

ASTRAZENECA PLC
Form 6-K
March 20, 2014

FORM 6-K

SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Report of Foreign Issuer

Pursuant to Rule 13a-16 or 15d-16 of
the Securities Exchange Act of 1934

For the month of March 2014

Commission File Number: 001-11960

AstraZeneca PLC

2 Kingdom Street, London W2 6BD

Indicate by check mark whether the registrant files or will file annual reports under cover of Form 20-F or Form 40-F.

Form 20-F Form 40-F

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(1):

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(7): _____

Indicate by check mark whether the registrant by furnishing the information contained in this Form is also thereby furnishing the information to the Commission pursuant to Rule 12g3-2(b) under the Securities Exchange Act of 1934.

Yes No

If "Yes" is marked, indicate below the file number assigned to the Registrant in connection with Rule 12g3-2(b): 82-_____

ANNUAL FINANCIAL REPORT

AstraZeneca PLC (the Company) announced today the publication of its Annual Report and Form 20-F Information 2013 (Annual Report); Notice of Annual General Meeting 2014 and Shareholders' Circular; a covering letter from the Chairman; and 'AstraZeneca 2013 In Brief'.

Copies of the documents have been submitted to the National Storage Mechanism and will shortly be available for inspection at www.morningstar.co.uk/uk/nsm. The documents will be despatched to shareholders shortly. The documents are also available on the Company's website at www.astrazeneca.com/agm.

The meeting place for the Annual General Meeting (AGM) will be the Lancaster London Hotel, Lancaster Terrace, London, W2 2TY and the AGM will commence at 2.30 pm (BST) on 24 April 2014.

EXPLANATORY NOTE AND WARNING

Solely for the purposes of complying with Disclosure Rules and Transparency Rules (DTR) 6.3.5R and the requirements it imposes on issuers as to how to make public annual financial reports, we set out below:

- in Appendix A, the principal risks and uncertainties facing the Company;
- in Appendix B, the Directors' responsibility statement made in respect of the Financial Statements and Directors' Report contained in the Annual Report; and
- in Appendix C, a statement regarding related party transactions.

The appendices have been extracted from the Annual Report in unedited full text. This information should be read in conjunction with the Company's fourth quarter and full year results 2013 announcement, issued on 6 February 2014, which contained a condensed set of financial statements and which can be found at www.astrazeneca.com/Investors/financial-information/Financial-results. Together, these constitute the material required by DTR 6.3.5R to be communicated to the media in unedited full text through a Regulatory Information Service.

Page numbers and section cross-references in the appendices refer to pages and sections in the Annual Report. Defined terms used in the appendices refer to terms as defined in the Annual Report.

This material is not a substitute for reading the full Annual Report.

A C N Kemp
Company Secretary
20 March 2014

APPENDIX A

Principal risks and uncertainties

Operating in the pharmaceutical sector carries a number of inherent risks and uncertainties that may affect our business. In the remainder of this section we describe the principal risks and uncertainties which we consider to be 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. Other risks, unknown or not currently considered material, could have a similar effect. We believe that the forward-looking statements about AstraZeneca in this Annual Report, identified by words such as 'anticipates', 'believes', 'expects' and 'intends', and that include, among other things, the statements made in the Chairman's Statement - Outlook on page 7, and Our strategic priorities - Financial expectations on page 17, 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.

Product pipeline risks

Failure to meet development targets

The development of any pharmaceutical product candidate is a complex, risky and lengthy process involving significant financial, R&D and other resources, which may fail at any stage of the process due to a number of factors. These include: failure to obtain the required regulatory or marketing approvals for the product candidate or its manufacturing facilities; unfavourable clinical efficacy data; safety concerns; failure of R&D to develop new product candidates; failure to demonstrate adequate cost-effective benefits to reimbursement authorities; and the emergence of competing products.

Production and release schedules for biologics may be more significantly impacted by regulatory processes than other products. This is due to more complex and stringent regulation on the manufacturing of biologics and their supply chain.

Difficulties of obtaining and maintaining regulatory approvals for new products

We are subject to strict controls on the commercialisation processes for our pharmaceutical products, including their development, manufacture, distribution and marketing. Safety, efficacy and quality must be established before a drug can be marketed for a given indication. The criteria for establishing safety, efficacy and quality may vary by country or region and the submission of an application to regulatory authorities may or may not lead to the grant of marketing approval. Regulators can refuse to grant approval or may require additional data before approval is given, even though the medicine may already be launched in other countries. Approved products are also subject to regulations, and a failure to comply can potentially result in losing regulatory approval to market our products.

Impact

A succession of negative drug project results and a failure to reduce development timelines effectively, or produce new products that achieve commercial success, could adversely affect the reputation of our R&D capabilities, and is likely to materially adversely affect our business or results of operations.

Impact

The predictability of the outcome and timing of review processes remains challenging due to evolving regulatory science, competing regulatory priorities and downward pressure on health authority resources.

Delays in regulatory reviews and approvals could impact patient and market access. In addition, the increase in post-approval activities requires increased resources and could impact the labelling and approval status of currently marketed products.

Factors including advances in science and technology, evolving regulatory science, and changes in benefit/risk tolerance by health authorities, the general public, and other third party public interest groups influence the initial approvability of new drugs. Existing marketed products are also subject to these same forces, and new data and meta-analyses have the potential to drive changes in the approval status or labelling. Recent years have seen an increase in post-marketing regulatory requirements and commitments, and an increased call for third party access to regulatory and clinical trial data packages for independent analysis and interpretation.

Failure to obtain and enforce effective IP protection

Our ability to obtain and enforce patents and other IP rights in relation to our products is an important element of our ability to protect our investment in R&D and create long-term value for the business. A number of the countries in which we operate are still developing their IP laws or may even be limiting the applicability of these laws to pharmaceutical inventions. Adverse political perspectives on the desirability of strong IP protection for pharmaceuticals in certain emerging and even developed markets may limit the scope for us to obtain effective IP protection for our products. As a result, certain countries may seek to limit or deny effective IP protection for pharmaceuticals.

Delay to new product launches

Our continued success depends on the development and successful launch of innovative new drugs. The anticipated launch dates of major new products have a significant impact on a number of areas of our business, including investment in large clinical studies, the manufacture of pre-launch product stocks, investment in marketing materials pre-launch, sales force training and the timing of anticipated future revenue streams from new product sales. These launch dates are primarily driven by the development programmes that we run and the demands of the regulatory authorities in the approvals process, as well as pricing negotiations. Delays to anticipated launch dates can result from a number of factors including adverse findings in pre-clinical or clinical studies, regulatory demands, price negotiation, competitor activity and technology transfer.

Strategic alliances and acquisitions may be unsuccessful

We seek technology licensing arrangements and strategic collaborations to expand our product portfolio and geographical presence as part of our business strategy.

Impact

Limitations on the availability of patent protection or the use of compulsory licensing in certain countries in which we operate could have a material adverse effect on the pricing and sales of our products and, consequently, could materially adversely affect our revenues from those products. More information about protecting our IP is contained in the Intellectual Property section on page 72. Information about the risk of patent litigation and the early loss of IP rights is contained in the Expiry or loss of, or limitations on, IP rights risk on page 204.

Impact

Significant delays to anticipated launch dates of new products could have a material adverse effect on our financial condition and/or results of operations. For example, for the launch of products that are seasonal in nature, delays in regulatory approvals or manufacturing difficulties 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. In addition, a delay in the launch may lead to increased costs if, for example, marketing and sales efforts need to be rescheduled or protracted for longer than expected.

Impact

If we fail to complete these types of collaborative projects in a timely manner, on a cost-effective basis, or at all, this may limit our ability to access a greater portfolio of products, IP technology and

Such licensing arrangements and strategic collaborations are key, enabling us to grow and strengthen the business. The success of such arrangements is largely dependent on the technology and other IP we acquire rights to, and the resources, efforts and skills of our partners. Also, under many of our strategic alliances, we make milestone payments well in advance of the commercialisation of the products, with no assurance that we will recoup these payments.

Furthermore, we experience strong competition from other pharmaceutical companies in respect of licensing arrangements, strategic collaborations, and acquisition targets, and therefore, we may be unsuccessful in implementing some of our intended projects.

We may also seek to acquire complementary businesses as part of our business strategy. The integration of an acquired business could involve incurring significant debt and unknown or contingent liabilities, as well as having a negative effect on our reported results of operations from acquisition related charges, amortisation of expenses related to intangibles and charges for the implementation of long-term assets. We may also experience difficulties in integrating geographically separated organisations, systems and facilities, and personnel with different organisational cultures.

Commercialisation and business execution risks

Challenges to achieving commercial success of new products

The successful launch of a new pharmaceutical product involves substantial investment in sales and marketing activities, launch stocks and other items. The commercial success of our new medicines is of particular importance to us in order to replace lost sales following patent expiry. We may ultimately be unable to achieve commercial success for any number of reasons. These include 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 and failure to show a differentiated product profile.

As a result, we cannot be certain that compounds currently under development will achieve success, and our ability to accurately assess, prior to launch, the eventual efficacy or safety 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.

The commercialisation of biologics is often more complex than for small molecule pharmaceutical products, primarily due to

shared expertise.

Additionally, disputes or difficulties in our relationship with our collaborators or partners may arise, often due to conflicting priorities or conflicts of interest between parties, which may erode or eliminate the benefits of these alliances.

The incurrence of significant debt or liabilities as a result of integration of an acquired business could cause deterioration in our credit rating and result in increased borrowing costs and interest expense.

Further, if, following an acquisition, liabilities are uncovered in the acquired business, the Group may suffer losses and may not have remedies against the seller or third parties. The integration process may also result in business disruption, diversion of management resources, the loss of key employees and other issues, such as a failure to integrate IT and other systems.

Impact

If a new product does not succeed as anticipated or its rate of sales growth is slower than anticipated, there is a risk that we may be unable to fully recoup the costs incurred in launching it, which could materially adversely affect our business or results of operations.

Due to the complexity of the commercialisation process for biologics, the methods of distributing and marketing biologics could materially adversely impact our revenues from the sales of products, such as Synagis and FluMist/Fluenz.

differences in the mode of administration, technical aspects of the product and rapidly changing distribution and reimbursement environments.

Illegal trade in our products

Illegal trade covers the theft, illegal diversion and counterfeiting of our products. Illegal trade in pharmaceutical products is estimated to exceed \$75 billion per year and is generally considered by the industry, non-governmental organisations and governmental authorities to be increasing. We suffer a commensurate financial exposure to illegal trade and there is also a risk to public health. Regulators and the public expect us to secure the integrity of our supply chain and to co-operate actively in the reduction of illegal trade in AstraZeneca products, through surveillance, investigation and legal action against others engaged in illegal trade.

Developing our business in Emerging Markets

The development of our business in Emerging Markets is a critical factor in determining our future ability to sustain or increase our global product revenues. This poses various challenges including: more volatile economic conditions; competition from multinational and local companies with existing market presence; the need to identify correctly and to leverage appropriate opportunities for sales and marketing; poor IP protection; inadequate protection against crime (including counterfeiting, corruption and fraud); the need to impose developed market compliance standards; the need to meet a more diverse range of national regulatory, clinical and manufacturing requirements; inadvertent breaches of local and international law; not being able to recruit appropriately skilled and experienced personnel; identification of the most effective sales channels and route to market; and interventions by national governments or regulators restricting access to market and/or introducing adverse price controls.

Expiry or loss of, or limitations on, IP rights

Pharmaceutical products are only protected from being copied during the limited period of protection under patent rights and/or related IP rights such as Regulatory Data Protection or orphan drug status. Expiry or loss of these rights typically leads to the immediate launch of generic copies of the product in the country where the rights have expired or been lost. See the Patent Expiries section on page 198, which contains a table of certain patent expiry dates for our key marketed products.

Impact

Public loss of confidence in the integrity of pharmaceutical products as a result of counterfeiting could materially adversely affect our reputation and financial performance. In addition, undue or misplaced concern about the issue may induce some patients to stop taking their medicines, with consequential risks to their health. There is also a direct financial loss where counterfeit medicines replace sales of genuine products and where genuine products are recalled following discovery of counterfeit, stolen and/or illegally traded products in an effort to regain control of the integrity of the supply chain.

Impact

The failure to exploit potential opportunities appropriately in Emerging Markets may materially adversely affect our reputation, business or results of operations.

Impact

Products under patent protection or within the period of Regulatory Data Protection typically generate significantly higher revenues than those not protected by such rights. Our revenues, financial condition and results of operations may be materially adversely affected upon expiry or early loss of our IP rights, due to generic entrants into the market for the applicable product. Additionally, the loss of patent rights covering major products of

Additionally, the expiry or loss of patents covering other innovator companies' products may also lead to increased competition for our own, still-patented, products in the same product class due to the availability of generic products in that product class. Further, there may be increased pricing pressure on our still-patented products as a result of the lower prices of generic entrants.

other pharmaceutical companies may materially adversely affect the growth of our still-patented products in the same product class in that market.

Pressures resulting from generic competition

Impact

Our products compete not only with other products approved for the same condition, marketed by research-based pharmaceutical companies, but also with generic drugs marketed by generic pharmaceutical manufacturers. These competitors may invest more of their resources into the marketing of their products than we do depending on the relative priority of these competitor products within their company's portfolio. Generic versions of products are often sold at lower prices than branded products as the manufacturer does not have to recoup the significant cost of R&D investment and market development. The majority of our patented products, including Nexium, Crestor and Seroquel XR, are subject to price pressures as a result of competition from generic copies of these products and from generic forms of other drugs in the same product class (for example, generic forms of Losec/Prilosec and Lipitor, and generic forms of Seroquel IR).

If challenges to our patents by generic drug manufacturers succeed and generic products are launched, or generic products are launched 'at risk' on the expectation that challenges to our IP will be successful, this may materially adversely affect our financial condition and results of operations. In 2013, US sales for Nexium, Crestor and Seroquel XR were \$2,123 million (2012: \$2,272 million), \$2,912 million (2012: \$3,164 million), and \$743 million (2012: \$811 million), respectively. Furthermore, if limitations on the availability, scope or enforceability of patent protection are implemented in jurisdictions in which we operate, generic manufacturers in these countries may be increasingly able to introduce competing products to the market earlier than they would have been able to, had more robust patent or Regulatory Data Protection been available.

As well as facing generic competition upon expiry or loss of IP rights, we also face the risk that generic drug manufacturers seek to market generic versions of our products prior to expiries of our patents and/or the Regulatory Exclusivity periods. For example, we are currently facing challenges in the US from numerous generic drug manufacturers regarding our patents for Nexium and Pulmicort, two of our key products. Generic manufacturers may also take advantage of the failure of certain countries to properly enforce Regulatory Data Protection and may launch generics during this protected period. This is a particular risk in some Emerging Markets where appropriate patent protection may be difficult to obtain or enforce.

Effects of patent litigation in respect of IP rights

Impact

Any of the IP rights protecting our products may be asserted or challenged in IP litigation initiated against or by external parties. Such IP rights may also be the subject of validity challenges in patent offices. We expect our most valuable products to receive the greater number of challenges. Despite our efforts to establish and defend robust patent protection for our products, we may not succeed in protecting our patents from such litigation or other challenges.

If we are not successful in maintaining exclusive rights to market one or more of our major products, particularly in the US where we achieve our highest revenue, our revenue and margins could be materially adversely affected. If we are ultimately unsuccessful in patent litigation, we may incur liabilities to third parties for damages incurred after enforcing our IP rights.

Where we assert our IP rights and allege infringement, we bear the risk that courts may decide that third parties do not infringe our IP rights. This may result in AstraZeneca losing exclusivity and/or erosion of revenues. Non-infringement defences are typically filed by third parties in response to patent infringement lawsuits including in so-called 505(b)(2) cases in the US. Details of 505(b)(2) actions can be found in Note 25 to the Financial Statements from page 176.

Where we assert our IP rights but are ultimately unsuccessful, third parties may seek damages, alleging, for example, that they have been inappropriately restrained from entering the market. In such cases, we bear the risk that we incur liabilities to those third parties.

We also bear the risk that we may be found to infringe patents owned or licensed exclusively by third parties, including research-based and generic pharmaceutical companies and individuals. Infringement accusations may implicate, for example, our manufacturing processes, product intermediates or use of research tools. Details of significant infringement claims against us by third parties enforcing IP rights can be found in Note 25 to the Financial Statements from page 176.

Price controls and reductions

Most of our key markets have experienced the implementation of various cost control or reimbursement mechanisms in respect of pharmaceutical products.

For example, in the US, realised prices are being depressed through restrictive reimbursement policies and cost control tools such as restricted lists and formularies, which employ 'generic first' strategies and require physicians to obtain prior approval for the use of a branded medicine where a generic alternative exists. These mechanisms can be used by payers to limit the use of branded products and put pressure on manufacturers to reduce net prices. Many of these mechanisms shift a greater proportion of the cost of medicines to the patient via out-of-pocket payments at the pharmacy counter. The patient out-of-pocket spend is generally in the form of a co-payment or, in some cases, a co-insurance, which is designed, principally, to encourage patients to use generic medicines.

A summary of the principal aspects of price regulation and how price pressures are affecting our business in our most important markets is set out in the Pricing pressure section from page 15 and these economic pressures are also further discussed below in the following risk factor.

Economic, regulatory and political pressures

We face continued economic, regulatory and political pressures to limit or reduce the cost of our products.

Managing or litigating infringement disputes over so-called 'freedom to operate' can be costly. We may be subject to injunctions against our products or processes and be liable for damages or royalties. We may need to obtain costly licences. These risks may be greater in relation to biologics and vaccines, where patent infringement claims may relate to discovery or research tools, and manufacturing methods and/or biological materials. While we seek to manage such risks by, for example, acquiring licences, foregoing certain activities or uses, or modifying processes to avoid infringement claims and permit commercialisation of our products, such steps can entail significant cost and there is no guarantee that they will be successful.

Impact

Due to these pricing pressures, there can be no certainty that we will be able to charge prices for a product that, in a particular country or in the aggregate, enable us to earn an adequate return on our product investment. These pressures, including the increasingly restrictive reimbursement policies to which we are subject and the continued potential of new legislation expanding the scope of permitted commercial importation of medicines into the US, could materially adversely affect our business or results of operations.

We expect that these pressures on pricing will continue, and may increase.

Impact

It is not possible to accurately estimate the financial impact of the potential consequences resulting from

In 2010, the US passed the Affordable Care Act, a comprehensive health reform package with provisions taking effect between 2010 and 2018. The law expands insurance coverage, implements delivery system reforms and places a renewed focus on cost and quality. In terms of specific provisions impacting our industry, the law mandates higher rebates and discounts on branded drugs for certain Medicare and Medicaid patients as well as an industry-wide excise fee. Implementation of several health system delivery reforms included in the law has commenced and will continue until 2018.

The Affordable Care Act expands the patient population eligible for Medicaid and will provide new insurance coverage for individuals through state-operated and federal-operated health insurance exchanges from 2014. The pharmaceutical industry could be adversely impacted by such shifts if the health insurance exchanges do not offer a prescription drug benefit that is as robust as benefits historically provided by large employers. We anticipate further government intervention in the US in connection with the recent initiative to contain federal spending. For more information see the Regulatory requirements and Pricing pressure sections from page 14 and 15, respectively.

In the EU, efforts by the European Commission to reduce inconsistencies and to improve standards in the disparate national pricing and reimbursement systems have met with little immediate success as Member States guard their right to make healthcare budget decisions. The industry continues to be exposed in Europe to a range of disparate pricing systems, ad hoc cost-containment measures and reference pricing mechanisms, which impact prices. This pressure is likely to continue for several years as the Member States try to re-balance their sovereign debt levels.

Concurrently, many markets are adopting the use of Health Technology Assessment (HTA) to provide a rigorous evaluation of the clinical efficacy of a product, at, or post, launch. HTA evaluations are also increasingly being used to assess the clinical as well as cost-effectiveness of products in a particular health system. This comes as payers and policymakers attempt to drive increased efficiencies in the use and choice of pharmaceutical products.

Further information regarding these pressures is contained in the Regulatory requirements and Pricing pressure sections from page 14 and page 15, respectively.

Abbreviated approval processes for biosimilars

While no application for a biosimilar has been made in relation to an AstraZeneca biologic, various regulatory authorities are implementing or considering abbreviated approval processes for biosimilars that would compete with patented biologics.

the Affordable Care Act or related legislative changes when taken together with the number of other market-related and industry-related factors that can also result in similar impacts. While the overall reduction in our profit before tax for the year due to higher minimum Medicaid rebates on prescription drugs, discounts on branded pharmaceutical sales to Medicare Part D beneficiaries and an industry-wide excise fee was \$933 million, this reflects only the limited number of known, quantifiable and isolatable effects of these legislative developments. Other potential indirect or associated consequences of these legislative developments, which continue to evolve and which cannot be estimated, could have similar impacts. These include broader changes in access to, or eligibility for, coverage under Medicare, Medicaid or similar governmental programmes. These continued disparities in pricing systems could lead to marked price differentials between markets, which, by way of the implementation of existing or new reference pricing mechanisms, increases the pricing pressure affecting the industry. The importation of pharmaceutical products from countries where prices are low due to government price controls, or other market dynamics, to countries where prices for those products are higher, is already prevalent and may increase. In particular, as discussed in the Pricing pressure section on page 15, eurozone crisis countries such as Greece and Portugal have introduced particularly tough measures to lower healthcare spending, including mandatory discounts, clawbacks and price referencing rules, which could have a material adverse effect on our business or results of operations.

Impact

The extent to which biosimilars would be differentiated from patented biologics on price is unclear. However, due to their complex nature, it is uncertain whether biosimilars would have the same

For example, in 2010, the US enacted the Biologics Price Competition and Innovation Act within the Affordable Care Act, which contains general directives for biosimilar applications. The FDA issued draft guidance in February 2012 on implementing an abbreviated biosimilar approval pathway. However, significant questions remain, including standards for designation of interchangeability. In 2012, the FDA also implemented user fee programmes to support biosimilar product review and policy development. In Europe, the EMA published final guidelines on similar biological medicinal products containing MABs and in May, the first MAB biosimilar application was made. Notably, a number of jurisdictions have adopted either the EMA guidelines or those recently set forth by the WHO to enable biosimilars to enter the market after discrete periods of data exclusivity.

impact on patented biologics that generic products have had on patented small molecule products. In addition, it is uncertain when any such abbreviated approval processes may be fully realised, particularly for more complex protein molecules such as MABs. Any such processes may materially adversely affect the future commercial prospects for patented biologics, such as the ones that we produce.

Increasing implementation and enforcement of more stringent anti-bribery and anti-corruption legislation

Impact

There is an increasing global focus on the implementation and enforcement of anti-bribery and anti-corruption legislation. For example, in the UK, the Bribery Act 2010 came into force in July 2011. It has extensive extra-territorial application, implements significant changes to existing UK anti-bribery legislation and broadens the scope of statutory offences and the potential applicable penalties, including organisational liability for any bribe paid by persons or entities associated with an organisation where the organisation failed to have adequate preventative procedures in place at the time of the offence. In the US, there has been significant enforcement activity in respect of the Foreign Corrupt Practices Act by the SEC and DOJ against US companies and non-US companies listed in the US.

We devote significant resources to the considerable challenge of compliance with this legislation, including in emerging and developing markets, at considerable cost. Investigations from governmental agencies require additional resources. Despite taking significant measures to prevent breaches of applicable anti-bribery and anti-corruption laws by our personnel and associated third parties, breaches may result in the imposition of significant penalties, such as fines, the requirement to comply with monitoring or self-reporting obligations, or debarment or exclusion from government sales or reimbursement programmes, any of which could materially adversely affect our reputation, business or results of operations.

We are the subject of current anti-corruption investigations and there can be no assurance that we will not, from time to time, continue to be subject to informal inquiries and formal investigations from governmental agencies. In the context of our business, governmental officials interact with us in a variety of roles that are important to our operations, such as in the capacity of a regulator, partner or healthcare payer, reimbursor or prescriber, among others. Details of these matters are included in Note 25 to the Financial Statements from page 176.

Any expected gains from productivity initiatives are uncertain

Impact

We continue to implement various productivity initiatives and restructuring programmes with the aim of enhancing the long-term efficiency of the business. However, anticipated cost savings and other benefits from these programmes are based on estimates and the actual savings may vary significantly. In

If inappropriately managed, the expected value of these initiatives could be lost through low employee engagement and hence productivity, increased absence and attrition levels, and industrial action.

particular, these cost reduction measures are often based on current conditions and cannot always take into account any future changes to the pharmaceutical industry or our operations, including new business developments, wage or price increases.

Our failure to successfully implement these planned cost reduction measures, either through the successful conclusion of employee relations processes (including consultation, engagement, talent management, recruitment and retention), or the possibility that these efforts do not generate the level of cost savings we anticipate, could materially adversely affect our business or results of operations.

Failure to attract and retain key personnel and failure to successfully engage with our employees

Impact

We rely heavily on recruiting and retaining talented employees with a diverse range of skills and capabilities to meet our strategic objectives. For example, the success of our science activities is particularly dependent on our ability to attract and retain sufficient numbers of high quality researchers and development specialists. We face intense competition for well qualified individuals, as the supply of people with specific skills and significant leadership potential or in specific geographic regions may be limited.

The inability to attract and retain highly skilled personnel, in particular those in key scientific and leadership positions and in our talent pools, 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.

Our ability to achieve high levels of employee engagement in the workforce, and hence benefit from strong commitment and motivation, is key to the successful delivery of our business objectives.

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 adversely impact our business or results of operations.

While we are committed to working on improving drivers of engagement, such as increasing our employees' understanding of our new strategy and our ongoing efforts to reduce organisational complexity, our efforts may be unsuccessful.

Failure of information technology and cybercrime

Impact

We are dependent on effective IT systems. These systems support key business functions such as our R&D, manufacturing, supply chain and sales capabilities, and are an important means of safeguarding and communicating data, including critical or sensitive information, the confidentiality and integrity of which we rely on. The size and complexity of our IT systems, and those of our third party vendors (including outsource providers) with whom we contract, has significantly increased over the past decade and makes such systems potentially vulnerable to service interruptions and security breaches from attacks by malicious third parties, or from intentional or inadvertent actions by our employees or vendors.

Any significant disruption to these IT systems, including breaches of data centre security or cybersecurity, or failure to integrate new and existing IT systems, could harm our reputation and materially adversely affect our financial condition or results of operations.

While we have invested heavily in the protection of our data and IT, we may be unable to prevent breakdowns or breaches in our systems that could adversely affect our business.

Significant changes in the business footprint and the implementation of the new IT strategy including the setting up of captive offshore Global Technology Centres could lead to temporary loss of capability while the changes are being implemented.

The inability to effectively back-up and restore data could lead to permanent loss of data that could result in non-compliance with applicable laws and regulations.

We and our vendors could be susceptible to third party attacks on our information security systems, which attacks are of ever increasing levels of sophistication and are made by groups and individuals with a wide range of motives and expertise, including criminal groups, 'hacktivists' and others. From time to time we experience malicious intrusions and computer viruses.

Impact

A failure to successfully manage and implement the integration of IT infrastructure services provided by our outsourcing providers could create disruption, which could materially adversely affect our business or results of operations. Failure of outsource providers to deliver timely services, and to the required level of quality, and failure of outsource providers to co-operate with each other, could materially adversely affect our financial condition or results of operations. In addition, such failures could adversely impact our ability to meet business targets, maintain a good reputation within the industry and with stakeholders, and result in non-compliance with applicable laws and regulations.

Failure of outsourcing

We have outsourced a number of business critical operations to third party providers. This includes certain R&D processes, IT systems, HR, and finance and accounting services.

Supply chain and delivery risks

Manufacturing biologics

Manufacturing biologics, especially in large quantities, is complex and may require the use of innovative technologies to handle living micro-organisms and facilities specifically designed and validated for this purpose, with sophisticated quality assurance and control procedures.

Final market release of a biologic depends on a number of in-process manufacturing and supply chain parameters to ensure the product conforms with its safety, identity and strength requirements and meets its quality and purity characteristics.

Biologics production facilities, especially for drug substance manufacture, are very specialised and can take years to develop and bring on line as licensed facilities. Predicting demand for certain classes of biologics, especially prior to launch, can be

Impact

Slight variations in any part of the manufacturing process or components may lead to a product that does not meet its stringent design specifications. Failure to meet these specifications may lead to recalls, spoilage, drug product shortages, regulatory action and/or reputational harm.

challenging.

Difficulties and delays in the manufacturing, distribution and sale of our products

Impact

We may experience difficulties and delays in manufacturing our products, such as (i) supply chain continuity, including as a result of disruptions such as a natural or man-made disaster at one of our facilities or at a critical supplier or vendor; (ii) delays related to the construction of new facilities or the expansion of existing facilities, including those intended to support future demand for our products; (iii) seizure or recalls of products or shutdown of manufacturing plants; and (iv) other manufacturing or distribution problems including changes in manufacturing production sites, limits to manufacturing capacity due to regulatory requirements, changes in the types of products produced, or physical limitations or other business interruptions that could impact continuous supply.

Manufacturing distribution and sale difficulties may result in product shortages and significant delays, which may lead to lost sales.

Reliance on third parties for goods

Impact

We increasingly rely on third parties for the timely supply of goods, such as raw materials (for example, the API in some of our medicines), equipment, formulated drugs and packaging, all of which are key to our operations.

Third party supply failure could materially adversely affect our financial condition or results of operations. This may lead to significant delays and/or difficulties in obtaining goods and services on commercially acceptable terms.

Unexpected events and/or events beyond our control could result in the failure of the supply of goods. For example, suppliers of key goods we rely on may cease to trade. In addition, we may experience limited supply of biological materials, such as cells, animal products or by-products. Furthermore, government regulations in multiple jurisdictions could result in restricted access to, use or transport of such materials.

Loss of access to sufficient sources of key goods and biological materials may interrupt or prevent our research activities as planned and/or increase our costs. Further information is contained in the Managing risk section on page 44.

Legal, regulatory and compliance risks

Adverse outcome of litigation and/or governmental investigations

Impact

We may be subject to legal proceedings and governmental investigations. Litigation, particularly in the US, is inherently unpredictable and unexpectedly high awards for damages can result from an adverse verdict. In many cases, plaintiffs may claim compensatory, punitive and statutory damages in extremely high amounts. In particular, the marketing, promotional, clinical and pricing practices of pharmaceutical manufacturers, as well as the manner in which manufacturers interact with purchasers, prescribers and patients, are subject to extensive regulation, litigation and governmental investigation. Many companies, including AstraZeneca, have been subject to

Investigations (for example, the DOJ investigative demand in relation to the Brilinta PLATO trial, described in further detail in Note 25 to the Financial Statements from page 176) or legal proceedings, regardless of their outcome, could be costly, divert management attention, or damage our reputation and demand for our products. 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, require us to make

claims related to these practices asserted by federal and state governmental authorities and private payers and consumers, which have resulted in substantial expense and other significant consequences. Note 25 to the Financial Statements from page 176 describes the material legal proceedings in which we are currently involved.

significant provisions in our accounts relating to legal proceedings and could materially adversely affect our business or results of operations.

Substantial product liability claims

Impact

Pharmaceutical companies have, historically, been subject to large product liability damages claims, settlements and awards for injuries allegedly caused by the use of their products. Adverse publicity relating to the safety of a product or of other competing products may increase the risk of product liability claims.

Substantial product liability claims that result in court decisions against us or in the settlement of proceedings 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 Limited third party insurance coverage risk on page 213.

Failure to adhere to applicable laws, rules and regulations

Impact

Any failure to comply with applicable laws, rules and regulations may result in civil and/or criminal legal proceedings being filed against us, or in us becoming subject to regulatory sanctions. Regulatory 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.

Failure to comply with applicable laws, including ongoing control and regulation, could materially adversely affect our business or results of operations. For example, once a product has been approved for marketing by the regulatory authorities, it is subject to continuing control and regulation, such as the manner of its manufacture, distribution, marketing and safety surveillance. For example, if regulatory issues concerning compliance with current Good Manufacturing Practice or safety monitoring regulations for pharmaceutical products (often referred to as pharmacovigilance) arise, this could lead to loss of product approvals, product recalls and seizures, and interruption of production, which could create product shortages and delays in new product approvals, and so negatively impact patient access, and reputation.

Failure to adhere to laws, rules and regulations relating to anti-competitive behaviour

Impact

Any failure to comply with laws, rules and regulations relating to anti-competitive behaviour may expose us to regulatory sanctions or lawsuits from private, non-governmental entities. Certain of our commercial arrangements with generics companies, which have sought to settle patent challenges on terms acceptable to both innovator and generics manufacturer, may be subject to challenge by competition authorities.