AstraZeneca

What science can do

AstraZeneca Risk Supplement 2021

Risk

References to Notes and page numbers, and capitalised terms not defined in this supplement, can be found in AstraZeneca's Annual Report and Form 20-F Information 2021 at www.astrazeneca.com/annualreport2021.

Risks and uncertainties

In this section, we describe the risks and uncertainties that we consider material to our business, in that they may have a significant effect on our financial condition, results of operations, and/or reputation.

These risks are not listed in any particular order of priority. We believe that the forward-looking statements about AstraZeneca, identified by words such as 'anticipates', 'believes', 'expects' and 'intends', and that include, among other things, future prospects in the Financial Review on page 52, are based on reasonable assumptions. However, forward-looking statements involve inherent risks and uncertainties such as those summarised below. They relate to events that may occur in the future, that may be influenced by factors beyond our control and that may have actual outcomes materially different from our expectations. Therefore, other risks, unknown or not currently considered material, could have a material adverse effect on our financial condition, results of operations and/or reputation.

Product pipeline risks	Impact
Failure or delay in the delivery of our pipeline or launch of new medicines	
Our continued success depends on the development and successful launch of innovative new drugs. The development of pharmaceutical product candidates is a complex, risky and lengthy process involving significant resources. A project may fail at any stage of the process due to various factors, including: failure to obtain the required regulatory or marketing approvals, unfavourable clinical efficacy data, safety concerns, failure to demonstrate adequate cost-effective benefits to regulatory authorities and/or payers, and the emergence of competing products. More details of projects that have suffered setbacks or failures during 2021, can be found in the Disease Area Review from page 16. Launch activities may be delayed by a number of factors, including: adverse findings in pre-clinical or clinical studies, regulatory demands, price negotiation, large-scale natural disasters or global pandemics, competitor activity and technology transfer. In addition to developing products in-house, we continue to expand our portfolio through licensing arrangements and strategic collaborations which may not ultimately be successful.	Failure or delay in development of new product candidates could damage the reputation of our R&D capabilities, and materially adversely affect our future business and results of operations. See also Failure to achieve strategic plans or meet targets or expectations on page 51. Delays to launches can lead to excess expenses in the manufacture of pre-launch product stocks, marketing materials and sales force training. For the launch of products that are seasonal in nature, delays in regulatory approvals or manufacturing may delay launch to the next season which, in turn, may significantly reduce the return on costs incurred in preparing for the launch for that season. Furthermore, in immuno-oncology in particular, speed to market is critical given the large number of clinical trials being conducted by competitors. Delay of launch can also erode the term of patent exclusivity. Competition from other pharmaceutical companies means that we may have to pay a significant premium over book or market values for our acquisitions. Failure to complete collaborative projects in a timely, cost-effective manner may limit our ability to access a greater portfolio of products, IP, technology and shared expertise. In many cases we make milestone payments in advance of the commercialisation of the products, with no assurance of recouping costs.
Failure to meet regulatory or ethical requirements for medicine development or approval	
We are subject to laws and regulations that control our ability to market our pharmaceutical products. Our development programmes must meet many standards in order to prove that our products are safe, effective and of high quality. These standards vary by country and region. Health authorities, such as the FDA in the US and the EMA in the EU, can refuse to grant approval for our products, or they may require us to conduct additional clinical trials or scientific testing for our products, or provide additional data before they will approve our products for marketing. The EU Clinical Trials Regulation, which is intended to create a favourable environment for conducting clinical trials while maintaining high standards for patient safety, came into application on 31 January 2022. EMA expects pharmaceutical companies to submit product data in Identification of Medicinal Products (IDMP) format, presenting a significant challenge to the industry as the requirements are complex. Many factors influence a health authority's decision to approve or reject a marketing application for a pharmaceutical product. These include: advances in science and technology; new laws, regulations and policies; different standards for evaluating safety and effectiveness by health authorities; and input from the general public and public interest groups.	Delays in regulatory approvals could impact our ability to market our products and may adversely affect our revenue. In addition, post-approval requirements, including additional clinical trials, could result in increased costs. We seek to manage these risks, but policymaking by governments and health authorities is unpredictable at times, and unforeseen circumstances, such as public health emergencies, may strain health authority resources. These factors may delay the approval of our products.
Following approval, a health authority may require us to conduct additional clinical trials or scientific testing to address concerns raised after our products have been used by patients in the marketplace.	New data may impact a product's approval status or lead to labelling changes that may limit the use of a product. While we support transparency efforts to make clinical trial data more publicly accessible, inappropriate or incorrect independent analyses may damage a product's integrity and our Company's reputation.

Commercialisation risks	Impact
Failures or delays in the quality or execution of the Group's commercial strategies	
The successful launch of a new pharmaceutical product involves substantial investment in sales and marketing activities, launch stocks and other areas. We may ultimately be unable to achieve commercial success for various reasons, including: difficulties in manufacturing sufficient quantities of the product candidate for development or commercialisation in a timely manner; the impact of price control measures imposed by governments and healthcare authorities; the outcome of negotiations with third-party payers; erosion of IP rights, including infringement by third parties; failure to show a differentiated product profile and changes in prescribing habits.	Failure to execute our commercial strategies or failure to achieve the level of sales anticipated to recoup launch and development investment, could materially adversely impact our business or results of operations.
The ability to successfully carry out business in emerging markets can be more challenging than in established markets. Such challenges may include: volatility in economic or political climates; inadequate protection against crime (including counterfeiting, corruption and fraud) and inadvertent breaches of local and international law.	Failure to leverage potential opportunities or appropriately manage risks in emerging markets, may materially adversely affect our reputation, business or results of operations.
The commercialisation of biologics and rare disease therapies is often more complex than for small molecule pharmaceutical products, primarily due to differences in the mode of administration, technical aspects of the product, and rapidly changing distribution and reimbursement environments.	Failure to effectively commercialise biologics and rare disease therapies could prevent us realising the full value of a significant proportion of our pipeline, as well as result in delays to launch and material write-offs.
Pricing, affordability, access and competitive pressures	
Operating in more than 100 countries, we are subject to political, socio-economic and financial factors around the world. A sustained global economic downturn may adversely impact our business. Global pressures to reduce healthcare spending mean many of our key markets experience the implementation of various controls, reimbursement mechanisms or cost-containment measures for pharmaceutical products, including: > drug pricing system reforms > restrictive reimbursement policies > payer consolidation in the US > price transparency > reference pricing > expedited approval of generic drugs and introduction of policies which encourage generic utilisation > cost transparency. A summary of the principal aspects of price regulation and how pricing pressures are affecting our business in our most important markets is set out in the Impact section to the right. Geopolitical tensions and the escalation of trade disputes may lead to sanctions, such as the unilateral imposition of tariffs, or non-tariff barriers. Price control measures could have a relatively high impact on our Rare Disease portfolio, given higher annual prices of orphan medicines and small patient populations.	Deterioration of, or lack of improvement in, socio-economic conditions, could adversely affect supply and/or distribution in affected countries, and the ability or willingness of customers to purchase our medicines, putting pressure on price and/or volumes. This could adversely affect our business or results of operations – for example, those health systems most severely impacted by downturn may seek alternative ways to settle their debts at a discount. Other customers may cease to trade, which may result in losses from writing off debts, or a reduction in demand for products. A downturn may exacerbate pressure from governments and other healthcare payers on medicine prices and volumes of sales, and may cause a slowdown in growth, or sales decline, in some markets. For example, in the US, any future changes to the Affordable Care Act (ACA), or any significant spending reductions or cost controls affecting Medicare, Medicaid or other publicly funded or subsidised health programmes, could adversely affect our business and financial results. Additionally, in the US, consolidation and integration of drug distributors, retail pharmacy chains, private insurers, managed care organisations and other purchasing organisations may continue to have an effect on pharmaceutical manufacturers, including AstraZeneca. Another example of commercial pressure is pricing control in China; 119 medicines, including AstraZeneca medicines, were added to the National Reimbursement Drug List (NRDL) in March 2021, with an average price reduction of 51%. Volume-based procurement (VBP) was also expanded in 2021, placing downward pressure on the price of medicines that have lost exclusivity and are facing local competition from Generic Quality Consistency Evaluation (GQCE)-validated products. In Europe, governments continue to implement and expand price control measures for medicines. The EU has also committed to introducing a joint health technology assessment (HTA) review, which may delay reimbursement decisions. In other markets, there has been a trend towards rigorous and consistent application of pricing regulations, including reference pricing and group purchasing. The implementation of tariffs or non-tariff barriers may increase the cost to supply medicines, or reduce the volumes sold in markets, adversely impacting our financial results.

Risk
continued

Supply chain and business execution risks	Impact
Failure to maintain supply of compliant, quality medicines	
Manufacturing and supply difficulties, delays and interruptions, including: > Product demand significantly in excess of what has been forecasted, or supply chain disruptions (e.g. due to natural disasters, COVID-19), may lead to supply shortages. > Delays in construction of new facilities or the expansion of existing facilities to support future demand for our products, including new types of medicine. > The inability to supply products due to a product quality failure (including a failure to manufacture in accordance with Good Manufacturing Practices (GMP) or other regulations) or regulatory compliance action, such as licence withdrawal, product recall or product seizure. > Reliance on third-party suppliers for active ingredients, packaging components etc.	Difficulties with manufacturing and supply, forecasting, distribution or third-party suppliers, may result in product shortages, which may lead to lost product sales and materially adversely affect our reputation and revenues. Even slight variations in components or any part of the manufacturing process may lead to a product that is non-compliant and does not meet quality standards. This could lead to recalls, spoilage, product shortage, regulatory action and/or reputational harm. In the event of insolvency of third-party suppliers, it would be difficult to substitute in a timely manner or at all.
Illegal trade in the Group's medicines	
The illegal trade of our pharmaceutical products, including counterfeiting, tampering, theft and illegal diversion (where products are found in a market where we did not send them and where they are not approved to be sold) may lead to a loss of public confidence in the integrity of our medicines.	Illegal trade could materially adversely affect our reputation, financial performance, and pose a direct risk to patient safety. In addition, concern about this issue may cause some patients to stop taking their medicines, with consequent risks to their health. If we are found liable for breaches in our supply chain, authorities may take action, financial or otherwise, that could restrict the distribution of our products.
Reliance on third-party goods and services	
We spend approximately $20 billion each year with trade suppliers. The spend supports the length of our value chain from discovery to manufacture and commercialisation of our medicines. Many of our business-critical operations, including certain R&D processes, IT systems, HR, finance, tax and accounting services, are outsourced to third-party providers. We are therefore heavily reliant on these third parties, not just to deliver timely and high-quality goods and services, but also to comply with applicable laws and regulations and adhere to our ethical business expectations of third-party providers.	The failure of suppliers to deliver timely goods and services, and to the required level of quality, or the failure of suppliers to cooperate with each other, could materially adversely affect our financial condition or results of operations. Any breach of security, whether physical, cyber or data related, or failure of these third parties to operate in a way that is consistent with laws or regulations, may lead to regulatory penalties, materially affect the results of operations and adversely impact our reputation. Failure to successfully manage either the integration of outsourced services or the transition process of insourcing services from third parties may lead to business disruption.

Supply chain and business execution risks *continued*	Impact
Failure in information technology or cybersecurity	
We are dependent on effective IT systems to support critical business functions. They provide an essential means of safeguarding and communicating data, including critical or strictly confidential information, the confidentiality and integrity of which we rely upon. We must ensure personal data that we or our third-party providers manage is protected and complies with increasingly stringent global privacy laws. Examples of strictly confidential information that we hold includes clinical trial records, personal information, intellectual property, R&D data, and compliance information. The size and complexity of our IT systems, cloud utilisation, and third-party vendors we engage, continue to increase significantly. As a result, such systems are potentially vulnerable to service interruptions and security breaches from attacks by malicious third parties or intentional or inadvertent actions by our employees or vendors. Significant changes in the business footprint or in the implementation of the IT strategy could lead to a temporary loss of capability.	Any significant disruption to these IT systems (including breaches of data security or cybersecurity, failure to integrate new and existing IT systems) or failure to comply with additional requirements under applicable laws, could harm our reputation and materially adversely affect our financial condition or results of operations. While we invest heavily in the protection of our data and IT, we may be unable to prevent breakdowns or breaches which could result in disclosure of confidential information, damage to our reputation, regulatory penalties or sanctions or financial loss. The inability to back up and restore data effectively could lead to permanent loss of data that could in turn result in non-compliance with applicable laws and regulations, and otherwise harm our business.
We increasingly use the internet, digital content, social media, mobile applications, the Internet of Things (IoT), artificial intelligence, and other forms of new technology to process our data and communicate internally and externally.	The accessibility and instantaneous nature of interactions with such media may exacerbate the risk of unauthorised data loss from AstraZeneca. This could lead to the unauthorised or unintentional public disclosure of confidential information which may damage our reputation, adversely affect our business or results of operations, and expose us to legal risks and/or additional legal obligations. Similarly, the involuntary public disclosure of commercially sensitive information could adversely affect our business or results of operations. In addition, negative posts, or comments about us (or, for example, the safety of our products) on social media websites or other digital channels, could harm our reputation, brand image or goodwill.
Privacy legislation in various jurisdictions includes obligations to report data protection breaches, whether intentional or inadvertent, to regulators and affected individuals within expedited timeframes.	Expedited reporting, often before the nature and impact of a data breach can be fully understood, could cause reputational damage and a loss of public trust that may be disproportionate to the extent of the breach.
We and our vendors could be susceptible to third-party or internal attacks on our information security systems. Such attacks are of ever-increasing levels of sophistication and are made by groups and individuals with a wide range of motives and expertise, including organised criminal groups, 'hacktivists', nation states, employees and others. Occasionally we experience intrusions, including as a result of computer-related malware.	Although we maintain cybersecurity insurance, there can be no guarantee that our insurance coverage limits will protect against any future claim or that such insurance proceeds will be paid to us in a timely manner.
Failure of critical processes	
Unexpected events and/or events beyond our control could result in the failure of critical processes within the Company or at third parties on whom we are reliant. The business faces threats to business continuity from many directions. Examples of material threats include: > Disruption to our business or the global markets if there is instability in a particular geographic region, including as a result of war, terrorism, pandemics, armed conflicts, riots, unstable governments, civil insurrection or social unrest. > Natural disasters in areas of the world prone to extreme weather events, which may increase in frequency or severity as a result of climate change, and such phenomena as earthquakes. > Cyber threats similar to those detailed in the 'Failure in information technology or cybersecurity' section above.	Crystallisation of such material threats may heighten certain other risks, such as those relating to the delivery of the pipeline or launch of new medicines or the manufacture and supply of medicines, and may lead to loss of revenue and have an adverse impact on our financial results.

Supply chain and business execution risks *continued*	Impact
Failure to collect and manage data in line with legal and regulatory requirements and strategic objectives	
AstraZeneca is obliged to meet legal, regulatory and ethical requirements when it collects, shares and utilises personal information and is required to operate a privacy framework, deploying people, processes and technology to manage and mitigate privacy risks. The COVID-19 pandemic has exacerbated privacy risks, changing practices relating to the collection and sharing of sensitive health data, including our employees' health data, and accelerated third-party due diligence of COVID-19 related suppliers.	Failure to demonstrate how AstraZeneca meets these obligations could cause reputational damage, significant regulatory sanctions, reduced ability to utilise personal data for scientific and business purposes and prevent access to wider industry data-sharing initiatives. Given the evolving external and internal data environment it is important that AstraZeneca ensures that there is a consistent level of engagement of senior data ownership and stewardship across the different business areas, aligned to the data risk profile.
Evolving third-party relationships beyond the traditional vendor/supplier model and the increased use of digital solutions and applications represents privacy challenges. In addition, there is increasing regulatory interest in emerging technologies, including a move towards regulations relating to the utilisation of Artificial Intelligence (AI) and data other than personal data. This will require appropriate updates to AstraZeneca's approach and capabilities in these areas.	Partnerships with entities such as smaller biotech companies and start-ups in hubs and emerging markets, potentially with less mature privacy regulations and varying ethical standards, may impact our ability to demonstrate compliance with core privacy requirements. In addition, greater reliance on third-parties means less direct oversight of day-to-day conduct and compliance, with a need for enhanced third-party risk management.
We continue to see regulatory developments that impact the ability for personal data to be shared freely across international borders. Recent examples include data localisation requirements in China's new personal information law, alongside new EU regulatory guidance further limiting the ability to transfer personal data from the EU to the rest of the world.	Responding to these developments in the short term will require additional controls around personal information transfers, including the use of contractual commitments with third-parties and the deployment of additional technical measures. Long term we may see a trend to more local data storage and access including regional data centres.
Failure to attract, develop, engage and retain a diverse, talented and capable workforce	
We rely heavily on recruiting and retaining talented employees with a diverse range of skills and capabilities to meet our strategic objectives. There is intense competition for well-qualified individuals, as the supply of people with certain skills or in specific geographic regions may be limited.	The inability to attract and retain highly-skilled personnel may weaken our succession plans for critical positions in the medium term, may materially adversely affect the implementation of our strategic objectives, and could ultimately impact our business or results of operations.
The successful delivery of our business objectives is dependent on high levels of engagement and commitment of the workforce, particularly as employees return to working in office locations following the pandemic. In addition, we need to effectively integrate Alexion employees to ensure they are engaged and committed to the AstraZeneca business priorities.	Failure to engage effectively with our employees could lead to business disruption in our day-to-day operations, reduce levels of productivity and/or increase levels of voluntary turnover, all of which could ultimately materially adversely affect our business or results of operations.

Legal, regulatory and compliance risks	Impact
Failure to meet regulatory or ethical expectations on environmental impact, including climate change	
Environmental issues will become more material in the marketplace as the wider healthcare system embraces net-zero climate targets. The environmental targets and performance of our business will come under increased scrutiny by investors, governments and non-governmental organisations. Environmental considerations are starting to become embedded in the public procurement of goods and services, including medicinal products and devices. Specific intermediates used to manufacture medicines, or those used as excipients or propellants, are coming under increased regulation and some may be subject to time-limited exemptions or potential phase-out. The physical impacts of climate change could impact the resilience of our business operations and supply chain.	Investors will increasingly target companies with strong Environmental, Social and Governance (ESG) performance. We continue to see an increased requirement to disclose our ESG strategy, targets and performance. This includes a requirement to quantify the impact of specific ESG issues on our business and associated mitigation plans (e.g. the impact of climate change through TCFD and CDP). Failure to maximise the sustainability credentials of our business, products and the processes used to make our medicines could expose us to increased regulatory risk, and put us at a commercial disadvantage relative to our peers. This could adversely impact our financial results. Failure to proactively manage the physical risks associated with climate change could impact the resilience of our operations and supply chain. This could result in supply interruptions, loss of stock and adversely impact our financial results.

Legal, regulatory and compliance risks *continued*	Impact

Safety and efficacy of marketed medicines is questioned

Our ability to accurately assess, prior to launch, the eventual safety or efficacy of a new product once in broader clinical use can only be based on data available at that time, which is inherently limited due to relatively short periods of product testing and relatively small clinical study patient samples.

Any unforeseen safety concerns or adverse events relating to our products, or failure to comply with laws, rules and regulations relating to provision of appropriate warnings concerning the dangers and risks of our products that result in injuries, could expose us to large product liability damages claims, settlements and awards, particularly in the US. Adverse publicity relating to the safety of a product, or of other competing products, may increase the risk of product liability claims.

Details of material product liability litigation matters can be found in Note 30 to the Financial Statements from page 189.

Serious safety concerns or adverse events relating to our products could lead to product recalls, seizures, loss of product approvals, declining sales and interruption of supply, and could materially adversely impact patient access, our reputation and financial revenues.

Significant product liability claims could also arise which could be costly, divert management attention, or damage our reputation and demand for our products.

Unfavourable resolution of such current and similar future product liability claims could subject us to enhanced damages, consumer fraud and/or other claims, including civil and criminal governmental actions. This could require us to make significant provisions in our accounts relating to legal proceedings, and could materially adversely affect our financial condition or results of operations, particularly where such circumstances are not covered by insurance.

For more information, see the Unexpected deterioration in the Group's financial position on page 7 of the Risk Supplement.

Adverse outcome of litigation and/or governmental investigations

We may be subject to various legal proceedings and governmental investigations. Our many business operations are subject to a wide range of laws, rules and regulations from around the world. Any failure to comply with these applicable laws, rules and regulations may result in AstraZeneca being investigated by relevant governmental agencies and authorities and/or subject to legal proceedings brought by private citizens. Relevant authorities have wide-ranging administrative powers to deal with any failure to comply with continuing regulatory oversight and this could affect us, whether such failure is our own or that of our contractors or external partners. In particular, the manufacturing, marketing, exportation, promotional, clinical, pharmacovigilance, and pricing practices of pharmaceutical manufacturers, as well as the manner in which manufacturers interact with regulatory agencies, purchasers, prescribers and patients, are subject to extensive regulation, litigation and governmental investigation. Moreover, such laws, rules and regulations are subject to change.

Many companies, including AstraZeneca, have been subject to legal claims asserted by federal and state governmental authorities and private payers and consumers, which have resulted in substantial expense and other significant consequences. Governmental investigations or proceedings could result in us becoming subject to civil or criminal sanctions and/or being forced to pay fines or damages. Civil litigation, particularly in the US, is inherently unpredictable and unexpectedly high awards for damages can result from an adverse result. In many cases, litigation adversaries may claim enhanced damages in extremely high amounts. Government investigations, litigations, and other legal proceedings, regardless of their outcome, could be costly, divert management attention, or damage our reputation and demand for our products. Note 30 to the Financial Statements from page 189 describes the material legal proceedings in which we are currently involved. Unfavourable resolution of current and similar future proceedings against us could subject us to criminal liability, fines, penalties or other monetary or non-monetary remedies, including enhanced damages, require us to make significant provisions in our accounts relating to legal proceedings and could materially adversely affect our business or results of operations.

IP-related risks to our products

IP protection provides the foundation for continued investment in developing innovative medicines to improve patient health. However, the pharmaceutical industry is experiencing pressure from governments and other healthcare payers to impose limits on IP protections in an effort to manage healthcare costs. Additionally, policymakers are progressively leveraging regulations to expedite the approval of generic drugs and encourage generic drug utilisation. These policies may drive accelerated utilisation of generic alternatives to our products following expiry or loss of our IP rights. We also recognise increasing use of compulsory licensing in some countries in which we operate.

We are subject to numerous patent challenges relating to various products or processes and assertions of non-infringement of our patents. A loss in any of these challenges could result in loss of patent protection on the covered product, and a risk to the revenue generated by the product. We also face the risk that our products may be found to infringe patents owned or licensed by third parties and be subject to monetary damages, or compelled to cease sales of the infringing product, resulting in a potential risk to revenue.

These challenges threaten the value of our investment in pharmaceutical development.

Details of material patent litigation matters can be found in Note 30 to the Financial Statements from page 189.

Following expiry of our IP rights, or if we are unable to obtain, defend and enforce IP that protects our products, we may experience accelerated and intensified competition from third parties. Also, if our products are found to infringe a third-party patent, we may be subject to monetary damages or compelled to cease sales of the infringing product. These negative outcomes could have an adverse, material impact on our financial results.

Economic and financial risks	Impact
Failure to achieve strategic plans or meet targets or expectations	
From time to time, we communicate our business strategy, our targets or performance expectations (for example, the expectations described in Future prospects in the Financial Review on page 66). All such statements are of a forward-looking nature and based on assumptions and judgements, all of which are subject to significant inherent risks and uncertainties.	There can be no guarantee that our financial targets or expectations will materialise. Actual results may deviate materially and adversely from any target or expectation. Any failure to successfully implement our business strategy may frustrate the achievement of our targets, which may therefore materially damage our brand, business, financial position or results of operations.
Following the acquisition of Alexion in July 2021, we may experience difficulties in integrating geographically separated organisations, systems and facilities, and personnel with different organisational cultures.	Failure to effectively integrate Alexion into the Group may delay the realisation of anticipated benefits from the acquisition, incur higher than anticipated costs of integration, or result in ongoing operational inefficiencies which may adversely impact the results of operations. Furthermore, our reported results of operations may be negatively impacted from acquisition-related charges, amortisation of expenses related to intangibles, charges for the implementation of long-term assets, or previously unknown or unidentified contingent liabilities.
Failure in financial control or the occurrence of fraud	
Effective internal controls assist in the provision of reliable Financial Statements and the detection and prevention of fraud. Testing of internal controls provide only limited assurance over the accuracy of Financial Statements and may not prevent or detect misstatements or fraud.	Significant resources may be required to remediate any deficiency in internal controls. Any such deficiency may trigger related investigations and may result in fines being levied against individual directors or officers. Serious fraud may lead to prosecution of senior management.
Unexpected deterioration in the Group's financial position	
Product sales in countries other than the US are predominantly in currencies other than the US dollar, including the Chinese renminbi, the euro, Japanese yen and pound sterling.	Currency fluctuations can significantly affect our results of operations, which are reported in US dollars. Movements in exchange rates against the US dollar may materially adversely affect our financial condition or results of operations.
A number of our existing or future commercial agreements, such as borrowings, derivative financial instruments and commercial contracts, utilise or may utilise various London Interbank Offered Rates (LIBOR), or other similar rates as benchmark reference rates. These rates are the subject of ongoing regulatory reform, the result of which is expected to see some or all of them partially or fully replaced by alternative reference rates.	This may result in potential adjustments or renegotiations being necessary to our agreements. While different alternative reference rates are developing, there is a risk that we fail to renegotiate or adjust our agreements. This could have an adverse effect on the cost, cash flows, value, return on and trading market of (as appropriate) our borrowings, derivative financial instruments and other agreements.
The majority of our cash investments are managed centrally and are invested in AAA credit-rated institutional money market funds, collateralised bank deposits, fixed income securities in government, and financial and non-financial securities. This means our credit exposure is a mix of US, EU and rest of world sovereign default risk, financial institution and non-financial institution default risk.	In a sustained economic downturn, financial institutions may cease to trade and there can be no guarantee that we will be able to access monies owed to us.
Our consolidated balance sheet contains significant investments in intangible assets, including goodwill. The pharmaceutical business is high risk, and we invest in a large number of projects in an effort to develop a successful portfolio of approved products. Our ability to realise value on these investments depends on regulatory approvals, market acceptance, competition and legal developments.	We expect that some of our intangible assets will become impaired in the future. Impairment losses may materially adversely affect our financial condition or results of operations. Details of the carrying values of goodwill and intangible assets are included in Notes 9 and 10 to the Financial Statements from page 156.
Our defined benefit post-retirement obligations (the most significant of which are for the UK, Sweden and US) can materially change in value, but are largely backed by invested assets.	Solvency levels could fall, leading to higher contributions if there are: falls in assets; increases in liability valuations (driven by falls in bond yields, increases in future inflation or lower than expected mortality); or changes in regulations. A material increase in deficit may cause credit agencies to downgrade our rating, negatively affecting our ability to borrow. Note 22 from page 168 has further details.

Economic and financial risks *continued*	Impact
Unexpected deterioration in the Group's financial position *continued*	
We maintain relevant insurance coverage for risks arising within the Group.	Financial liabilities arising where we do not have insurance coverage, or where an insurer successfully denies coverage, could materially adversely affect our financial condition. For more information, see Adverse outcome of litigation and/or governmental investigations on page 6 of this Risk Supplement.
Revenue authorities can make conflicting claims as to the profits to be taxed in individual countries. The Organisation for Economic Co-operation and Development (OECD) has introduced a number of changes under the Base Erosion and Profit Shifting (BEPS) Action Plans which are now being progressively implemented by tax authorities around the world. In December 2021, the OECD published the Global Anti-Base Erosion (GloBE) rules, setting out the framework the 130 countries which are members of the Inclusive Framework are expected to introduce from 2023, which taxes profits of large groups at a minimum rate of 15% in each country in which they operate. It is also considering further potential actions, which would potentially include allocating taxing rights over a higher proportion of profits to end market jurisdictions, and is now seeking a consensus amongst the Inclusive Framework members on those changes.	The resolution of tax disputes regarding the profits to be taxed in individual territories can result in a reallocation of profits or losses between jurisdictions, or even double taxation, and an increase or decrease in related tax costs, and has the potential to affect our cash flows, EPS and post-tax earnings. Claims, regardless of their merits or their outcome, are costly, divert management attention and may adversely affect our reputation. If tax treaties are withdrawn or amended, this could materially adversely affect our financial condition or results of operations, as could a negative outcome of a tax dispute or a failure by tax authorities to agree to eliminate double taxation. Changes to the application of tax treaties or the availability of the EU arbitration convention following Brexit could also result in adverse consequences, such as those described above. For more information, see Financial Review on page 66 for tax risk management policies and Note 30 to the Financial Statements from page 195 for details of current tax disputes. Changes in tax regimes could result in a material impact on the Group's cash tax liabilities and tax charge, resulting in either an increase or a reduction in financial results. Specific OECD BEPS recommendations that we expect to impact the Group include changes to patent box regimes, restrictions of interest deductibility, global minimum tax rate and revised transfer pricing guidelines allocating more profits to end user markets.