ASTRAZENECA PLC
Form 6-K
March 08, 2016

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 2016

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 X 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 X

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 2015 (Annual Report).

A copy of the Annual Report will be submitted to the National Storage Mechanism and will shortly be available for inspection at www.morningstar.co.uk/uk/nsm.

The Annual Report is also available on the Company’s website at http://www.astrazeneca-annualreports.com/2015/.

The Annual Report, together with the Notice of Annual General Meeting 2016 and Shareholders' Circular, ‘AstraZeneca 2015 In Brief' and a covering letter from the Chairman will be despatched to shareholders on or about 18 March 2016.

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 29 April 2016.

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 2015 announcement, issued on 4 February 2016, 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
8 March 2016

APPENDIX A

Risks and uncertainties
Operating in the pharmaceutical sector carries various inherent risks and uncertainties that may affect our business. 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 and have been categorised consistently with the Principal risks detailed from page 21. 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, Future prospects in the Financial Review on page 76, 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 and IP risks

Failure to meet development targets	Impact
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 various 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 regulatory authorities and/or payers; and the emergence of competing products. Because our business model and strategy rely on the success of relatively few compounds, the failure of any in line production may have a significant negative effect on our business or results of operations. 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.	A succession of negative drug project results and a failure to reduce development timelines effectively, or produce new products that achieve the expected commercial success, could frustrate the achievement of development targets, adversely affect the reputation of our R&D capabilities, and is likely to materially adversely affect our business and results of operations. See also Failure to achieve strategic priorities or to meet targets or expectations on page 225.

Delay to new product launches	Impact
Our continued success depends on the development and successful launch of innovative new drugs. The anticipated launch dates of major new products significantly affect 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. Launch dates are primarily driven by our development programmes and the demands from various factors, including adverse findings in pre-clinical or	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 delayed launch may lead to increased costs if, for example,

clinical studies, regulatory demands, price negotiation, competitor activity and technology transfer.	marketing and sales efforts need to be rescheduled or performed for longer than expected.
Acquisitions and strategic alliances, including licensing and collaborations, may be unsuccessful	Impact
We seek licensing arrangements and strategic collaborations to expand our product portfolio and geographical presence as part of our business strategy. 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 rights we acquire, and the resources, efforts and skills of our partners. Also, under many of our licensing arrangements and strategic collaborations, we make milestone p ayments well in advance of the commercialisation of the products, with no assurance that we will recoup these payments. We may also seek to acquire complementary businesses or enter into other strategic transactions. 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. 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 or we may have to pay a significant premium over book or market values for our acquisitions.	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 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 due to the integration of an acquired business could cause deterioration in our credit rating and result in increased borrowing costs and interest expense. We may issue additional shares to pay for acquired businesses, which would result in the dilution of our then existing shareholders. Further, if liabilities are uncovered in an acquired business, an acquired business fails to perform in line with expectations, or a strategic transaction does not deliver the results we intended, then the Group or our shareholders may suffer losses and may not have adequate remedies against the seller or third parties. Integration processes 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.
Difficulties obtaining and maintaining regulatory approvals for new products	Impact
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	Delays in regulatory reviews and approvals impact patient and market access. In addition, post-approval requirements result in increased costs and may impact the labelling and approval status of currently marketed products.

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. Regulations may require a company to conduct additional clinical trials after a drug's approval, which can result in increased costs, labelling challenges or loss of regulatory approval.

Factors, including advances in science and technology, evolving regulatory science, and different approaches to benefit/risk tolerance by regulatory 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, and broader data transparency.

Unanticipated and unpredictable policy making by governments and regulators can adversely influence regulatory decision making, often leading to severe delays in regulatory approval. The predictability of the outcome and timing of review processes remains challenging due to evolving regulatory science, competing regulatory priorities, unpredictable policy making and limits placed on regulatory authority resources.

Failure to obtain and enforce effective IP protection	Impact
Our ability to obtain and enforce patents and other IP rights in relation to our products is an important element in protecting our investment in R&D and creating long-term value for the business. Some countries in which we operate are still developing their IP laws, others are limiting the applicability of their IP laws to certain pharmaceutical inventions. Certain countries may seek to limit or deny effective IP protection for pharmaceuticals because of adverse political perspectives around the desirability of appropriate IP protection for pharmaceuticals.	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, the risk of patent litigation and the early loss of IP rights is contained in the Intellectual Property section on page 60, the Effects of patent litigation in respect of IP rights risk on page 218 and the Expiry or loss of, or limitations to, IP rights and

consequential pressure from generic competition risk on page 215.

Commercialisation risks

Expiry or loss of, or limitations to, IP rights and consequential pressure from generic competition	Impact
A pharmaceutical product is protected from being copied for the limited period of protection under patent rights and/or related IP rights such as Regulatory Data Protection or Orphan Drug status. This period of protection helps us recoup our overall R&D investment. Early loss of IP rights may threaten our ability to recoup our investment in a patent product. Expiry or loss of these rights can materially adversely affect our revenues and financial condition due to the launch of generic copies of the product in the country where the rights have expired or been lost (see the Patent Expiries section on pages 210 and 211, which contains a table of certain patent expiry dates for our key marketed products). Products protected by our IP account for a significant proportion of our revenues. For example, in 2015, US Product Sales for Crestor and Seroquel XR were $2,844 million (2014: $2,918 million) and $716 million (2014: $738 million), respectively. Additionally, the expiry or loss of patents covering other innovator companies' products may also lead to increased competition and pricing pressure for our own, still-patented, products in the same product class due to the availability of lower priced generic products in that product class. Typically, products under patent protection or within the period of Regulatory Data Protection generate significantly higher revenues than those not protected by such rights.	If challenges to our IP 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 revenues and financial condition. 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 protection or Regulatory Data Protection been available.
A pharmaceutical product competes with other products marketed by research-based pharmaceutical companies and approved for the same condition, as well as with generic drugs for that condition marketed by generic drug manufacturers. 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 pricing pressures due to 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, Lipitor and Seroquel IR). Additionally, generic manufacturers are often able to invest more resources in the marketing of their products than we do, due to their lack of R&D expenses.

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, as detailed in Note 27 to the Financial Statements from page 186, we are currently facing challenges from numerous generic drug manufacturers regarding our patents relating to key products, including Brilinta, Faslodex, Seroquel XR, Byetta, Daliresp, Onglyza and Crestor (which goes off-patent in the US in May 2016). Patent challenges are also discussed in the Effects of patent litigation in respect of IP rights risk on page 218. 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.

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.

For example, in 2010, the US enacted the Biologics Price Competition and Innovation Act within the ACA, which contains general directives for biosimilar applications. The FDA issued final guidance in April 2015 on implementing an abbreviated biosimilar approval pathway. In March 2015, the FDA approved the first biosimilar product submitted under the abbreviated biosimilar pathway. However, significant questions remain, including standards for designation of interchangeability and data collection requirements to support extrapolation of indications. In addition, due to the recent submissions and approvals of abbreviated biosimilar applications, a number of legal challenges construing the requirements of the abbreviated biosimilar pathway are under review. For example, in July 2015, the US Court of Appeals for the Federal Circuit held

Impact

The extent to which biosimilars would differ from patented biologics on price is unclear. However, due to their complex nature, it is uncertain whether biosimilars would have the same 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. Such processes may materially and adversely affect the future commercial prospects for patented biologics, such as the ones that we produce.

that biosimilar applicants were not required to provide copies of the biosimilar application or manufacturing information but needed to provide 180-day commercial marketing notice to the reference sponsor. Although this decision and other ongoing legal challenges do not directly impact an AstraZeneca biologic, uncertainty regarding the abbreviated biosimilar approval pathway may remain until these initial legal challenges reach final conclusion. In Europe, the EMA published final guidelines on similar biologics containing MAbs and in May 2012, the first MAb biosimilar application was submitted with recommendation for approval made by the EMA. Notably, various jurisdictions have adopted either the EMA guidelines or those set forth by WHO to enable biosimilars to enter the market after discrete periods of data exclusivity.	
Political and socio-economic conditions We operate in over 100 countries around the world, some of which may be subject to political and social instability. There may be disruption to our business if there is instability in a particular geographic region, including as a result of war, terrorism, riot, unstable governments, civil insurrection or social unrest. For instance, our operational risks in Ukraine have increased due to growing political and economic uncertainty in the region.	Impact Deterioration of, or failure to improve, socio-economic conditions, and situations and/or resulting events, depending on their severity, could adversely affect our supply and/or distribution chain in the affected countries and the ability of customers or ultimate payers to purchase our medicines. This could adversely affect our business or results of operations. Broader economic developments, such as potential international sanctions and global oil price developments, could exacerbate this effect in the Ukrainian and Russian markets.
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 Sales. This poses various challenges including: more volatile economic conditions and/or political environments; competition from multinational and local companies with existing market presence; the need to identify and to leverage appropriate opportunities for sales and marketing; poor IP protection; inadequate protection against crime (including counterfeiting, corruption and fraud); inadequate infrastructure to address disease outbreaks (such as the Ebola virus); the need to impose developed market compliance standards; the need to meet a more diverse	Impact The failure to exploit potential opportunities appropriately in Emerging Markets or materialisation of the risks and challenges of doing business in such markets, including inadequate protection against crime (including counterfeiting, corruption and fraud) or inadvertent breaches of local and international law may materially adversely affect our reputation, business or results of operations.

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 and marketing channels and route to market; and interventions by national governments or regulators restricting market access and/or introducing adverse price controls.	
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 particularly important to replace lost Product 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, failure to show a differentiated product profile and changes in prescribing habits. 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 differences in the mode of administration, technical aspects of the product, and rapidly changing distribution and reimbursement environments. Our products are subject to competition by other products approved for the same or similar indication, and the approval of a competitive product that is considered superior, or equivalent to, one of our products may result in immediate and significant decreases in our revenues.	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 biologics medicines, such as Synagis and FluMist/Fluenz.
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 and/or patent office proceedings initiated against or by external parties. We expect our most valuable products to receive the greatest number of challenges. Despite our efforts to establish and defend robust patent protection for our products, we may not succeed in protecting or enforcing our patents in such litigation or other challenges.

We bear the risk that courts may decide that third parties do not infringe our asserted IP rights. This may result in AstraZeneca losing exclusivity and/or erosion of revenues.

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. Third parties may seek damages for alleged patent infringement. In the US, they may also seek enhanced (ie up to treble) damages for alleged wilful infringement of their patents.

Details of material patent litigation matters can be found in Note 27 to the Financial Statements from page 186.

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, forgoing 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.

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 Product Sales, our revenue and margins could be materially adversely affected.

Unfavourable resolution of such current and similar future patent litigation matters could subject us to damages (including enhanced damages), require us to make significant provisions in our accounts relating to legal proceedings and/or could materially adversely affect our financial condition or results of operations.

Price controls and reductions

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

For example, in the US, prices are being depressed through restrictive reimbursement policies and cost control tools such as restricted lists and formularies, which employ ‘generic first’ strategies and/or 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. In addition, payers are shifting a greater proportion of the cost of branded 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

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, as well as potential legislation that expands the commercial importation of medicines into the US, could materially adversely affect our business or results of operations.

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

medicines.

In Emerging Markets, governments are increasingly controlling pricing in the self-pay sector and favouring locally manufactured drugs.

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 Pricing of medicines in the Marketplace section on page 14 and overleaf 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.

In 2010, the US enacted the ACA, a comprehensive health reform law that 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 ACA has commenced and will continue through 2018. The ACA expands the patient population eligible for Medicaid and provides new insurance coverage for individuals through state and federally operated health insurance exchanges. In general, patients enrolled in the exchanges are subject to higher cost sharing obligations and may not have as robust access to prescription drugs as compared to patients enrolled in Medicare Part D or commercial plans. Based, in part, on the impact of ACA to other healthcare sectors, there is ongoing scrutiny of the US pharmaceutical industry that could result in further government intervention and financial constraint. Many stakeholders, including some in Congress and others in the broader healthcare system, such as health plans, have dramatically increased their criticism over the value of medicines in the US and have placed a stronger emphasis on innovative therapies. Such criticism and focus on the value of medicines has resulted in proposed policy and legislative changes at the state and federal levels aimed at imposing price controls on medicines and increasing price transparency. For more information, please see Regulatory requirements and Pricing of medicines in the Marketplace section from page 13 and page 14, respectively.

In the EU, efforts by the EC to reduce inconsistencies and improve standards in the disparate national pricing and

Impact

While new patients entering the US healthcare system due to the ACA may lead to a slight increase in prescription drug utilisation, we expect that our financial and other costs resulting from the ACA, many of which we are unable to accurately estimate, will far outweigh any increase in Product Sales.

The continued disparities in EU and US 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. Increased transparency of net prices and strengthened collaboration by governments may accelerate the development of further cost containment policies (such as procurement or the comparison of net prices etc).

reimbursement systems 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 various ad hoc cost-containment measures and reference pricing mechanisms, which impact prices. There is a trend towards increasing transparency and comparison of prices among EU Member States. Recent controversy regarding the high price of a drug marketed by one of our competitors for chronic hepatitis C may provoke further EU collaboration and may eventually lead to a change in the overall pricing and reimbursement landscape. 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 effect, as well as cost-effectiveness, of products in a particular health system. This comes as payers and policymakers attempt to increase efficiencies in the use and choice of pharmaceutical products.
Further information regarding these pressures is contained in Regulatory requirements and Pricing of medicines in the Marketplace section from page 13 and page 14, respectively.

Illegal trade in our products	Impact
The illegal trade in pharmaceutical products is widely recognised by industry, non-governmental organisations and governmental authorities to be increasing. Illegal trade includes counterfeiting, theft and illegal diversion (that is, when our products are found in a market where we did not send them and where they are not approved or not permitted/allowed to be sold). There is a risk to public health when illegally traded products enter the supply chain, as well as associated financial risk. Authorities and the public expect us to help reduce opportunities for illegal trade in our products through securing the integrity of our supply chain, surveillance, investigation and supporting legal action against those found to be engaged in illegal trade.	Public loss of confidence in the integrity of pharmaceutical products as a result of illegal trade could materially adversely affect our reputation and financial performance. In addition, undue or misplaced concern about this issue may cause some patients to stop taking their medicines, with consequential risks to their health. Authorities may take action, financial or otherwise, if they believe we are liable for breaches in our own supply chains. There is also a direct financial loss when counterfeit and/or illegally diverted products replace sales of genuine products; or genuine products are recalled following discovery of counterfeit products; or products which have been the subject of theft or illegal diversion are recalled; or illegally diverted products replace sales of products which are approved/allowed for sale in a market.
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 has extensive extra-territorial application, and imposes organisational liability for any bribe paid by persons or entities associated with an organisation where the organisation failed to have adequate preventative controls 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. China and other countries are also enforcing their own anti-bribery laws more aggressively and/or adopting tougher new measures.

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 various roles that are important to our operations, such as in the capacity of a regulator, partner or healthcare payer, reimburser or prescriber, among others. Details of these matters are included in Note 27 to the Financial Statements from page 186.

Despite taking measures to prevent breaches of applicable anti-bribery and anti-corruption laws by our personnel and associated third parties, breaches may still occur, potentially resulting 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.

Failure to adhere to applicable laws, rules and regulations

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.

Impact

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 negatively impact patient access and our reputation.

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.

Examples of sensitive information that we protect include loss of clinical trial records (patient names and treatments), personal information (employee bank details, home address), intellectual property of manufacturing process and compliance, key research science techniques, AstraZeneca property (theft) and privileged access (rights to perform IT tasks).

The size and complexity of our IT systems, and those of our third party vendors (including outsource providers) with whom we contract, have 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 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 result in disclosure of confidential information, damage to our reputation, regulatory penalties, financial losses and/or other costs.

Significant changes in the business footprint and the implementation of the IT strategy, including the creation and
use of captive offshore Global Technology Centres, could lead to temporary loss of capability.

The inability to effectively backup 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. 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 criminal groups, ‘hacktivists’ and others. From time to time we experience intrusions, including as a result of computer-related malware.

Any expected gains from productivity initiatives are uncertain

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 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 or wage or price increases.

Impact

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.

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 of outsourcing

Impact

We have outsourced various business-critical operations to third party providers. This includes certain R&D processes, IT systems, HR and finance, tax and accounting services.	The failure of outsource providers to deliver timely services, and to the required level of quality, and the 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. A failure to successfully manage and implement the integration of IT infrastructure services provided by our outsource providers could create disruption, which could materially adversely affect our business or results of operations. In addition, failure to manage outsourcing or insourcing transition processes may disrupt our business. For instance, as we transition services that previously were outsourced to our service centre in Chennai (India), incumbent outsource providers may cease to continue to provide the same level of resources and quality of service.

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 depends largely 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. 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.	The inability to attract and retain highly skilled personnel, in particular those in key scientific and leadership positions and those 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. 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 strategy and our ongoing efforts to reduce organisational complexity, our efforts may be unsuccessful.

Supply chain and business execution risks

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: > Supply shortages associated with gaps between forecasted and actual demand for products. > Supply chain disruptions, including those due to natural or man-made disasters at one of our facilities or at a critical supplier or vendor. > Delays related to the construction of new facilities or the expansion of existing facilities, including those intended to support future demand for our products. > Inability to supply products due to a product quality failure or regulatory agency compliance action such as licence withdrawal, product recall or product seizure. > 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, forecasting, distribution and sales difficulties may result in product shortages and significant delays, which may lead to lost Product Sales and materially adversely affect our business, financial condition or results of operations.

Reliance on third party goods and services	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, and services, all of which are key to our operations. Many of these goods are difficult to substitute in a timely manner or at all.	Third party supply failure could lead to significant delays and/or difficulties in obtaining goods and services on commercially acceptable terms and/or adversely affect AstraZeneca's reputation. This may materially adversely affect our business, financial condition or results of operations.
Unexpected events and/or events beyond our control could result in the failure of the supply of goods and services. For example, suppliers of key goods may cease to trade or experience supply chain failures such as those described under the risk above. In addition, we may experience limited supply of biological materials, such as cells, animal products or by-products. Furthermore, government regulations could result in restricted access to, use or transport of such materials.	Loss of access to sufficient sources of key goods and biological materials or services may interrupt or prevent planned research activities and/or increase our costs. Further information is contained in Working with suppliers in Manufacturing and Supply on page 47.

Impact

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 challenging. We expect that external capacity for biologics drug substance production will remain constrained for the next several years and, accordingly, may not be readily available for supplementary production in the event that we experience unforeseen need for such capacity.	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.
Legal; regulatory and compliance risks	
Adverse outcome of litigation and/or governmental investigations	Impact
We may be subject to various product liability, consumer commercial, anti-trust, environmental, employment or tax litigation or other 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 enhanced 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 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 27 to the Financial Statements from page 186	Governmental investigations for example, under the Foreign Corrupt Practices Act or federal or state False Claims Acts 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, 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.

describes the material legal proceedings in which we are currently involved.	
Failure to adhere to applicable laws, rules and regulations relating to anti-competitive behaviour Any failure to comply with laws, rules and regulations relating to anti-competitive behaviour may expose us to regulatory sanctions and/or lawsuits from governmental authorities and private, nongovernmental 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. Details of material litigation matters which raise allegations of anticompetitive behaviour can be found in Note 27 to the Financial Statements from page 186.	Impact Where a government authority investigates our adherence to competition laws, or we become subject to private party lawsuits, this may result in inspections of our sites or requests for documents and other information. Competition investigations or legal proceedings could be costly, divert management attention or damage our reputation and demand for our products. Unfavourable resolution of such current and similar future proceedings against us could subject us to fines and penalties, including enhanced (ie up to treble) damages, require us to make significant provisions in our accounts relating to legal proceedings and could materially adversely affect our business results of operations, including, by requiring us to change our commercial practice.
Substantial product liability claims Any failure to comply with laws, rules and regulations relating to the manufacturing, design, and provision of appropriate warnings concerning the dangers and risks of our medicines that result in injuries allegedly caused by the use of our medicines 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 27 to the Financial Statements from page 186.	Impact Significant product liability claims can result in requests for documents and other information. These legal proceedings 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, 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 Limited third party insurance coverage risk on page 226.
Failure to adhere to applicable laws, rules and regulations relating to environment, health and safety; environmental and occupational health and safety liabilities Any failure to comply with laws, rules and regulations relating to the environment or occupational health or safety may expose us to regulatory sanctions and/or lawsuits from governmental authorities and private, non-governmental entities. Additionally, the failure to adequately anticipate and proactively manage emerging policy and legal developments associated with the	Impact While we carefully manage compliance and any known liabilities, and work to stay ahead of policy and legislative developments, if a significant compliance issue, environmental, occupational health or safety incident or legal requirement for which we are responsible were to arise, this could result in us being responsible for fines and penalties, damages, and other costs. In some circumstances, such liability could materially adversely

environment, health and safety could adversely affect our licence to operate and/or reputation.

We have environmental and/or occupational health and safety-related liabilities at some currently and formerly owned, leased and third party sites, the most significant of which are detailed in Note 27 to the Financial Statements from page 186.

affect our business or results of operations. In addition, our financial provisions for any obligations that we may have relating to environmental or occupational health and safety liabilities may be insufficient if the assumptions underlying the provisions, including for example our assumptions regarding the portion of waste at a site for which we are responsible, prove incorrect or if we are held responsible for additional contamination or occupational health and safety-related claims.

Misuse of social media platforms and new technology

We increasingly use the internet, digital content, social media, mobile applications and other forms of new technology to communicate internally and externally. The accessibility and instantaneous nature of interactions with such media may facilitate or exacerbate the risk of data leakages from within AstraZeneca or false or misleading statements being made about AstraZeneca, which may damage our reputation. As existing social media platforms expand and evolve, and new social media platforms emerge, it becomes increasingly challenging to identify new points of entry and to put structures in place to secure and protect information.

Impact

Inappropriate use of certain media vehicles could lead to the unauthorised or unintentional public disclosure of sensitive information (such as personally identifiable information on employees, healthcare professionals or patients, for example, those enrolled in our clinical trials), which may damage our reputation, adversely affect our business or results of operations and expose us to legal risks, as well as additional legal obligations. Similarly, the involuntary public disclosure of commercially sensitive information, such as trade secrets through external media channels, or an information loss could adversely affect our business or results of operations. In addition, negative posts or comments on social media websites or other digital channels or new forms of technology about us or, for example, the safety of our products, could harm our reputation.

Economic and financial risks

Failure to achieve strategic priorities or to meet targets or expectations

We may from time to time communicate our business strategy or our targets or expectations regarding our future financial or other performance (for example, the expectations described in Future prospects in the Financial Review on page 76). All such statements are of a forward-looking nature and are based on assumptions and judgements we make, all of which are subject to significant inherent risks and uncertainties, including risks and uncertainties that we are unaware of and/or that are beyond our control.

Impact

There can be no guarantee that our financial targets or expectations will materialise on the expected timeline or at all. Actual results may deviate materially and adversely from any such target or expectation, including if one or more of the assumptions or judgements underlying any such target or expectation proves to be incorrect in whole or in part.

Any failure to successfully implement our business strategy may frustrate the achievement of our financial or

Impact

other targets or expectations and, in turn, materially damage our brand and materially adversely affect our business, financial position or results of operations.

Adverse impact of a sustained economic downturn

A variety of significant risks may arise from a sustained global economic downturn including for example the economic slowdown in China, our second largest market. Additional pressure from governments and other healthcare payers on medicine prices and volumes of sales in response to recessionary pressures on budgets may cause a slowdown or a decline in growth in some markets. In some cases, those governments most severely impacted by the economic downturn may seek alternative ways to settle their debts through, for example, the issuance of government bonds which might trade at a discount to the face value of the debt.

In addition, our customers may cease to trade, which may result in losses from writing off debts, or the sustained economic downturn may unfavourably affect the spending patterns of the consumers of our products.

We are highly dependent on being able to access a sustainable flow of liquid funds due to the high fixed costs of operating our business and the long and uncertain development cycles of our products. In a sustained economic downturn, financial institutions with whom we deal may cease to trade and there can be no guarantee that we will be able to access monies owed to us without a protracted, expensive and uncertain process, if at all.

More than 95% of our cash investments are managed centrally and are invested in collateralised bank deposits or AAA credit rated institutional money market funds. Money market funds are backed by institutions in the US and the EU, which, in turn, invest in other funds, including sovereign funds. This means our credit exposure is a mix of US and EU sovereign default risk and financial institution default risk.

Fluctuations in exchange rates

As a global business, currency fluctuations can significantly affect our results of operations, which are reported in US dollars. Approximately 40% of our global 2015 Product Sales were in the US, which is expected to remain our largest single market for the foreseeable future. Product Sales in other countries are predominantly in currencies other than the US dollar, including the euro, Japanese yen, Chinese renminbi, Australian dollar and Canadian dollar. We have a growing exposure to Emerging Market currencies, some of which are subject to exchange

While we have adopted cash management and treasury policies to manage this risk (see the Financial risk management policies section of the Financial Review on page 76), we cannot be certain that these will be as effective as they are intended to be, in particular in the event of a global liquidity crisis. In addition, open positions where we are owed money and we have made in financial institutions or money market funds cannot be guaranteed to be recoverable. Additionally, if we need access to external sources of financing to sustain and/or grow our business, such as the debt or equity capital financial markets, this may not be available on commercially acceptable terms, if at all, in the event of a severe and/or sustained economic downturn. This may, for instance, be the case in the event of any default by the Group on its debt obligations, which may materially adversely affect our ability to secure debt funding in the future or our financial condition in general. Further information on debt funding arrangements is contained in the Financial risk management policies section of the Financial Review on page 76.

Impact

Movements in the exchange rates used to translate foreign currencies into US dollars may materially adversely affect our financial condition or results of operations.

Additionally, some of our subsidiaries import and export goods and services in currencies other than their own functional currency, and so the financial results of such subsidiaries could be affected by currency fluctuations arising between the transaction dates and the settlement dates for these transactions. In addition, there are foreign exchange differences arising on the translation of equity investments in subsidiaries.

Impact

controls, and these currencies, such as that of Venezuela, may be subject to material devaluations against the US dollar. Major components of our cost base are located in the UK and Sweden, where an aggregate of approximately 20% of our employees are based.

Limited third party insurance coverage

In recent years, the costs associated with product liability litigation have increased the cost of, and narrowed the coverage afforded by, pharmaceutical companies' product liability insurance. To contain insurance costs in recent years, we have continued to adjust our coverage profile, accepting a greater degree of uninsured exposure. The Group has not held any material product liability insurance since February 2006. In addition, where claims are made under insurance policies, insurers may reserve the right to deny coverage on various grounds. For example, product liability litigation cases relating to Crestor and Nexium in the US are not covered by third party product liability insurance. See Note 27 to the Financial Statements from page 186 for details.

Taxation

The integrated nature of our worldwide operations can produce conflicting claims from revenue authorities as to the profits to be taxed in individual countries. The majority of the jurisdictions in which we operate have double tax treaties with other foreign jurisdictions, which provide a framework for mitigating the incidence of double taxation on our revenues and capital gains.

AstraZeneca's worldwide operations are taxed under laws in the jurisdictions in which they operate. International standards governing the global tax environment regularly change. The Organisation for Economic Co-operation and Development (OECD) has proposed a number of changes under the Base Erosion and Profit Shifting (BEPS) Action Plans.

Pensions

If we are found to have a financial liability due to product liability or other litigation, in respect of which we do not have insurance coverage, or if an insurer's denial of coverage is ultimately upheld, this could require us to make significant provisions in our accounts relating to legal proceedings and could materially adversely affect our business or results of operations.

For more information, please see the Substantial product liability claims risk on page 223.

Impact

The resolution of these disputes can result in a reallocation of profits between jurisdictions and an increase or decrease in related tax costs, and has the potential to affect our cash flows and EPS. Claims, regardless of their merits or their outcome, are costly, divert management attention and may adversely affect our reputation.

If any of these double tax treaties should be withdrawn or amended, especially in a territory where a member of the Group is involved in a taxation dispute with a tax authority in relation to cross-border transactions, such withdrawal or amendment could materially adversely affect our business or results of operations, as could a negative outcome of a tax dispute or a failure by the tax authorities to agree through competent authority proceedings. See the Financial risk management policies section of the Financial Review on page 76 for tax risk management policies and Note 27 to the Financial Statements on page 186 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 depending upon the nature of the change. We represent views to OECD, governments and tax authorities through public consultations to ensure international institutions and governments understand the business implications of law changes. Specific OECD BEPS recommendations that we expect to impact the Group include changes to patent box regimes, restrictions of interest deductibility and revised transfer pricing guidelines.

Impact

Our pension obligations are largely backed by assets invested across the broad investment market. Our most significant obligations relate to the UK pension fund.	Sustained falls in these asset values could reduce pension fund solvency levels, which may result in requirements for additional cash, restricting the cash available for business growth. Similarly, if the present value of the liabilities increase due to a sustained low interest rate environment, an increase in expectations of future inflation, or an improvement in member longevity (above that already assumed), this could also reduce pension fund solvency ratios. The likely increase in the IAS 19 accounting deficit generated by any of these factors may cause the credit rating agencies to review our credit rating, with the potential to negatively affect our ability to raise debt. See Note 20 to the Financial Statements from page 166 for further details of the Group’s pension obligations.

APPENDIX B

This statement relates to and is extracted from the Annual Report. It is repeated here solely for the purpose of complying withDTR 6.3.5. It is not connected to the information presented in this announcement or in the Company's fourth quarter and full year results 2015 announcement that was published on4 February 2016.

Directors' responsibility statement pursuant to DTR 4

The Directors confirm that to the best of our knowledge:

- The Financial Statements, prepared in accordance with the applicable set of accounting standards, give a true and fair view of the assets, liabilities, financial position and profit or loss of the Company and the undertakings included in the consolidation taken as a whole.
- The Directors' Report includes a fair review of the development and performance of the business and the position of the issuer and the undertakings included in the consolidation taken as a whole, together with a description of the principal risks and uncertainties that they face.

On behalf of the Board of Directors on 4 February 2016

Pascal Soriot
Director

APPENDIX C

Related party transactions

The Group had no material related party transactions which might reasonably be expected to influence decisions made by the users of these Financial Statements.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

AstraZeneca PLC

Date: 08 March 2016

By: /s/ Adrian Kemp
Name: Adrian Kemp
Title: Company Secretary