Europe and Asia Pacific regions. It is expected that the pandemic will continue to ebb and flow, with **our company** different jurisdictions having higher levels of infections than others over the course of the pandemic. New variants of the SARS- CoV- 2 virus have emerged , including the delta and omicron variants and its subvariants, and have been shown to be present in many geographies and appear to spread more easily and quickly than other variants. Further, although some studies suggest that antibodies generated with currently authorized vaccines may be effective against these variants, it remains uncertain whether currently available vaccines will retain their efficacy against future variants of the virus. Further, even while vaccine booster shots are available for certain patients, persistent vaccine hesitancy may result in under- vaccinated populations which may prolong **divert our management' s attention from** the **other business issues** duration of the COVID- 19 pandemic and continue to disrupt **opportunities and restrict** the availability **full realization** of healthcare services to the patients we serve **anticipated benefits of such transactions within the expected timeframe or at all** . Jurisdictions **We** may implement **pay substantial amounts of cash** , **incur debt** continue or reinstate border closures, impose or reimpose prolonged quarantines and further restrict travel and business activity. These measures could significantly affect our **or** ability **issue equity securities** to **pay** support our operations and customers and the ability of our employees to get to their workplaces to discover, study, develop and produce our product candidates and products, disrupt the movement of our products through the supply chain, and further prevent or discourage patients from participating in our clinical trials, seeking healthcare services and the administration of certain of our products. The increased availability of remote working arrangements in response to the COVID- 19 pandemic has expanded the pool of companies that can compete for **acquisition** our employees and employment candidates. Further, in connection with the global outbreak and spread of COVID- 19 and in an effort to increase the wider availability of needed medical products, we or our suppliers may elect to, or governments may require us or our suppliers to, allocate manufacturing capacity (for example pursuant to the U. S. Defense Production Act) in a way that adversely affects our regular operations, customer relationships and financial results. In the United States, on January 21, 2021, President Biden issued an Executive

~~Order instructing federal agencies to use all available legal authorities, including the Defense Production Act, to improve current and future pandemic response and biological threat preparedness. The rapid reallocation of resources for the treatment and prevention of COVID- 19 (including the production of COVID- 19 vaccines or related therapies, such as our agreement to contribute to the production of COVID- 19 antibody therapies for Lilly) and / or disruptions and shortages in the global supply chain caused by the pandemic, could also result in increased competition for, or reduced availability of, materials or components used in the development, manufacturing, distribution or administration of our products. For example, during the second quarter of 2021, an industry- wide shortage of certain lab kit supplies necessary for some~~ activities ~~that support our clinical trials has developed that we are actively monitoring and managing. We have also experienced challenges in obtaining certain COVID- 19- related supplies, including COVID- 19 antigen rapid test kits for our staff, as a result of high demand and limited supplies during the omicron variant surge. In addition, unpredictable increases in demand for certain of our products could exceed our capacity to meet such demand~~ , which could adversely affect our ~~financial~~ **liquidity or** ~~results~~ **result** ~~and customer relationships~~ **in dilution to our stockholders, respectively** . ~~The COVID- 19 pandemic and~~ **For example, the primary sources of funds for our acquisition of Horizon were** ~~the~~ **those received** ~~volatile global economic conditions stemming~~ from ~~it~~ **our $ 24 billion of senior notes issued on March 2, 2023, together with the $ 4 billion drawn down from our term loan facility, and while the Company currently has investment grade credit ratings, this substantial additional indebtedness has resulted in downgrades to our credit ratings. Further, failures or difficulties in integrating or retaining new personnel or in integrating the operations of the businesses, products or assets we acquire (including related technology, research, development and commercial operations, compliance programs, manufacturing, distribution and general business operations and procedures and ESG activities)** may ~~precipitate~~ **affect** ~~or~~ **our** ~~amplify~~ **ability to realize** the **benefits of the transaction and grow our business and may result in us incurring asset impairment or restructuring charges. These and** other ~~risks described~~ **challenges may arise** in ~~this " Risk Factors " section~~ **connection with our acquisitions of Otezla, Five Prime, Teneobio, ChemoCentryx, Horizon and / or our collaborations with BeiGene and Kyowa Kirin, or with other acquisition activities** , which could **have a** ~~materially~~ -- **material** ~~adversely affect our business, operations and financial condition and results. For example, if a natural disaster or other potentially disruptive event occurs concurrently with the COVID- 19 pandemic, such disaster or event could deplete our inventory levels and we could experience a disruption to our manufacturing or ability to supply our products. The rapid development and fluidity of the pandemic precludes any prediction as to the ultimate effect of COVID- 19 on us. The duration of the measures being taken by the authorities to mitigate against the spread of COVID- 19 (including the distribution and / or availability of vaccines and boosters), and the extent to which such measures are effective, if at all, remain highly uncertain. The magnitude and degree of COVID- 19' s~~ adverse effect on our business **, results of operations and stock price. We may not realize the anticipated strategic benefits of our acquisition of Horizon, including our efforts to leverage Amgen' s global presence and commercial and medical capabilities in inflammation and nephrology to accelerate revenue growth of Horizon' s products. Our assumptions and estimates about the future revenue growth of Horizon' s products may prove to be incorrect. Sales of our rare disease products acquired through our acquisition of Horizon will depend on our ability to increase awareness and educate physicians on the rare conditions that such medicines are designed to treat, as well as successfully identifying target patients and educating them about our treatments. We may also face greater than expected challenges associated with rare disease drug development (such as challenges obtaining patients for clinical trials and / or regulatory approvals) and reimbursement (such as obtaining reimbursement of orphan drugs by public health systems). We are in the process of integrating the Horizon business into ours, including a large number of complex operational and administrative systems, to form a unified combined company, including with respect to human resources, intellectual property management, research and development activities, finance, accounting and internal control processes and systems, sales operations, product distribution, commercialization efforts, information and information security systems, compliance programs and policies and supply chain systems and third party relationships** (including **vendors** ~~our product development, product sales, operating results~~ and ~~resulting cash flows~~ **third party manufacturers**) **. For example, Horizon adds more than 30 contract manufacturing organizations (CMOs) to our operations, many of which are single source suppliers (including the CMO that produces TEPEZZA drug substance** and **the CMO that produces all of our KRYSTEXXA drug substance in Israel that is affected by the current conflict in Israel and Gaza). Business integrations generally, and our integration of Horizon specifically, are complex, time consuming and expensive, and we may experience unanticipated costs, delays or other operational or** financial **challenges. These integration efforts may also divert our management** ~~condition will be driven by the severity and duration of the pandemic, the pandemic~~ ' s **attention and resources away from other business operations, which may disrupt to some degree our ongoing business. Failure to successfully integrate the Horizon business into ours and / or achieve its anticipated strategic benefits may result in our incurring significant asset impairment or restructuring charges, and could have a material adverse** effect on **our business, results of operations and stock price. The capital and credit markets may experience extreme volatility and disruption, which may lead to uncertainty and liquidity issues for both borrowers and investors. For example, in early 2020,** ~~the~~ **there** ~~United States~~ **were significant disruptions in the commercial paper market** and ~~global economies~~ **several borrowers were unable to obtain funding at normal rates or maturities, which resulted in a significant increase in draws of corporate credit lines with banks. Similarly, the bond markets experienced extreme volatility in terms of interest rates** and **credit spreads, with several days without new issuances of corporate bonds. While we have historically accessed capital markets to supplement our existing funds and cash generated from operations to satisfy our needs for capital expenditures, debt service requirements, to pay dividends and repurchase stock, and engage in** ~~the~~ **other** ~~timing~~ **business initiatives** , ~~scope~~ **including acquisitions** and **licensing activities** ~~effectiveness of federal~~ , ~~state~~ **in 2023** , ~~local and international governmental responses~~ **we substantially increased our outstanding indebtedness in connection with our acquisition of Horizon, which**

may limit our ability to **timely obtain additional financing on desired terms. See Our efforts to collaborate with or acquire** ~~the~~ **other** ~~pandemic. If mitigation of the pandemic continues~~ **companies, products, or technology, and** to **integrate the operations of companies or to support the products or technology we have acquired, may not be successful, and may result in unanticipated costs, delays or failures to realize the benefits of the transactions. While our plans include reducing our debt leverage levels before returning to the capital or credit markets for new funds, if we are** ~~require~~ **required** ~~further shelter~~ **to access the capital and credit markets at an inopportune time, including when adverse capital and credit market conditions prevail, we may be unable to obtain financing on favorable terms, or at all, which could have a material adverse effect on our business and results of operations or our ability to complete business acquisitions. Changes in credit ratings issued by nationally recognized credit** - **rating agencies could also adversely affect** ~~in- place and shutdown orders and / or~~ **our** ~~restrictions~~ **ability to obtain capital and credit market financing and the cost of such financing and have an adverse effect** on ~~individual and /~~ **the market price of** ~~or~~ **our securities** ~~group conduct, any adverse effects of the COVID- 19 pandemic will likely grow and could be enduring, and our business and financial position could be materially adversely affected~~. To achieve our business objectives, we rely on sophisticated information technology systems, including **hardware,** software **, technology infrastructure, online sites and networks for both internal and external operations** , mobile applications, cloud services and network- connected control systems, some of which are managed, hosted, provided or serviced by third parties. Internal or external events that compromise the confidentiality, integrity and availability of our systems and data may significantly interrupt the operation of our business, result in significant costs and / or adversely affect our reputation. Our information technology systems are highly integrated into our business, including our R & D efforts, our clinical and commercial manufacturing processes and our product sales and distribution processes. Further, as the majority of our employees work remotely for some portion of their jobs in our hybrid work environment, our reliance on our and third- party information technology systems has increased substantially and is expected to continue to increase. **Remote and hybrid working arrangements, including those of at many third- party providers, can increase cybersecurity risks due to the challenges associated with managing remote computing assets and security vulnerabilities that are present in many non- corporate and home networks.** The complexity and interconnected nature of **software, hardware and** our systems ~~makes~~ **make** them ~~potentially~~ vulnerable to breakdown or other service interruptions **, and to software errors or defects, misconfiguration and other security vulnerabilities** . Upgrades or changes to our systems or the software that we use ~~may~~ **have resulted and we expect, in the future, will** result in the introduction of new cybersecurity vulnerabilities and risks. In 2022 **,** we identified a number of security vulnerabilities introduced into our information systems as a result of flaws that we subsequently identified in software that we **had** purchased and installed, and these flaws required that we apply emergency patches to certain of our systems. While we did not experience any significant adverse effects as a result of these vulnerabilities, there can be no assurance that we will timely identify and address ~~any~~ future vulnerabilities. Our systems are also subject to frequent perimeter network reconnaissance and scanning, phishing and other cyberattacks. **For example, as a result of our cybersecurity monitoring of the Horizon legacy information systems, we detected phishing activity in the accounts of two Horizon executives. These accounts were de- activated, the incidents were investigated and the determination was made separately by both our internal cybersecurity team and our external digital forensics and incident response supplier that no confidential information had been exfiltrated.** As the cyber- threat landscape evolves, these attacks are growing in frequency, sophistication **,** and intensity, and are becoming increasingly difficult to detect **and increasingly sophisticated in using techniques and tools — including artificial intelligence — that circumvent security controls, evade detection and remove forensic evidence** . Such attacks could include the use of harmful and virulent malware, including ransomware or other denials of service, ~~that~~ **which** can be deployed through various means, including the software supply chain, e- mail, malicious websites and / or the use of social engineering **/ phishing** . We have also experienced denial of service attacks against our network, and **,** although such attacks did not succeed, there can be no assurance that our efforts to guard against the wide and growing variety of potential attack techniques will be successful in the future. Attacks such as those experienced by ~~governmental~~ -- **government** entities (including those that approve and / or regulate our products, such as the EMA) and other multi- national companies, including some of our peers, could leave us unable to utilize key business systems or access or protect important data **,** and could have a material adverse effect on our ability to operate our business, including developing, gaining regulatory approval for, manufacturing, selling and / or distributing our products. For example, in 2017, a pharmaceutical company experienced a cyberattack involving virulent malware that significantly disrupted its operations, including its research and sales operations and the production of some of its medicines and vaccines. As a result of the cyberattack, its orders and sales for certain products ~~in certain markets~~ were negatively affected. In late 2020, SolarWinds Corporation, a leading provider of software for monitoring and managing information technology infrastructure, disclosed that it had suffered a cybersecurity incident whereby attackers had inserted malicious code into legitimate software updates for its products that were installed by myriad private and government customers, enabling the attackers to access a backdoor to such systems. In 2022, Okta, Inc., a provider of software that helps companies manage user authentication, disclosed that several hundred of its corporate customers were vulnerable to a security breach that allowed attackers to access Okta' s internal network. Although this breach did not have a significant effect on our business, there can be no assurance that a similar future breach would not result in a material adverse effect on our business or results of operations. Our systems also contain and ~~utilize~~ **use** a high volume of sensitive data, including intellectual property, trade secrets **and other proprietary business information** , financial information, regulatory information, strategic plans, sales trends and forecasts, litigation materials and / or personal **identifiable** information belonging to us, our staff, our patients, customers and / or other parties. In some cases, we utilize third- party service providers to **collect,** process, store, manage or transmit such data, which ~~may~~ **have** ~~increase~~ **increased** our risk. Intentional or inadvertent data privacy or security breaches (including cyberattacks) resulting from attacks or lapses by employees, service providers (including providers of information technology- specific services), business partners, nation states

(including groups associated with or supported by foreign intelligence agencies), organized crime organizations, " hacktivists " or others, create risks that our sensitive data may be exposed to unauthorized persons, our competitors or the public. System vulnerabilities and / or cybersecurity breaches experienced by our third- party service providers have constituted a substantial share of the information security risks that have affected us. For example, in the first half of 2021, a supplier experienced a data breach in which an unauthorized third party acquired access to certain information provided to the supplier in the course of its provision of services to us, including business documents and certain personally identifiable patient information (not including social security or other financial or health insurance information). As required, we promptly notified the applicable state attorneys general and the individuals whose personally identifiable information was affected of this data breach at the supplier. In the third quarter of 2022, another service provider experienced a similar cybersecurity breach in which an attacker exfiltrated certain data (including non- significant Amgen data) from the service provider' s systems. Although these supplier data breaches have not resulted in material adverse effects on our business, there can be no assurance that a similar future cybersecurity incident would not result in a material adverse effect on our business or results of operations. Further, the timeliness of our awareness of a cybersecurity incident affects our ability to respond to and work to mitigate the severity of such events. For example, in 2020 and 2022, two of our vendors experienced cyberattacks and each initially reported to us that neither event involved our data. However, upon further investigation, they each subsequently informed us that the attackers had accessed limited, non- significant Amgen information. Although neither of these breaches had a significant adverse effect on our business, in the future we may again not receive timely reporting of cybersecurity events and such events could have a material adverse effect on our business. Cyberattackers are also increasingly exploiting vulnerabilities in commercially available software from shared or open- source code. We rely on third party commercial software that **have had and** may have such vulnerabilities, but as use of open- source code is frequently not disclosed, our ability to fully assess this risk to our systems is limited. For example, in December 2021, a remote code execution vulnerability was discovered in a ~~widely used~~ software library that is **widely** used in a variety of commercially available software and services. Although this vulnerability has not resulted in any significant adverse effects on us, there can be no assurances that a similar future vulnerability in the software and services that we use would not result in a material adverse effect on our business or results of operations. Domestic and global government regulators, our business partners, suppliers with whom we do business, companies that provide us or our partners with business services and companies we have acquired or may acquire face similar risks **.** ~~, and security~~ **Security** breaches of their systems or service outages **have adversely affected systems and** could ~~adversely~~ **, in the future,** affect our **systems and** security, leave us without access to important systems, products, raw materials, components, services or information **,** or expose our confidential data or sensitive personal information. For example, in 2019, two vendors that perform testing and analytical services that we use in developing and manufacturing our products experienced cyberattacks, and in April and September of 2020, vendors that provide us with information technology services and clinical data services, respectively, each experienced ransomware attacks. Although there was no breach of our systems, each of these incidents required us to disconnect our systems from those vendors' systems. While we were able to reconnect our systems following restoration of these vendors' capabilities without significantly affecting product availability, a more extended service outage affecting these or other vendors, particularly where such vendor is the single source from which we obtain the services, could have a material adverse effect on our business or results of operations. In addition, we distribute our products in the United States primarily through three pharmaceutical wholesalers, and a security breach that impairs the distribution operations of our wholesalers could significantly impair our ability to deliver our products to healthcare providers and patients. **There can be no assurance that our cybersecurity risk management program and processes, including our policies, controls, or procedures, will be fully implemented, complied with or effective in protecting our information technology systems and sensitive data.** Although we have experienced system breakdowns, attacks and information security breaches, we do not believe such breakdowns, attacks and breaches have had a material adverse effect on our business or results of operations. We **will continue to experience varying degrees of cyberattacks and other incidents in the future. Even though we** continue to invest in the monitoring, protection and resilience of our critical and / or sensitive data and systems ~~. However~~ , there can be no assurances that our efforts will detect, prevent or fully recover systems or data from all breakdowns, service interruptions, attacks and / or breaches of our systems that could adversely affect our business and operations and / or result in the loss or exposure of critical, proprietary, private, confidential or otherwise sensitive data, which could result in material financial, legal ~~,~~ business or reputational harm to us or negatively affect our stock price. While we maintain cyber- liability insurance, our insurance is not sufficient to cover us against all losses that could potentially result from a service interruption, breach of our systems or loss of our critical or sensitive data. We are also subject to various laws and regulations globally regarding privacy and data protection, including laws and regulations relating to the collection, storage, handling, use, disclosure, transfer and security of personal data. The legislative and regulatory environment regarding privacy and data protection is continuously evolving and developing and the subject of significant attention globally. For example, we are subject to the EU' s GDPR, which became effective in May 2018, and the CCPA, which became effective in January 2020, both of which provide for substantial penalties for noncompliance. The CCPA was amended in late 2020, to create the California Privacy Rights Act to create opt in requirements for the use of sensitive personal data and the formation of a new dedicated agency for the enforcement of the law, the California Privacy Protection Agency. ~~Virginia, Colorado, Utah and Connecticut have all subsequently passed similar~~ **Similar** consumer privacy laws ~~, which~~ went into effect in Virginia ~~as of January 1~~ , **Colorado, Utah, Connecticut and Florida in** 2023 **. Consumer privacy laws were also passed in eleven other states , with the earliest** ~~and will go into effect~~ **effective dates** ~~in Colorado, Utah and Connecticut~~ later **this year, and proposed** in ~~2023~~ **three additional states** . **Outside the United States,** ~~Other~~ **other** jurisdictions where we operate have passed, or continue to propose, similar legislation and / or regulations. For example, in China, the Personal Information Protection Law and the Data Security Law, which regulate data processing activities associated with personal and nonpersonal data, are in effect and build upon the existing Cybersecurity Law. Failure to comply with these current and future laws could result in significant

penalties and reputational harm and could have a material adverse effect on our business and results of operations. As we continue our expansion efforts in emerging markets around the world, through acquisitions and licensing transactions as well as through the development and introduction, both independently and through collaborations such as our collaboration with BeiGene, of our products in new markets, we face numerous risks to our business. There is no guarantee that our efforts and strategies to expand sales in emerging markets will succeed. Our international business, including in China and emerging market countries, may be especially vulnerable to periods of global and local political, legal, regulatory and financial instability, including issues of geopolitical relations, the imposition of international sanctions in response to certain state actions and / or sovereign debt issues ~~. Further~~ , ~~in 2022~~ and **management** ~~continuing through early 2023, the Asia Pacific region also experienced a surge~~ of **health policy** ~~COVID- 19 infections. While one country~~ in ~~the region initially responded~~ - **response** to **pressures** ~~the surge by activating strict containment measures, in late 2022 that country abruptly reversed those measures, resulting in a significant COVID- 19 outbreak, causing issues~~ such as **global pandemics** ~~lack of capacity at hospitals that could lead to a local health emergencies~~ . If relations between the United States and other governments deteriorate, our business and investments in such markets may also be adversely affected. We may also be required to increase our reliance on third- party agents and unfamiliar operations and arrangements including those previously utilized by companies we partner with or acquire in emerging markets. See We must conduct clinical trials in humans before we commercialize and sell any of our product candidates or existing products for new indications. Our expansion efforts in China and emerging markets around the world are dependent upon the establishment of an environment that is predictable, navigable and supportive of biopharmaceutical innovation, sustained access for our products and predictable pricing controls. For example, China continues to strengthen regulations on the collection, use and transmission of Chinese human genetic resources, and has expanded regulations on the conduct of biotechnology R & D activities in China. Between 2020 and 2022, we experienced delays in our applications to the Human Genetic Resources Administration of China that sought approval to conduct clinical trials in China. Our international operations and business may also be subject to less protective intellectual property or other applicable laws, diverse data privacy and protection requirements, changing tax laws and tariffs, trade restrictions or other barriers designed to protect industry in the home country against foreign competition, far- reaching antibribery and anticorruption laws and regulations and / or evolving legal and regulatory environments. **For example, recent cross- border data transfer compliance requirements in China may also impose additional costs of doing business, including costs associated with localizing operations.** In response to the ongoing armed conflict in Ukraine, the U. S. government, numerous state governments, the EU and other countries in which we conduct business have imposed a wide range of economic sanctions that restrict commerce and business dealings with Russia, certain regions of Ukraine and certain entities and individuals. ~~This~~ **Additionally, the armed** conflict **in the Middle East that has been ongoing since October 2023 has caused regional disruptions to economic activity. For a description of the conflict' s impact on our third- party contract manufacturing of KRYSTEXXA, see Our efforts to collaborate with or acquire other companies, products, or technology, and to integrate the operations of companies or to support the products or technology we have acquired, may not be successful, and may result in unanticipated costs, delays or failures to realize the benefits of the transactions. These conflicts** may also precipitate or amplify the other risks described herein, including risks relating to cybersecurity, global economic conditions, clinical trials and supply chains, which could adversely affect our business, operations and financial condition and results. As we expand internationally, we are subject to fluctuations in foreign currency exchange rates relative to the U. S. dollar. While we have a program in place that is designed to reduce our exposure to foreign currency exchange rate fluctuations through foreign currency hedging arrangements, our hedging efforts do not completely offset the effect of these fluctuations on our revenues and earnings. Overall, the legal and operational challenges of our international business operations, along with government controls, the challenges of attracting and retaining qualified personnel and obtaining and / or maintaining necessary regulatory or pricing approvals of our products, may result in material adverse effects on our international product sales, business and results of operations. RISKS..... have a material adverse effect on our business and results of operations. RISKS RELATED TO COMPETITION We operate in a highly competitive environment. See Item 1. Business — Marketing, Distribution and Selected Marketed Products — Competition. We expect that our products and product candidates will compete with existing drugs, new drugs currently in development, drugs currently approved for other indications that may later be approved for the same indications as those of our products and drugs approved for other indications that are used off- label. Large pharmaceutical companies and generics manufacturers of pharmaceutical products have expanded into, and are expected to continue expanding into, the biotechnology field, and some pharmaceutical companies and generics manufacturers have formed partnerships to pursue biosimilars. With the proliferation of companies pursuing biopharmaceuticals, several of our biosimilar products have entered, and a number of our product candidates may enter, markets with one or more competitors or with competitors soon to arrive. In addition, some of our competitors may have technical, competitive or other advantages over us for the development of technologies and processes or greater experience in particular therapeutic areas, and consolidation among pharmaceutical and biotechnology companies can enhance such advantages. These advantages may make it difficult for us to compete with them successfully to discover, develop and market new products and for our current products to compete with new products or new product indications they may bring to market. As a result, our products have been competing and may continue to compete, and our product candidates may compete, against products or product candidates that offer higher rebates or discounts, lower prices, equivalent or superior efficacy, better safety profiles, easier administration, earlier market availability or other competitive features. If we are unable to compete effectively, this could reduce our sales, which could have a material adverse effect on our business and results of operations. Our success depends in part on our ability to obtain and defend patent rights and other intellectual property rights that are important to the commercialization of our products and product candidates. The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and often involve complex legal, scientific and factual questions. Driven by cost pressures, efforts to limit or weaken patent protection for our industry are increasing. For example, the COVID- 19 pandemic has resulted in

increased interest in compulsory licenses, march- in rights or other governmental interventions, both in the United States and internationally, related to the procurement of drugs, and the World Trade Organization has agreed to a waiver of COVID- 19 vaccine intellectual property protections through the Trade- Related Aspects of Intellectual Property Rights waiver process. ~~See The COVID~~ **Also, in December 2023, the Administration released a proposed framework that would consider price as a factor when determining whether to exercise march** - **in rights pursuant** ~~19 pandemic, and the public and governmental effort~~ to ~~mitigate against~~ the **Bayh- Dole Act with respect** ~~spread of the disease, have had, and are expected~~ to **drugs** ~~continue to have, an adverse effect, and may have a material adverse effect, on our~~ - **or other taxpayer- funded inventions** ~~clinical trials, operations, manufacturing, supply chains, distribution systems, product development, product sales, business and results of operations~~ . Third parties have challenged and may continue to challenge, invalidate or circumvent our patents ~~and~~ **(including any** patent applications **, term extensions, term adjustments and supplemental protection certificates)** relating to our products, product candidates and technologies **. See Part IV — Note 20, Contingencies and commitments, to the Consolidated Financial Statements** . Challenges to patents may come from potential competitors or from parties other than those who seek to market a potentially- infringing product. In addition, our patent positions might not protect us against competitors with similar products or technologies because competing products or technologies may not infringe our patents. For certain of our product candidates, there are third parties who have patents or pending patent applications that they may claim necessitate payment of a royalty or prevent us from commercializing these product candidates in certain territories. **Further, disputes may arise with third parties from whom we have licensed rights to intellectual property necessary for the development and commercialization of some of our products. For example, we are in a dispute with Roche regarding a license agreement that we acquired through our acquisition of Horizon for patents and know- how for TEPEZZA.** Patent disputes are frequent, costly and can preclude, delay or increase the cost of commercialization of products. We have been in the past, are currently and expect to be in the future, involved in patent litigation. These matters have included, and may in the future include, litigation with manufacturers of products that purport to be biosimilars of certain of our products for patent infringement **, invalidity, unenforceability** and ~~for~~ failure to comply with certain provisions of the BPCIA. A determination made by a court, agency or tribunal concerning infringement, validity, enforceability, injunctive or economic remedy, or the right to patent protection, for example, are typically subject to appellate or administrative review. Upon review, such initial determinations may be afforded little or no deference by the reviewing tribunal and may be affirmed, reversed or made the subject of reconsideration through further proceedings. A patent dispute or litigation has not discouraged, and may not in the future discourage, a potential violator from bringing the allegedly infringing product to market prior to a final resolution of the dispute or litigation. The period from inception until resolution of a patent dispute or litigation is subject to the availability and schedule of the court, agency or tribunal before which the dispute or litigation is pending. We have been, and may in the future be, subject to competition during this period and may not be able to recover fully from the losses, damages and harms we incur from infringement by the competitor product even if we prevail. Moreover, if we lose or settle current or future litigations at certain stages or entirely, we could be subject to competition and / or significant liabilities, be required to enter into third- party licenses for the infringed product or technology or be required to cease using the technology or product in dispute. In addition, we cannot guarantee that such licenses will be available on terms acceptable to us, or at all. Further, under the Hatch – Waxman Act, our products approved by the FDA under the FDCA have been, and may in the future be, the subject of patent litigation with generics competitors before expiry of the five- year period of data exclusivity provided for under the Hatch- Waxman Act and prior to the expiration of the patents listed for the product. Likewise, our innovative biologic products have been, and may in the future be, the subject of patent litigation prior to the expiration of our patents and, with respect to competitors seeking approval as a biosimilar or interchangeable version of our products, prior to the 12- year exclusivity period provided under the BPCIA. In addition, we have faced, and may in the future face, patent litigation involving claims that ~~the~~ **our** biosimilar product candidates ~~we are working to develop~~ infringe the patents of other companies, including those that manufacture, market or sell the applicable reference products or who are developing or have developed other biosimilar versions of such products. Alternatively, patents held by other entities have contributed, and may in the future contribute, to a decision by us to not pursue all of the same labeled indications as are held by these companies. While we have attempted, and expect to continue to attempt, to challenge the patents held by other companies, our efforts may be unsuccessful. For examples of and information related to our patent litigation, see Part IV — Note ~~19~~ **20** , Contingencies and commitments, to the Consolidated Financial Statements. Certain of the existing patents on our products have expired or will soon expire. See Item 1. Business — Marketing, Distribution and Selected Marketed Products — Patents. As our patents expire, competitors are able to legally produce and market similar products or technologies, including biosimilars, which has had, and may continue to have, a material adverse effect on our product sales, business and results of operations. In addition, competitors have been, and may continue to be, able to invalidate, design around or otherwise circumvent our patents and sell competing products. We currently face competition from biosimilars and generics in most of the territories in which we operate, including the United States and Europe, and we expect to face increasing biosimilar and / or generics competition this year and beyond. Expiration or successful challenge of applicable patent rights or expiration of an applicable exclusivity period has accelerated such competition, and we expect to face more litigation regarding the validity and / or scope of our patents. Our products have also experienced greater competition from lower cost biosimilars or generics that come to market when branded products that compete with our products lose their own patent protection. To the extent that governments adopt more permissive regulatory approval standards and competitors are able to obtain broader or expedited marketing approval for biosimilars and generics, the rate of increased competition for our products ~~could~~ **would likely** accelerate. In the EU, biosimilars are evaluated for marketing authorization pursuant to a set of general and product class- specific guidelines. In addition, in an effort to spur biosimilar utilization and / or increase potential healthcare savings, some EU countries and some Canadian provinces have adopted, or are considering the adoption of, biosimilar uptake measures such as physician prescribing quotas or automatic pharmacy substitution of biosimilars for the corresponding reference

products. Some EU countries impose automatic price reductions upon market entry of one or more biosimilar competitors. In September 2022, the EMA and the EU Heads of Medicines' Agencies (HMA) issued a joint statement providing that biosimilar medicines approved in the EU are " interchangeable " with their reference products and other biosimilars of the same reference product. This EMA- HMA statement could further contribute to the prescribing of biosimilars and to greater competition in Europe. While the degree of competitive effects of biosimilar competition differs between EU countries and between products, in the EU the overall use of biosimilars and the rate at which product sales of innovative products are being affected by biosimilar competition is increasing. In the United States, the BPCIA authorizes the FDA to approve biosimilars via a separate, abbreviated pathway. See Item 1. Business — Government Regulation — Regulation in the United States — Approval of Biosimilars. In the United States, the FDA has approved numerous biosimilars, including biosimilar versions of Neulasta, EPOGEN and ENBREL, and a growing number of companies have announced that they are also developing biosimilar versions of our products. For example, six biosimilar versions of Neulasta are now approved in the United States, **including an on- body injector presentation that was approved in December 2023 for a Neulasta biosimilar,** and we expect that other biosimilar versions of Neulasta may be marketed or receive approval in the future. Impact to our Neulasta sales has accelerated as additional competitors have launched. See Item 1. Business — Marketing, Distribution and Selected Marketed Products — Competition. Manufacturers of biosimilars have attempted, and may in the future attempt, to compete with our products by offering lower list prices, greater discounts or rebates, or contracts that offer longer- term pricing or a broader portfolio of other products. Companies pursuing development of biosimilar versions of our products have challenged and may continue to challenge our patents well in advance of the expiration of our material patents. For examples of and information related to our biosimilars and generics patent litigation, see Part IV — Note ~~19~~ **20** , Contingencies and commitments, to the Consolidated Financial Statements. See Our ~~intellectual property positions may be challenged, invalidated or circumvented, or we may fail to prevail in current and future intellectual property litigation.~~ The U. S. biosimilar pathway includes the option for biosimilar products that meet certain criteria to be approved as interchangeable with their reference products. Some companies currently developing or already marketing biosimilars may seek to obtain interchangeable status from the FDA, which could potentially allow pharmacists to substitute those biosimilars for our reference products without prior approval from the prescriber in most states under state law. The FDA approved the first interchangeable biosimilar in 2021 and has subsequently granted interchangeability designations to ~~three~~ additional biosimilars ~~. In 2019~~ , **including without always requiring a switching study** ~~the FDA issued draft guidance that provides that comparative immunogenicity studies will not generally be expected for biosimilar and interchangeable insulin products. This has opened the door for other product- specific guidance development and the removal of the expectation for certain studies, which may contribute to increased biosimilar competition for our innovative products~~ . For example, in August 2022, the FDA designated a monoclonal antibody biosimilar as interchangeable without requiring a switching study to support the interchangeability determination ~~. Further~~ , **and has** ~~in September 2022, the FDA indicated that while comparative clinical trials will continue~~ **continued** to **make** ~~be a requirement for many biosimilar development programs, the~~ **other** ~~agency is focused~~ **such designations of interchangeability** on ~~reducing the need for them in the future through~~ a **case- by- case basis** ~~range of statistical, analytical and pharmacologic approaches~~ . In addition, critics of the 12- year exclusivity period in the biosimilar pathway law will likely continue to seek to shorten the data exclusivity period and / or to encourage the FDA to interpret narrowly the law' s provisions regarding which new products receive data exclusivity. In 2019, the Administration agreed to remove from the United States- Mexico- Canada Agreement a requirement for at least 10 years of data exclusivity for biologic products. Also, the FDA is considering whether subsequent changes to a licensed biologic would be protected by the remainder of the reference product' s original 12- year exclusivity period (a concept known in the generic drug context as " umbrella exclusivity "). If the FDA were to decide that umbrella exclusivity does not apply to biological reference products or were to make other changes to the exclusivity period, this could expose us to biosimilar competition at an earlier time. There also have been, and may continue to be, legislative and regulatory efforts to promote competition through policies enabling easier generic and biosimilar approval and commercialization, including efforts to lower standards for demonstrating biosimilarity or interchangeability, **eliminate the standard for interchangeability and declare by law that all biosimilars are de facto interchangeable with their reference products,** limit patents that may be litigated and / or patent settlements, implement preferential reimbursement policies for biosimilars and pass new laws requiring more disclosure in the FDA' s Orange **Book** and Purple ~~Books~~ **Book** . For example, in 2021 the FDA sent a letter to the USPTO describing ways to strengthen coordination between the two agencies, offered training to help identify prior art, and seeking USPTO' s views on practices that extend market exclusivities, whether pharmaceutical patent examiners need additional resources, and the effect of post- grant challenges at the Patent Trial and Appeal Board on drug patents. The USPTO responded in July 2022 with a letter to the FDA stating that it is prepared to create formal mechanisms to collaborate with the FDA on patent issues that may affect the timing of generic and biosimilar entry. In January 2023, the USPTO held a joint listening session with the FDA on USPTO- FDA collaboration efforts. Upon the expiration or loss of patent protection and / or applicable exclusivity for one of our products, we can lose the majority of revenues for that product in a very short period of time. See Item 1. Business — Marketing, Distribution and Selected Marketed Products — Competition. Additionally, if one of our products is the subject of an FDA Written Request for pediatric studies and we are unable to adequately complete these studies, we may not obtain the pediatric exclusivity award that extends unexpired regulatory exclusivity for the product (and existing patents for a small molecule product) by an additional six months. **Further, in 2023, FDA draft guidance contemplates that the agency may no longer grant pediatric exclusivity for studies conducted solely to fulfill Pediatric Research Equity Act (PREA) requirements.** While we are unable to predict the precise effects of biosimilars and generics on our products, we are currently facing and expect to face greater competition in the United States, Europe and elsewhere as a result of biosimilar and generic competition and, in turn, downward pressure on our product prices and sales. This competition has had, and could increasingly have, a material adverse effect on our product sales, business and results of operations. State laws may also have an impact on

our business. For example, California is the first state to have passed legislation, effective on January 1, 2020, against " pay for delay " settlements of patent infringement claims filed by manufacturers of generics or biosimilars where anything of value is given in exchange for settlement. Under this law, such settlement agreements are presumptively anticompetitive. The law may result in prolonged litigation and fewer settlements. **Similar legislation based on California' s law continues to be introduced in** ~~Other~~ **other** states, including Connecticut ~~,~~ **and** New York **. Efforts to target such settlements are also active** ~~, Illinois and Minnesota, may adopt similar laws or a similar law could be adopted~~ at the federal level **, including legislation introduced such as the Preserving Access to Affordable Generics and Biosimilars Act that adopts California' s anticompetitive presumption approach** . Certain of our distributors, customers and payers have substantial purchasing leverage, due to the volume of our products they purchase or the number of patient lives for which they provide coverage. The substantial majority of our U. S. product sales is made to three pharmaceutical product wholesaler distributors: McKesson Corporation, **Cencora, Inc. (formerly** AmerisourceBergen Corporation **)** and Cardinal Health, Inc. These distributors, in turn, sell our products to their customers, which include physicians or their clinics, dialysis centers, hospitals and pharmacies. Similarly, as discussed above, there has been significant consolidation in the health insurance industry, including that a small number of PBMs now oversee a substantial percentage of total covered lives in the United States. See Our sales depend on coverage and reimbursement from government and commercial third- party payers, and pricing and reimbursement pressures have affected, and are likely to continue to affect, our profitability. ~~The~~ **For example,** ~~three~~ -- **the five** largest PBMs in the United States are now part of major health insurance providers **, and nationally account for 92 % of prescription drug claims** . The growing concentration of purchasing and negotiating power by these entities has, and may continue to, put pressure on our pricing due to their ability to extract price discounts on our products, fees for other services or rebates, negatively affecting our bargaining position, sales and / or profit margins. In addition, decisions by these entities to purchase or cover less or none of our products in favor of competing products could have a material adverse effect on our product sales, business and results of operations due to their purchasing volume. Further, if one of our significant wholesale distributors encounters financial or other difficulties and becomes unable or unwilling to pay us all amounts that such distributor owes us on a timely basis, or at all, it could negatively affect our business and results of operations. In addition, if one of our significant wholesale distributors becomes insolvent or otherwise unable to continue its commercial relationship with us in its present form, it could significantly disrupt our business and adversely affect our product sales, our business and results of operations unless suitable alternatives are timely found or lost sales are absorbed by another distributor. RISKS RELATED TO RESEARCH AND DEVELOPMENT Amgen invests heavily in R & D. Successful product development in the biotechnology industry is highly uncertain, and very few R & D projects yield approved and commercially viable products. Product candidates, including biosimilar product candidates, or new indications for existing products (collectively, product candidates) that appear promising in the early phases of development have failed to reach the market for a number of reasons, such as: • the product candidate did not demonstrate acceptable clinical trial results even though it achieved its primary endpoints and / or demonstrated positive preclinical or early clinical trial results, for reasons that could include changes in the standard of care of medicine or expectations of health authorities; • the product candidate was not effective or not more effective than currently available or potentially competitive therapies in treating a specified condition or illness; • the product candidate was not cost effective in light of existing or potentially competitive therapeutics; • the product candidate had harmful side effects in animals or humans; • the necessary regulatory bodies, such as the FDA or EMA, did not approve the product candidate for an intended use; • reimbursement for the product candidate is limited despite regulatory approval; • the product candidate was not economical for us to manufacture and commercialize; • **the patient population size is smaller than anticipated; •** other parties had or may have had proprietary rights relating to our product candidate, such as patent rights, and did not let us sell it on reasonable terms, or at all; • we and certain of our licensees, partners, contracted organizations or independent investigators failed to effectively conduct clinical development or clinical manufacturing activities; • the pathway to regulatory approval or reimbursement for product candidates was uncertain or not well- defined; • the biosimilar product candidate failed to demonstrate the requisite biosimilarity to the applicable reference product, or was otherwise determined by a regulatory authority to not meet applicable standards for approval; and • a companion diagnostic device that is required with the use of a product candidate is not approved by the necessary regulatory authority. We ~~have spent considerable time, energy and resources developing our expertise in human genetics and acquiring access to libraries of genetic information with the belief~~ **believe** that genetics **, together with the benefit of artificial intelligence and computational evidence,** could meaningfully aid our search for new medicines and help guide our R & D decisions and investments ~~. We~~ **, and** have focused our R & D strategy on drug targets validated by genetic or other compelling human evidence. **We have invested considerable time, energy and resources into developing our expertise in human genetics, acquiring access to libraries of genetic information, and are applying artificial intelligence to our R & D activities, including applying such technologies to advance our human data efforts and our generative biology platform that seek to discover and design new drugs.** However, product candidates based on genetically validated targets **or developed with the assistance of such technologies** remain subject to the uncertainties of the drug development process and may not reach the market for a number of reasons, including the factors listed above. Before a product may be sold, we must conduct clinical trials to demonstrate that our product candidates are safe and effective for use in humans. The results of those clinical trials are used as the basis to obtain approval from regulatory authorities such as the FDA and EMA. See Our current products and products in development cannot be sold without regulatory approval. We are required to conduct clinical trials using an appropriate number of trial sites and patients to support the product label claims. The length of time, number of trial sites and number of patients required for clinical trials vary substantially, and we may spend several years and incur substantial expense in completing certain clinical trials. In addition, we may have difficulty finding a sufficient number of clinical trial sites and / or patients to participate in our clinical trials, particularly if competitors are conducting clinical trials in similar patient populations ~~. See The COVID- 19 pandemic,~~ and **/ or in rare** ~~the public and governmental effort to mitigate against the spread of the~~ disease

therapy ~~, have had, and are expected to continue to have, an adverse effect, and may have a material adverse effect, on our~~ clinical trials **due to the inherently small patient population potentially served by such therapies** ~~, operations, supply chains, distribution systems, product development, product sales, business and results of operations~~ . Patients may withdraw from clinical trials at any time **(including trials in which patients believe that they may not be receiving a clinical benefit)** , and privacy laws and / or other restrictions in certain countries may restrict the ability of clinical trial investigators to conduct further follow- up on such patients, which may adversely affect the interpretation of study results. Delays and complications in planned clinical trials can result in increased development costs, associated delays in regulatory approvals and in product candidates reaching the market and revisions to existing product labels. Further, to increase the number of patients available for enrollment in our clinical trials, we have opened, and will continue to open, clinical sites and enroll patients in a number of locations where our experience conducting clinical trials is more limited, including India, China, South Korea, the Philippines, Singapore and some Central and South American countries, either through utilization of third- party contract clinical trial providers entirely or in combination with local staff. Conducting clinical trials in locations where we have limited experience requires substantial time and resources to understand the unique regulatory environments of individual countries. For other examples of the risks of conducting clinical trials in China, see also Our sales and operations are subject to the risks of doing business internationally, including in emerging markets. Further, we must ensure the timely production, distribution and delivery of the clinical supply of our product candidates to numerous and varied clinical trial sites. Additionally, regional disruptions, including natural and man- made disasters, health emergencies (such as novel viruses or pandemics ~~such as~~ **, including** the ~~one we are currently experiencing with~~ COVID- 19 **pandemic**), or geopolitical conflicts (such as the ongoing armed ~~conflict~~ **conflicts** in Ukraine **and the Middle East**) have significantly disrupted the timing of clinical trials, and in the future could disrupt the timing, execution and outcome of clinical trials. If we fail to adequately manage the design, execution and diverse regulatory aspects of our clinical trials or to manage the production or distribution of our clinical supply, or such sites experience disruptions as a result of a natural / man- made disaster, health emergency or geopolitical conflict, corresponding regulatory approvals may be delayed or we may fail to gain approval for our product candidates or could lose our ability to market existing products in certain therapeutic areas or altogether. For example, our clinical trials **were** ~~have been~~ adversely affected by the COVID- 19 pandemic ~~. See The COVID- 19 pandemic, and the public and governmental effort to mitigate against the spread of the disease, have had, and are expected to continue to have, an adverse effect, and may have a material adverse effect, on our clinical trials, operations, supply chains, distribution systems, product development, product sales, business and results of operations~~ . If we are unable to market and sell our products or product candidates or to obtain approvals in the timeframe needed to execute our product strategies, our business and results of operations could be materially and adversely affected. We rely on independent third- party clinical investigators to recruit patients and conduct clinical trials on our behalf in accordance with applicable study protocols, laws and regulations. Further, we rely on unaffiliated third- party vendors to perform certain aspects of our clinical trial operations. In some circumstances, we enter into co- development arrangements with other pharmaceutical and medical devices companies that provide for the other company to conduct certain clinical trials for the product we are co- developing or to develop a diagnostic test used in screening or monitoring patients in our clinical trials. See Some of our pharmaceutical pipeline and our commercial product sales rely on collaborations with third parties, which may adversely affect the development and sales of our products. We also may acquire companies that have past or ongoing clinical trials or rights to products or product candidates for which clinical trials have been or are being conducted. These trials may not have been conducted to the same standards as ours; however, once an acquisition has been completed we assume responsibility for the conduct of these trials, including any potential risks and liabilities associated with the past and prospective conduct of those trials. If regulatory authorities determine that we or others, including our licensees or co- development partners, or the independent investigators or vendors selected by us, our co- development partners or by a company we have acquired or from which we have acquired rights to a product or product candidate, have not complied with regulations applicable to the clinical trials, those authorities may refuse or reject some or all of the clinical trial data or take other actions that could delay or otherwise negatively affect our ability to obtain or maintain marketing approval of the product or indication. In addition, delays or failures to develop diagnostic tests for our clinical trials can affect the timely enrollment of such trials and lead to delays or inability to obtain marketing approval. If we were unable to market and sell our products or product candidates, our business and results of operations could be materially and adversely affected. In addition, some of our clinical trials utilize drugs **and combination products** manufactured and marketed by other pharmaceutical companies **or vendors** . These drugs **, devices and / or products** may be administered **or used** in clinical trials in combination with one of our products or product candidates or in a head- to- head study comparing the products' or product candidates' relative efficacy and safety. In the event that any of these vendors or pharmaceutical companies have unforeseen issues that negatively affect the quality of their work product or create a shortage of supply, or if we are otherwise unable to obtain an adequate supply of these other drugs, our ability to complete our applicable clinical trials and / or evaluate clinical results may also be negatively affected. As a result, such quality or supply problems could adversely affect our ability to timely file for, gain or maintain regulatory approvals worldwide. Clinical trials must generally be designed based on the current standard of medical care. However, in certain diseases, such as cancer, the standard of care is evolving rapidly. In some cases, we may design a clinical trial based on the standard of care we anticipate will exist at the time our study is completed. The duration of time needed to complete certain clinical trials may result in the design of such clinical trials being based on standards of medical care that are no longer or that have not become the current standards by the time such trials are completed, limiting the utility and application of such trials. Additionally, the views of regulatory agencies relating to the requirements for accelerated approval may change over time, and trial designs that were sufficient to support accelerated approvals for some oncology products may not be considered sufficient for later candidates. We may not obtain favorable clinical trial results and therefore may not be able to obtain regulatory approval for new product candidates or new indications for existing products and / or maintain our current product labels. Participants in clinical trials of

our products and product candidates may also suffer adverse medical events or side effects that could, among other factors, delay or terminate clinical trial programs and / or require additional or longer trials to gain approval. Even after a product is on the market, safety concerns may require additional or more extensive clinical trials as part of a risk management plan for our product or for approval of a new indication. Additional clinical trials we initiate, including those required by the FDA, could result in substantial additional expense, and the outcomes could result in further label restrictions or the loss of regulatory approval for an approved indication, each of which could have a material adverse effect on our product sales, business and results of operations. Additionally, any negative results from such trials could materially affect the extent of approvals, the use, reimbursement and sales of our products, our business and results of operations. Our business is subject to extensive regulation by numerous state and federal government authorities in the United States, including the FDA, and by foreign regulatory authorities, including the EMA. We are required in the United States and in the other regions and countries in which we, or our partners and affiliates, sell to obtain approval from regulatory authorities before we manufacture, market and sell our products. Once our products are approved, the FDA and other U. S. and ex- U. S. regulatory agencies have substantial authority to require additional testing and reporting, perform inspections, change product labeling or mandate withdrawals of our products. Failure to comply with applicable regulatory requirements may subject us to administrative and / or judicially imposed sanctions or monetary penalties as well as reputational and other harms. The sanctions could include the FDA' s or ex- U. S. regulatory authorities' refusals to approve pending applications, delays in obtaining or withdrawals of approvals, delays or suspensions of clinical trials, warning letters, product recalls or seizures, total or partial suspensions of our operations, injunctions, fines, civil penalties and / or criminal prosecutions. Obtaining and maintaining regulatory approvals have been, and will continue to be, increasingly difficult, time- consuming and costly. Legislative bodies or regulatory agencies could enact new laws or regulations, change existing laws or regulations or change their interpretations of laws or regulations at any time, which could affect our ability to obtain or maintain approval of our products or product candidates. The rate and degree of change in existing laws and regulations and regulatory expectations have accelerated in established markets, and regulatory expectations continue to evolve in emerging markets. We are unable to predict whether and when any further changes to laws or regulatory policies affecting our business could occur, such as changes to laws or regulations governing manufacturer communications concerning drug products and drug product candidates and whether such changes could have a material adverse effect on our product sales, business and results of operations. Further, we are reliant on regulators having the resources necessary to evaluate and approve our products. In the United States, a partial federal government shutdown halted the work of many federal agencies and their employees from late December 2018 through late January 2019. A subsequent extended shutdown could result in reductions or delays of FDA' s activities, including with respect to our ongoing clinical programs, our manufacturing of our products and product candidates and our product approvals. Regulatory authorities have questioned, and may in the future question, the sufficiency for approval of the endpoints we select for our clinical trials. A number of our products and product candidates have been evaluated in clinical trials using surrogate endpoints that measure an effect that is known to correlate with an ultimate clinical benefit. For example, a therapeutic oncology product candidate may be evaluated for its ability to reduce or eliminate minimal residual disease (MRD), or to extend the length of time during and after the treatment that a patient lives without the disease worsening, measured by **progression- free survival (** PFS **)** . Demonstrating that the product candidate induces MRD- negative responses or produces a statistically significant improvement in PFS does not necessarily mean that the product candidate will show a statistically significant improvement in overall survival or the time that the patients remain alive. In the **cardiovascular (** CV **)** setting, a heart disease therapeutic candidate may be evaluated for its ability to reduce LDL- C levels, as an elevated LDL- C level has been a surrogate endpoint for CV events such as death, heart attack and stroke. The use of surrogate endpoints such as PFS and LDL- C reduction, in the absence of other measures of clinical benefit, may not be sufficient for broad usage or approval even when such results are statistically significant. Regulatory authorities could also add new requirements, such as the completion of enrollment in a confirmatory study or the completion of an outcomes study or a meaningful portion of an outcomes study, as conditions for obtaining approval or obtaining an indication. For example, despite demonstrating that Repatha reduced LDL- C levels in a broad patient population, only after our large phase 3 outcomes study evaluating the ability of Repatha to prevent CV events met certain of its primary composite endpoint and key secondary composite endpoint did the FDA grant a broader approval of Repatha to reduce the risk of certain CV events. There may also be situations in which demonstrating the efficacy and safety of a product candidate may not be sufficient to gain regulatory approval unless superiority to other existing treatment options can be shown. The imposition of additional requirements or our inability to meet them in a timely fashion, or at all, has delayed, and may in the future delay, our clinical development and regulatory filing efforts, delay or prevent us from obtaining regulatory approval for new product candidates or new indications for existing products, or prevent us from maintaining our current product labels. Some of our products have been approved by U. S. and ex- U. S. regulatory authorities on an accelerated or conditional basis with full approval conditioned upon fulfilling the requirements of regulators. For example, ~~in May 2021, we announced that~~ the FDA **has** approved LUMAKRAS under accelerated approval for the treatment of adult patients with KRAS G12C- mutated local advanced or metastatic NSCLC ~~, as determined by an~~ **. Following our submission of the LUMAKRAS / LUMYKRAS CodeBreaK 200 Phase 3 confirmatory data submission in March 2023 to the** FDA **and EMA** ~~- approved test~~ , **we** ~~who have~~ received ~~at least one prior systemic therapy. Continued approval for this indication is contingent upon verification and description of clinical benefit in confirmatory trials, including~~ a ~~requirement by~~ **Complete Response Letter from** the FDA **and** ~~that we complete~~ a **new** post- marketing **requirement for** ~~trial to investigate whether a lower dose will have a similar clinical effect to the results demonstrated in our pre- marketing trial. We have since received the data from such post- marketing trial and~~ - **an** ~~intend~~ **additional confirmatory study** to **support full approval** ~~submit it to the FDA, as required~~ . Regulatory authorities are placing greater focus on ~~monitoring~~ **whether the sponsors of** products originally approved on an accelerated or conditional basis ~~and on whether the sponsors of such products~~ have met the conditions of the accelerated or conditional approvals. If we are unable to fulfill the

regulators' requirements that were conditions of a product' s accelerated or conditional approval and / or if regulators reevaluate the data or risk- benefit profile of our product, the conditional approval may not result in full approval or may be revoked or not renewed. Alternatively, we may be required to change the product' s labeled indications **, conduct an additional confirmatory clinical trial,** or even withdraw the product from the market. Regulatory authorities can also impose post- marketing pediatric study requirements. Failure to fulfill such requirements may result in regulatory or enforcement action, including financial penalties or the invalidation of a product' s marketing authorization. Safety problems or signals can arise as our products and product candidates are evaluated in clinical trials, including investigator sponsored studies, or as our marketed products are used in clinical practice. We are required continuously to collect and assess adverse events reported to us and to communicate to regulatory agencies these adverse events and safety signals regarding our products. Regulatory agencies periodically perform inspections of our pharmacovigilance processes, including our adverse event reporting. In the United States, for our products with approved **Risk Evaluation and Mitigation Strategies (** REMS ~~(~~**,** see **Part I,** Item 1. Business — Government Regulation — Postapproval Phase), we are required to submit periodic assessment reports to the FDA to demonstrate that the goals of the REMS are being met. REMS and other risk management programs are designed to help ensure that a drug' s benefits outweigh the risks and vary in the elements they contain. If the FDA is not satisfied with the results of the periodic assessment reports we submit for any of our REMS, the FDA may also modify our REMS or take other regulatory actions, such as implementing revised or restrictive labeling. The drug delivery devices approved for use in combination with our products are also subject to regulatory oversight and review for safety and malfunctions. See Some of our products are used with drug delivery or companion diagnostic devices that have their own regulatory, manufacturing and other risks. If regulatory agencies determine that we or other parties (including our clinical trial investigators, those operating our patient support programs or licensees of our products) have not complied with the applicable reporting, other pharmacovigilance or other safety or quality assessment requirements, we may become subject to additional inspections, warning letters or other enforcement actions, including fines, marketing authorization withdrawal and other penalties. Our product candidates and marketed products can also be affected by safety problems or signals occurring with respect to products that are similar to ours or that implicate an entire class of products. Further, as a result of clinical trials, including sub- analyses or meta- analyses of earlier clinical trials (a meta- analysis involves the use of various statistical methods to combine results from previous separate but related studies) performed by us or others, concerns may arise about the sufficiency of the data or studies underlying a product' s approved label. Such actual or perceived safety problems or concerns can lead to: • revised or restrictive labeling for our products, or the potential for restrictive labeling that has resulted, and may in the future result, in our decision not to commercialize a product candidate; • requirement of risk management or minimization activities or other regulatory agency compliance actions related to the promotion and sale of our products; • post- marketing commitments, mandated post- marketing requirements or pharmacovigilance programs for our approved products; • product recalls of our approved products; • required changes to the processes used in the manufacture of our products, which could increase our manufacturing costs and affect the availability of contract manufacturers we may utilize to assist in such manufacturing; • revocation of approval for our products from the market completely, or within particular therapeutic areas or patient types; • increased timelines or delays in being approved by the FDA or other regulatory bodies; and / or • treatments or product candidates not being approved by regulatory bodies. For example, after an imbalance in positively adjudicated CV serious adverse events was observed in one of the phase 3 clinical trials for EVENITY but not in another, larger phase 3 study, in April 2019 the FDA approved EVENITY for the treatment of osteoporosis in postmenopausal women at high risk for fracture, along with a post- marketing requirement. The requirement includes a five- year observational feasibility study that could be followed by a comparative safety study or trial. In addition to our innovative products, we are working to develop and commercialize biosimilar versions of a number of products currently manufactured, marketed and sold by other pharmaceutical companies. In some markets **outside the United States and EU** , there is not yet a legislative or regulatory pathway for the approval of biosimilars. In the United States, the BPCIA provided for such a pathway. Discussions within the FDA and other regulatory authorities, and between regulatory authorities and sponsors, continue as to the evidence needed to demonstrate biosimilarity or interchangeability for specific products. See We currently face competition from biosimilars and generics and expect to face increasing competition from biosimilars and generics in the future. Delays or uncertainties in the development or implementation of such pathways, or changes in existing regulatory pathways, including degradation of regulatory standards, could result in delays or difficulties in getting our biosimilar products approved by regulatory authorities, subject us to unanticipated development costs or otherwise reduce the value of the investments we have made in the biosimilars area. Further, we cannot predict the extent to which any potential legislative or policy initiatives would affect the biosimilar pathway or have a material adverse effect on our development of biosimilars ~~or ,~~ on our marketed biosimilars **or on our pursuit of interchangeability designations for any biosimilar** . In addition, if we are unable to bring our biosimilar products to market on a timely basis and secure " first- to- market " or other advantageous positions, our future biosimilar sales, business and results of operations could be materially and adversely affected. Many of our products and product candidates may be used in combination with a drug delivery device, such as an injector or other delivery system. For example, Neulasta is available as part of the Neulasta Onpro kit, ~~and~~ our AutoTouch reusable autoinjector is used with ENBREL Mini single- dose prefilled cartridges **, and Repatha can be administered with the Repatha SureClick autoinjector or Pushtronex automated mini doser** . In addition, some of our products or product candidates, including many of our oncology product candidates and products, including LUMAKRAS / LUMYKRAS and bemarituzumab, may also require the use of a companion or other diagnostic device such as a device that determines whether the patient is eligible to use our drug or that helps ensure its safe and effective use. In some regions, including the United States, regulatory authorities may require contemporaneous approval of the companion diagnostic device and the therapeutic product; in others the regulatory authorities may require a separate study of the companion diagnostic device. Our product candidates or expanded indications of our products used with such devices may not be approved or may be substantially delayed in receiving regulatory approval if development or approval of such devices is delayed, such

devices do not also gain or maintain regulatory approval or clearance, or if such devices do not remain commercially available. When approval of the product and device is sought under a single marketing drug application, the increased complexity of the review process may delay receipt of regulatory approval. In addition, some of these devices may be provided by single- source unaffiliated third- party companies. We are dependent on the sustained cooperation and effort of those third- party companies to supply and / or market the devices and, in some cases, to conduct the studies required for approval or clearance by the applicable regulatory agencies. We are also dependent on those third- party companies continuing to meet applicable regulatory or other requirements. Failure to successfully develop, modify, or supply the devices, delays in or failures of the Amgen or third- party studies, or failure of us or the third- party companies to obtain or maintain regulatory approval or clearance of the devices could result in increased development costs; delays in, or failure to obtain or maintain, regulatory approval; and / or associated delays in a product candidate reaching the market or in the addition of new indications for existing products. We are also required to collect and assess user complaints, adverse events and malfunctions regarding our devices, and actual or perceived safety problems or concerns with a device used with our product can lead to regulatory actions and adverse effects on our products. See Our current products and products in development cannot be sold without regulatory approval. Additionally, regulatory agencies conduct routine monitoring and inspections to identify and evaluate potential issues with our devices. For example, in 2017, the FDA reported on its adverse event reporting system that it was evaluating our Neulasta Onpro kit. Subsequently, we implemented device and labeling enhancements to address product complaints received on this device. We continuously monitor complaints and adverse events and implement additional enhancements as needed. Loss of regulatory approval or clearance of a device that is used with our product may also result in the removal of our product from the market. Further, failure to successfully develop, supply, or gain or maintain approval for these devices could adversely affect sales of the related approved products. We depend on alliances with other companies, including pharmaceutical and biotechnology companies, vendors and service providers, for the development of a portion of the products in our pharmaceutical pipeline and for the commercialization and sales of certain of our commercial products. For example, we have collaborations with third parties under which we share development rights, obligations and costs and / or commercial rights and obligations. See Item 1. Business — Business Relationships. Failures by these parties to meet their contractual, regulatory, or other obligations to us or any disruption in the relationships between us and these third parties, could have a material adverse effect on our pharmaceutical pipeline and business. In addition, our collaborative relationships for R & D and / or commercialization and sales often extend for many years and have given, and may in the future give, rise to disputes regarding the relative rights, obligations and revenues of us and our collaboration partners, including the ownership or prosecution of intellectual property and associated rights and obligations. This could result in the loss of intellectual property rights or protection, delay the development and sale of potential pharmaceutical products, affect the sale and delivery of our commercialized products and lead to lengthy and expensive litigation, administrative proceedings or arbitration. ~~We seek innovation through significant investment in both internal R & D and external transactions, including collaborations, partnerships, alliances, licenses, joint ventures, mergers and acquisitions (collectively, acquisition activity). Acquisition activities may be subject to regulatory approvals or other requirements that are not within our control. There can be no assurance that such regulatory or other approvals will be obtained or that all closing conditions required in connection with our acquisition activities will be satisfied or waived, which could result in us being unable to complete the planned acquisition activities. In addition, antitrust scrutiny by regulatory agencies and changes to regulatory approval process in the U. S. and foreign jurisdictions may cause approvals to take longer than anticipated to obtain, not be obtained at all, or contain burdensome conditions, which may jeopardize, delay or reduce the anticipated benefits of acquisitions to us and could impede the execution of our business strategy. Acquisition activities are complex, time consuming and expensive and may result in unanticipated costs, delays or other operational or financial problems related to integrating the acquired company and business with our company, which may divert our management' s attention from other business issues and opportunities and restrict the full realization of the anticipated benefits of such transactions within the expected timeframe or at all. We may pay substantial amounts of cash, incur debt or issue equity securities to pay for acquisition activities, which could adversely affect our liquidity or result in dilution to our stockholders, respectively. Further, failures or difficulties in integrating or retaining new personnel or in integrating the operations of the businesses, products or assets we acquire (including related technology, commercial operations, compliance programs, manufacturing, distribution and general business operations and procedures and ESG activities) may affect our ability to realize the benefits of the transaction and grow our business and may result in us incurring asset impairment or restructuring charges. These and other challenges may arise in connection with our acquisitions of Otezla, Five Prime, Teneobio, ChemoCentryx, Horizon and / or our collaborations with BeiGene and KKC, or with other acquisition activities, which could have a material adverse effect on our business, results of operations and stock price.~~ RISKS RELATED TO OPERATIONS The global supply of our products and product candidates for commercial sales and for use in our clinical trials is significantly dependent on the uninterrupted and efficient operation of our manufacturing facilities, in particular those in the U. S. territory of Puerto Rico and Thousand Oaks, California. See Manufacturing difficulties, disruptions or delays could limit supply of our products and limit our product sales. We currently perform a substantial majority of our clinical manufacturing that supports our product candidates at our facility in Thousand Oaks, California. A substantial disruption in our ability to operate our Thousand Oaks manufacturing facility could materially and adversely affect our ability to supply our product candidates for use in our clinical trials, leading to delays in development of our product candidates. In addition, we currently perform a substantial majority of our commercial manufacturing activities at our facility in the U. S. territory of Puerto Rico. In recent years, Puerto Rico has been affected by a number of natural disasters, including ~~Hurricane~~ **Hurricanes** Maria (2017) **and Fiona (2022)** , **as well as** earthquakes (2020 ~~) and Hurricane Fiona (2022~~). These natural disasters have affected, and may continue to affect, public and private properties and Puerto Rico' s electric grid and communications networks. While the critical manufacturing areas of our commercial manufacturing facility were not significantly affected by these natural disasters, the restoration of electrical service on the island after Hurricane Maria was a

slow process, and our facility relied on backup diesel powered generators for some time. We also operated on backup generators for a few weeks after the early 2020 earthquakes in Puerto Rico. In 2021, the baseload power generation units of the Puerto Rico Electric Power Authority malfunctioned due to the lack of adequate maintenance for over a decade, leading to selective outages across the island. In September 2022, Hurricane Fiona caused further damage to the island' s utility infrastructure which again resulted in widespread power outages and water supply issues. Although these events did not directly have a material effect on our business, they have resulted in disruptions to our third- party suppliers on the island. Further instability of the electric grid could require us to increase our use of our generators or to use them exclusively. In addition, future storms, earthquakes or other natural or man- made disasters or events (including political unrest or labor shortages) could have a more significant effect on our manufacturing operations. The COVID- 19 pandemic ~~has~~ also resulted in disruptions to activities on the island. In March 2020, the Governor of Puerto Rico issued Executive Orders requiring the lockdown of businesses and government facilities, imposing restrictions on business operations and a curfew on residents in response to COVID- 19. Additionally, during the summer of 2021, a labor dispute arose between the maritime terminal operation company and its employees, represented by the International Longshoremen' s Association (ILA), which resulted in a strike that delayed cargo movement from the San Juan Port Zone for several days. Hurricanes Maria and Fiona, the 2020 earthquakes, the COVID- 19 pandemic and the ILA strike have ~~also~~ placed greater stress on the island' s already challenged economy. Beginning in 2016, the government of Puerto Rico defaulted on its roughly $ 72 billion of debt. In response, the U. S. Congress passed the Puerto Rico Oversight, Management, and Economic Stability Act, which established a financial oversight board for Puerto Rico. After years of negotiations with bondholders and other creditors, this financial oversight board reached an agreement with the same, which was confirmed by the U. S. District Court for the District of Puerto Rico effective March 2022. Although our ability to manufacture and supply our products has not, to date, been significantly affected by natural disasters, unreliable electric utility services, strikes, pandemic lockdowns or the island' s economic challenges, these, or a combination of these challenges, or other issues that create a substantial disruption to our ability to operate our Puerto Rico manufacturing facility or get supplies and manufactured products transported to and from that location, could make it more expensive or difficult for us to operate in Puerto Rico, and could materially and adversely affect our ability to supply our products and affect our product sales. See Manufacturing difficulties, disruptions or delays could limit supply of our products and limit our product sales. We rely on unaffiliated third- party suppliers for certain raw materials, medical devices and components necessary for the manufacturing of our commercial and clinical products. Certain of those raw materials, medical devices and components are proprietary products of those unaffiliated third- party suppliers and are specifically cited in our drug applications with regulatory agencies so that they must be obtained from that specific sole source or sources and could not be obtained from another supplier unless and until the regulatory agency approved such supplier. For example, we rely on a single source for the SureClick autoinjectors used in the drug delivery of Repatha, ENBREL, Aimovig, **AMJEVITA /** AMGEVITA and Aranesp **, and we also rely on a single source for the Pushtronex automated mini doser used in the drug delivery of Repatha** . Also, certain of the raw materials required in the commercial and clinical manufacturing of our products are sourced from other countries and / or derived from biological sources, including mammalian tissues, bovine serum and human serum albumin. Among the reasons we may be unable to obtain these raw materials, medical devices and components include: • regulatory requirements or action by regulatory agencies or others; • adverse financial or other strategic developments at or affecting the supplier, including bankruptcy; • unexpected demand for or shortage of raw materials, medical devices or components; • failure to comply with our quality standards which results in quality and product failures **, complaints** , product contamination and / or recall; • a material shortage, contamination, recall and / or restrictions on the use of certain biologically derived substances or other raw materials; • discovery of previously unknown or undetected imperfections in raw materials, medical devices or components; • cyberattacks on supplier systems; • natural or other disasters, including hurricanes, earthquakes, volcanoes or fires; • labor disputes **(such as strikes)** or shortages, including from the effects of health emergencies (such as novel viruses or pandemics ~~such as the one we are currently experiencing with COVID- 19~~) or natural disasters; and • geopolitical conflicts **(such as the ongoing conflicts in Ukraine and the Middle East)** . For example, in prior years we have experienced shortages in certain components necessary for the formulation, fill and finish of certain of our products in our Puerto Rico facility, and we have also experienced shortages related to single use systems and packaging which has caused disruptions to our manufacturing plans. Further quality issues that result in unexpected additional demand for certain components have resulted in shortages and in the future may lead to shortages of required raw materials or components (such as we have experienced with EPOGEN glass vials). We may experience similar or other shortages in the future resulting in delayed shipments, supply constraints, clinical trial delays, contract disputes and / or stock- outs of our products. These or other similar events could negatively affect our ability to satisfy demand for our products or conduct clinical trials, which could have a material adverse effect on our product sales, business and results of operations. Manufacturing biologic and small molecule human therapeutic products is difficult, complex and highly regulated. We manufacture many of our commercial products and product candidates internally. In addition, we ~~currently~~ use third- party contract manufacturers to produce, or assist in the production of, a number of our products, and we currently use contract manufacturers to produce, or assist in the production of, a number of our late- stage product candidates and drug delivery devices. **The number of third- party contract manufacturers that we use has increased with our recent acquisition of Horizon, as Horizon required such contract manufacturers for all of its products.** See Item 1. Business — Manufacturing, Distribution and Raw Materials — Manufacturing **; see also Our efforts to collaborate with or acquire other companies, products, or technology, and to integrate the operations of companies or to support the products or technology we have acquired, may not be successful, and may result in unanticipated costs, delays or failures to realize the benefits of the transactions** . Our ability to adequately and timely manufacture and supply our products (and product candidates to support our clinical trials) is dependent on the uninterrupted and efficient operation of our facilities and those of our third- party contract manufacturers, which may be affected by: • capacity of manufacturing facilities; • contamination by microorganisms or viruses,

or foreign particles from the manufacturing process; • labor disputes or shortages, including the effects of health emergencies (such as novel viruses or pandemics ~~such as the one we are currently experiencing with COVID- 19~~) or natural disasters; • compliance with regulatory requirements; • changes in forecasts of future demand; • timing and actual number of production runs and production success rates and yields; • updates of manufacturing specifications; • contractual disputes with our suppliers and contract manufacturers; • timing and outcome of product quality testing; • power failures and / or other utility failures; • breakdown, failure, substandard performance or improper installation or operation of equipment (including our information technology systems and network- connected control systems or those of our contract manufacturers or third- party service providers); • delays in the ability of the FDA or foreign regulatory agencies to provide us necessary reviews, inspections and approvals, including as a result of a subsequent extended U. S. federal or other government shutdowns; and / or If any of these or other problems affect production in one or more of our facilities or those of our third- party contract manufacturers, or if we do not accurately forecast demand for our products or the amount of our product candidates required in clinical trials, we may be unable to start or increase production in our unaffected facilities to meet demand. If the efficient manufacture and supply of our products or product candidates is interrupted, we may experience delayed shipments, delays in our clinical trials, supply constraints, stock- outs, adverse event trends, contract disputes and / or recalls of our products. From time to time, we have initiated recalls of certain lots of our products. For example, in July 2014 we initiated a voluntary recall of an Aranesp lot distributed in the EU after particles were detected in a quality control sample following distribution of that lot, and in April 2018 we initiated a precautionary recall of two batches of Vectibix distributed in Switzerland after potential crimping defects were discovered in the metal seals on some product vials. If we are at any time unable to provide an uninterrupted supply of our products to patients, we may lose patients and physicians may elect to prescribe competing therapeutics instead of our products, which could have a material adverse effect on our product sales, business and results of operations. Our manufacturing processes, those of our third- party contract manufacturers and those of certain of our third- party service providers must undergo regulatory approval processes and are subject to continued review by the FDA and other regulatory authorities. It can take longer than five years to build, validate and license another manufacturing plant, and it can take longer than three years to qualify and license a new contract manufacturer or service provider. If we elect or are required to make changes to our manufacturing processes because of new regulatory requirements, new interpretations of existing requirements or other reasons, this could increase our manufacturing costs and result in delayed shipments, delays in our clinical trials, supply constraints, stock- outs, adverse event trends or contract negotiations or disputes. Such manufacturing challenges may also occur if our existing contract manufacturers are unable or unwilling to timely implement such changes, or at all. In addition, regulatory agencies conduct routine monitoring and inspections of our manufacturing facilities and processes as well as those of our third-party contract manufacturers and service providers. If regulatory authorities determine that we or our third- party contract manufacturers or certain of our third- party service providers have violated regulations, they may mandate corrective actions and / or issue warning letters, or even restrict, suspend or revoke our prior approvals, prohibiting us from manufacturing our products or conducting clinical trials or selling our marketed products until we or the affected third- party contract manufacturers or third-party service providers comply, or indefinitely. See also Our current products and products in development cannot be sold without regulatory approval. Such issues may also delay the approval of product candidates we have submitted for regulatory review, even if such product candidates are not directly related to the products, devices or processes at issue with regulators. Because our third- party contract manufacturers and certain of our third- party service providers are subject to the FDA and foreign regulatory authorities, alternative qualified third- party contract manufacturers and third- party service providers may not be available on a timely basis, or at all. If we or our third- party contract manufacturers or third- party service providers cease or interrupt production or if our third- party contract manufacturers and third- party service providers fail to supply materials, products or services to us, we may experience delayed shipments, delays in our clinical trials, supply constraints, contract disputes, stock- outs and / or recalls of our products. Additionally, we distribute a substantial volume of our commercial products through our primary distribution centers in Louisville, Kentucky for the United States and in Breda, Netherlands for Europe and much of the rest of the world. We also conduct most of the labeling and packaging of our products distributed in Europe and much of the rest of the world in Breda. Our ability to timely supply products is dependent on the uninterrupted and efficient operations of our distribution and logistics centers, our third- party logistics providers and our labeling and packaging facility in Breda. Further, we rely on commercial transportation, including air and sea freight, for the distribution of our products to our customers, which has been negatively affected by the ~~ongoing~~ COVID- 19 pandemic **, labor unrest,** ~~and may be negatively affected by~~ natural disasters ~~or~~ **and** geopolitical security threats. There have also been legislative and administrative proposals seeking to incentivize greater drug manufacturing in the United States with the stated goal of improving supply reliability in the United States. For example, on August 6, 2020, the previous Administration issued an Executive Order aimed at boosting domestic production of essential medicines, medical countermeasures, and critical inputs titled " Executive Order on Ensuring Essential Medicines, Medical Countermeasures, and Critical Inputs are Made in the United States. " Additionally, one legislative proposal would have prohibited the U. S. Department of Veterans Affairs from purchasing certain drugs that have active pharmaceutical ingredients manufactured outside the United States. While we perform a substantial majority of our commercial manufacturing activities in the United States, including in the U. S. territory of Puerto Rico, and a substantial majority of our clinical manufacturing activities at our facility in Thousand Oaks, California, the passage of such legislation could result in foreign governments enacting retaliatory legislation or regulatory actions, which may have an adverse effect on our product sales, business and results of operations. We continue to work towards operating our business in an environmentally responsible and socially inclusive manner. Stakeholders, including our investors and our employees, have increasingly focused on, and are expected to continue to focus on, our ESG practices. **Policymakers, regulators and investors globally have increased their focus on ESG matters, resulting in rapidly evolving and diverging expectations and standards. For example, California recently enacted the Climate Corporate Data Accountability Act that requires, among other things,**

disclosure of greenhouse gas emissions. In contrast, in other states, there are a growing number of anti- ESG initiatives that may conflict with certain of our stakeholders' expectations. For example, 11 states have enacted laws prohibiting the consideration of ESG factors in connection with state pension asset investment decisions. If our ESG practices fail to meet ~~these~~ **our** stakeholders' expectations and standards **, or if we fail to comply with ESG- related regulations across our global business** , there could be a material adverse effect on our reputation, business and, ultimately, our stock price. Our ESG report is made available on our website and describes our **current** ESG goals and the progress we have made on the ESG issues **that we believe** ~~deemed most important to~~ our external and internal stakeholders **consider to be important** , based on surveys, interviews and certain frameworks for corporate responsibility. Achieving our ESG goals requires long- term investments and broad, coordinated activity, and we may be required to incur additional costs or allocate additional resources towards monitoring, reporting and implementing our ESG ~~practices~~ **programs** . Further, we may fail to accurately assess our stakeholders' ESG priorities **and concerns** , as such priorities **and concerns** have **been rapidly changing** ~~evolved and will continue to evolve~~ . While we have achieved most of our goals set in prior years, whether we can achieve our current and future ESG goals continues to be uncertain and remains subject to numerous risks, including evolving regulatory requirements and social expectations affecting ESG practices, our ability to recruit, develop and retain a diverse workforce, the availability of suppliers and collaboration partners that can meet our ~~ESG~~ **environmental** goals, the effects of the organic growth of our business and potential acquisitions of other businesses on our ESG performance, and the availability and cost of technologies or resources, such as carbon credits, that support our ~~goals. For example, impacts on the commodity market and supply chains caused by the armed conflict in Ukraine could limit the availability of electric vehicle components, impairing our ability to meet some of our environmental sustainability~~ goals. Any failure or perceived failure to meet our ESG program priorities could result in a material adverse effect on our reputation, business and stock price. Many of our operations and facilities, including those essential to our manufacturing, R & D and distribution activities, are in locations that are subject to natural disasters, including droughts, fires, extreme temperatures, hurricanes, tropical storms and / or floods. For example, in 2017 Hurricane Maria caused catastrophic damage, compounded in 2022 by Hurricane Fiona, to the U. S. territory of Puerto Rico, where we perform a substantial majority of our commercial manufacturing activities. Although our site was well- protected and suffered minimal damage, there can be no assurances that we would have similar results in the face of future natural disasters. The severity and frequency of weather- related natural disasters has been amplified, and is expected to continue to be amplified by, global climate change. Such natural disasters have caused, and in the future may cause, damage to and / or disrupt our operations, which may result in a material adverse effect on our product sales, business and results of operations. Our suppliers, vendors and business partners also face similar risks, and any disruption to their operations could have an adverse effect on our supply and manufacturing chain. Further, many of our key facilities are located on islands, including Puerto Rico, Singapore and Ireland, which rely on essential port facilities that may be vulnerable to climate change- related or other natural disasters. Although we have detailed business continuity plans in place and periodic assessments of our natural disaster risk, any natural disaster may also result in prolonged interruption to our critical operational and business activities, and we may be required to incur significant costs to remedy the effects of such natural disasters and fully resume operations, which may result in a material adverse effect on our product sales, business and results of operations. See We perform a substantial majority of our commercial manufacturing activities at our facility in the U. S. territory of Puerto Rico and a substantial majority of our clinical manufacturing activities at our facility in Thousand Oaks, California; significant disruptions or production failures at these facilities could significantly impair our ability to supply our products or continue our clinical trials and Manufacturing difficulties, disruptions or delays could limit supply of our products and limit our product sales. GENERAL RISK FACTORS Our operations and performance have been, and may continue to be, affected by global economic conditions. The economic downturn resulting from the COVID- 19 pandemic precipitated a global recession, ~~and together with~~ **which was followed by** high rates of inflation and ~~energy supply issues experienced~~ **actions taken by financial regulators to raise interest rates. Instability** in ~~certain regions~~ **the financial system** , **tighter lending standards and higher interest rates** have ~~led to regional and / or~~ **added stress that may create additional vulnerabilities in the** global **economy** ~~macroeconomic challenges~~ , the effects of which may be of an extended duration. **Additionally** ~~In particular~~ , ~~acute rising energy costs~~ **with higher interest rates, deficits, and other fiscal pressures, governments** may **be unable to sustain their previously high levels of fiscal spending.** ~~further~~ **Further** ~~adversely affect productivity~~ **, in the United States, although Congress has approved stopgap measures to fund the government through early March, the federal government continues to be at risk of a shutdown if legislation providing funding for the fiscal year is not passed as a result of political divisions in Congress and** ~~and~~ **an** ~~economic conditions in Europe~~ **impasse on budgetary and spending matters** . ~~Additionally~~ **Consequently** , **these and other** financial pressures **have caused, and** may **continue to** cause **,** government or other third- party payers to more aggressively seek cost containment measures in healthcare and other settings. See Our sales depend on coverage and reimbursement from government and commercial third- party payers, and pricing and reimbursement pressures have affected, and are likely to continue to affect, our profitability. As a result of global economic conditions, some third- party payers may delay or be unable to satisfy their reimbursement obligations. Job losses or other economic hardships (including inflation) may also affect patients' ability to afford healthcare as a result of increased co- pay or deductible obligations, greater cost sensitivity to existing co- pay or deductible obligations, lost healthcare insurance coverage or for other reasons. We believe such conditions have led and could continue to lead to reduced demand for our products, which could have a material adverse effect on our product sales, business and results of operations. The current inflationary environment related to increased aggregate demand, supply chain constraints and the effects from the armed conflict in Ukraine (including the effects of the sanctions that were implemented in response to the conflict and the resulting impacts on the commodity market and supply chains) **and the Middle East** have also increased our operating expenses and may continue to affect our operating expenses. Our operational costs, including the cost of energy, materials, labor, distribution and our other operational and facilities costs are subject to market conditions and are being

adversely affected by inflationary pressures. Economic conditions may also adversely affect the ability of our distributors, customers and suppliers to obtain the liquidity required to buy inventory or raw materials and to perform their obligations under agreements with us, which could disrupt our operations. Although we monitor our distributors', customers' and suppliers' financial condition and their liquidity to mitigate our business risks, some of our distributors, customers and suppliers may become insolvent, which could have a material adverse effect on our product sales, business and results of operations. A significant worsening of global economic conditions could precipitate or materially amplify the other risks described herein. We maintain a significant portfolio of investments disclosed as cash equivalents and marketable securities on our consolidated balance sheets. ~~The~~ **In recent years, the** global ~~spread of~~ COVID- 19 ~~has also~~ **pandemic and interest rate increases have** led to disruption and volatility in the global capital markets. We have certain assets, including equity investments, that are exposed to market fluctuations that could, in a sustained or recurrent series of market disruptions, result in impairments. The value of our investments may also be adversely affected by interest rate fluctuations, inflation, downgrades in credit ratings, illiquidity in the capital markets **, geopolitical events** and other factors that may result in other- than- temporary declines in the value of our investments. Any of those events could cause us to record impairment charges with respect to our investment portfolio or to realize losses on sales of investments **. We also maintain a majority of our cash and cash equivalents in accounts with major multi- national financial institutions, and our deposits at these institutions exceed insured limits. Market conditions can adversely affect the viability of these institutions. In the event of failure of any of the financial institutions where we maintain our cash and cash equivalents, there can be no assurance that we would be able to access uninsured funds in a timely manner or at all. Inability to access, or a delay in accessing these funds, could adversely affect our business and financial position** . Our stock price, like that of our peers in the biotechnology and pharmaceutical industries, is volatile. Our revenues and operating results may fluctuate from period to period for a number of reasons. Events such as a delay in product development, changes to our expectations or strategy or even a relatively small revenue shortfall may cause financial results for a period to be below our expectations or projections. As a result, our revenues and operating results and, in turn, our stock price may be subject to significant fluctuations. Announcements or discussions, including via social media channels, of possible restrictive actions by government or private payers that would negatively affect our business or industry if ultimately enacted or adopted may also cause our stock price to fluctuate, whether or not such restrictive actions ever actually occur. Similarly, actual or perceived safety issues with our products or similar products or unexpected clinical trial results can have an immediate and rapid effect on our stock price, whether or not our operating results are materially affected. **53** ~~The capital and credit markets may experience extreme volatility and disruption, which may lead to uncertainty and liquidity issues for both borrowers and investors. For example, early in 2020, there were significant disruptions in the commercial paper market and several borrowers were unable to obtain funding at normal rates or maturities, which resulted in a significant increase in draws of corporate credit lines with banks. Similarly, the bond markets experienced extreme volatility in terms of interest rates and credit spreads, with several days without new issuances of corporate bonds. We expect to access the capital markets, from time to time, to supplement our existing funds and cash generated from operations to satisfy our needs for working capital; capital expenditure and debt service requirements; our plans to pay dividends and repurchase stock; and other business initiatives we strategically plan to pursue, including acquisitions (such as our acquisition of Horizon) and licensing activities. In the event of adverse capital and credit market conditions, we may be unable to obtain capital market financing on similar favorable terms, or at all, which could have a material adverse effect on our business and results of operations or our ability to complete business acquisitions. Changes in credit ratings issued by nationally recognized credit- rating agencies could adversely affect our ability to obtain capital market financing and the cost of such financing and have an adverse effect on the market price of our securities.~~