

MANAGING RISK, PRINCIPAL RISKS AND UNCERTAINTIES

As a global, research-based pharmaceutical company, we face a diverse range of risks and uncertainties that may adversely affect our business.

We work continuously to ensure that we have effective processes in place for identifying, assessing and managing these risks appropriately, in line with our strategic objectives, the material needs of our stakeholders and our core values. As part of this, we continue to monitor our business activities and our external and internal environments for new and emerging risks, including environmental, social and governance matters, to ensure that these are captured and managed at the appropriate level.

In this section we describe our key risk management and assurance mechanisms, together with the associated accountabilities and the principal areas of risks and uncertainties that we currently 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. Where relevant, specific risks and uncertainties are also discussed at various points in the Directors' Report.

EMBEDDED IN BUSINESS PROCESSES

Risk is an inherent part of doing business, and our approach to risk management is designed to encourage clear decisions on which risks we should take and to provide assurance that the commercial, financial, compliance and reputation implications of these risks are adequately understood and managed to an acceptable level.

We constantly strive to ensure that risk management is embedded within our existing business processes and performance management processes. The Group maintains a long-term business plan, updated annually, to support the delivery of its strategy. Each Senior Executive Team (SET) area and key functions are required to provide a comprehensive assessment of their risks as part of the annual business plan update. The Chief Executive Officer and the Chief Financial Officer undertake quarterly business reviews (QBRs) with each SET area at which the key risks are reviewed. To support this review, key functions within each SET area are required to provide quarterly updates on their key risks.

RISK MANAGEMENT & ASSURANCE PROCESSES

Our Code of Conduct and Global Policy framework require all employees to maintain consistent standards of responsible behaviour. Compliance with the Code of Conduct, the related policies and standards is mandatory. Employees are encouraged to raise questions about how to apply these standards and to report suspected breaches and incidents of non-compliance through our continuous assurance process or the AZethics line and other reporting channels described in the Code of Conduct. Compliance with mandatory standards is also subject to ongoing monitoring and review by our compliance functions and Group Internal Audit (GIA), in accordance with its annual plan, agreed with the SET and the Audit Committee.

To strengthen further our high-level corporate responsibility (CR) management capability, during late 2007/early 2008 we established a dedicated Global CR Team of experienced CR professionals from around the Group. The Global CR Team leads the development of our CR strategy and the alignment of tactical delivery, working closely with Global Compliance to ensure that the CR risks and opportunities are identified and managed appropriately, in line with business objectives.

In early 2009, we developed a combined Compliance and Corporate Responsibility 'Responsible Business' scorecard with defined objectives and accountabilities, to track performance consistently across all SET areas and enable quarterly reporting to SET, the Audit Committee and Professor Dame Nancy Rothwell (the Non-Executive Director with responsibility for overseeing CR within the Company), as well as annual reporting to the Board and SET. We plan to introduce this new scorecard during 2009.

KEY ACCOUNTABILITIES

The Board, and specifically the Audit Committee, are accountable for monitoring and overseeing the risk management systems and processes implemented by management and for assessing their adequacy and effectiveness. In addition to direct assurances from senior management through the performance management and monitoring process, they receive and review a Group-level risk summary from the annual business planning process and QBRs. They also receive quarterly incident reports and updates on compliance initiatives from the Global Compliance Officer, and information in respect of audits in relation to certain risks, carried out by GIA, in accordance with its annual audit plan.

SET members are accountable for ensuring sound risk management, control and assurance processes within their SET areas. They actively participate in the annual and quarterly risk review processes and receive quarterly reports on key compliance incidents and the outcomes of audits in their SET area. They are also required to complete an annual assurance statement to confirm that effective risk management and control processes have been operating throughout the year.

Line and project management are accountable for the management of risk within the context of their functional or cross-functional remit or project. To support and underpin the work of line and project management and the SET in managing risk, we have developed systems and processes to ensure the effective identification, management and reporting of key risks. A risk management policy, with guidelines and supporting tools ensures that managers can recognise, assess and actively manage the challenges in their areas.

Our compliance organisation is comprised of a wide range of specialist groups who work with line management and the SET to develop systems and processes for managing risk in specific regulated areas to ensure ongoing legal and regulatory compliance. These groups include Good Laboratory, Clinical and Manufacturing Compliance, SHE, Medical and Regulatory Affairs, Financial Control and Compliance, Information Security and Data Privacy, Sales and Marketing Compliance and Legal and Intellectual Property.

Both line management and these specialist functions are supported by the Global Compliance function that acts as the primary reporting channel to Board and SET on compliance matters and is accountable for overseeing compliance globally and managing the Group's compliance programme.

Against the background of the key accountabilities set out in this section, the Board believes that adequate information was made available to it in order to identify the key risks and uncertainties facing the business, further information of which is set out in the Principal Risks and Uncertainties section on page 76.

KEY COMMITTEES AND COUNCILS

Our quarterly business review process serves as the primary mechanism for monitoring the effectiveness of business performance and risk management and is embedded into existing management team meetings. In addition to this we operate a number of management committees and councils to monitor Group-wide compliance and reputation risks including the Global Compliance Committee (GCC) (further details of which can be found in the Compliance and Group Internal Audit section on page 93) and the Issues Management Council (IMC).

The IMC monitors our external environment for new and emerging issues relating to our business that affect or concern our stakeholders and works with the people who are responsible for managing the issues internally to agree appropriate actions, timelines and, where possible, key performance indicators. The Vice-President, Group Public Affairs chairs the IMC and is also a member of the GCC to ensure that any reputational risk is fully captured at the appropriate level.

BUSINESS RESILIENCE PLANS

Our approach to risk management includes the development of business resilience plans, and such plans are designed to provide for situations in which specific risks have the potential to have a severe impact on our business. During 2008, our business resilience planning activities focused on improving our existing crisis management processes, planning and response structures, including plans, escalation processes and crisis communications. A global standard for crisis management has been rolled out during 2008, and during 2009 a global policy for business resilience, to cover crisis management, business continuity and emergency response will be communicated. This will ensure alignment of documentation, appropriate training of line managers and the use of crisis simulation activities to test the new procedures.

WORKING WITH SUPPLIERS

We believe that effective risk management extends to managing any potential reputational risks associated with our purchasing activities. We are therefore committed to working only with those suppliers who embrace standards of ethical behaviour consistent with our own. This applies across the full range of our purchasing activities, from promotional items to pharmaceutical ingredients, and includes any specialised work for which we use external contractors to complement our in-house effort. It also applies as much to our expanding business in Emerging Markets as it does to our existing supplier relationships.

We are in the process of revising and strengthening our Corporate Responsibility Principles in Purchasing, which we first launched in 2003 to provide guidance for our purchasing community on integrating CR considerations into their activity. The strengthened guidance will become a new Global Responsible Procurement Standard and will provide the framework for developing and implementing the programmes needed to ensure that we effectively and consistently incorporate our standards of ethical behaviour into our procurement activity worldwide. Launch of the new standard is planned for the first half of 2009 and targeted training will be subsequently provided.

A rolling implementation

Integrating responsible business considerations into all of our supplier relationships around the world will take time. CR considerations are being included in all new contracts and master agreements in the US, the UK and Sweden – our three main business hubs where over 80% of our suppliers are based, and last year we extended the geographic reach to other countries where we have major marketing, manufacturing or research activities. These include Japan, China, India, Canada, Mexico and Puerto Rico, as well as more countries in Europe.

Monitoring performance

Our supplier evaluation procedure requires that comprehensive on-site audits of all our high-risk category suppliers be conducted at least once every four years. Medium risk suppliers are audited at the start of the business relationship and refresher audits are planned if there are any significant changes at the supplier. The auditing process will be further extended to regional and local suppliers in 2009.

In 2008, our audit programme covered 28 manufacturing sites at 27 different global suppliers. These audits included elements of safety, health, environment, corporate responsibility and security of supply. High-risk categories such as active pharmaceutical ingredients, formulation and packaging, and complex chemicals were a particular focus.

Within the scope of the audit programme, a critical deficiency in a known high risk R&D-area (hydrogenation) was identified at a proposed supplier. The supplier acknowledged the audit feedback, de-commissioned the facility and replaced it with a facility of an appropriate standard.

During the year, we updated our supplier evaluation process to include product security, comprising elements such as information security, logistics and waste handling related to packaging operations. We have also strengthened the social elements of the evaluation process in recent years, particularly in relation to human rights and labour standards, given our expanding presence in Emerging Markets.

Audit training continued during the year, with nine more people joining the audit team. We also conducted a focused 'Ethical Auditing' auditor-training programme as a part of the implementation of the new supplier evaluation process. Training will continue during 2009.

PRINCIPAL RISKS AND UNCERTAINTIES

The pharmaceutical sector is inherently risky and a variety of risks and uncertainties may affect our business. Here we summarise, under the headings Industry/Economic Environment Risks; Legal/Compliance/Regulatory Risks; and Business Execution Risks, the principal risks and uncertainties that we currently consider may have a significant effect on our financial condition, results of operations and/or reputation. These risks are not listed in any assumed order of priority. Other risks, known or not currently considered material, could have a similar effect. We believe the forward-looking statements about AstraZeneca in this Report, identified by words such as 'anticipates', 'believes', 'expects' and 'intends', are based on reasonable assumptions. However, forward-looking statements involve inherent risks and uncertainties such as those summarised below, and may be influenced by factors beyond our control and/or may have actual outcomes materially different from our expectations.

INDUSTRY/ECONOMIC ENVIRONMENT RISKS

Expiration of patents or marketing exclusivity

Pharmaceutical products or diagnostic or medical devices are normally only protected from competition from copying during the period of patent protection or marketing exclusivity. Following patent protection or marketing exclusivity expiry the product is generally open to competition from generic copies. Products under patent protection or having marketing exclusivity generally generate significantly higher revenues than those not protected by patents or marketing exclusivity.

Patent litigation and early loss of patents, marketing exclusivity or trademarks

Generic drug manufacturers are seeking to market generic versions of many of our more important products, prior to the expiration of our patents and marketing exclusivity periods. For example, we are currently facing challenges from multiple generic manufacturers to certain of our patents for *Nexium*, *Seroquel* and *Crestor*, some of our best-selling products in the US, our largest market. If such challenges are successful and generic products are launched, or launched 'at risk' on the expectation that challenges to our intellectual property will be successful, this may have a materially adverse effect on our financial condition and results of operations. US sales for *Nexium* in 2008 were \$3,101m, for *Seroquel* were \$3,015m and for *Crestor* were \$1,678m. The more significant patent

litigation relating to our products is described in Note 25 to the Financial Statements. In addition, the research-based pharmaceutical industry may exert intellectual property rights against other research-based companies and there continues to be examples of this. In the case of litigation both with generic manufacturers and other research-based companies, we expect that the greatest challenges will be focused on the most valuable products. Although we vigorously defend our intellectual property rights we cannot be certain we will be successful.

There is the risk that we may be found to infringe the patents of others, and managing such disputes can be costly. We may be liable for damages or royalties, have to obtain costly licences or stop manufacturing, using or selling our products. This risk may be greater in respect of biologics and vaccines where intellectual property protection is sometimes not so clear. In the event of such risks arising we may mitigate them through, for example, acquiring licences or making modifications to cease the infringement and permit commercialisation of our products.

Any of our currently patented products may be the subject of intellectual property litigation or other disputes involving patent offices, anti-trust authorities, other government or law enforcement agencies. Despite our efforts to establish and defend robust patent protection, we may not succeed in such litigation or disputes or be able to mitigate the risk through, for example: obtaining a licence to any third party patent on commercially reasonable terms; successfully developing non-infringing alternatives on a timely basis; or licensing alternative non-infringing technology, if any exists, on commercially reasonable terms. If we were not successful during the patent protection or data exclusivity periods in maintaining exclusive rights to market one or more of our major products, particularly in the US where we have our highest revenue and margins, our revenue and margins would be significantly adversely affected.

In addition to the challenges to our patented products from manufacturers of generic or other patented pharmaceutical products, there is a risk that some countries, particularly some of those in the developing world, may seek to impose limitations on the availability of patent protection for pharmaceutical products, or on the extent to which such protection may be obtained and/or enforced, within their jurisdictions. As a result, generic manufacturers in these countries may be increasingly and more easily able to introduce

competing products to the market earlier than they would have been able to, had the patent protection been available.

Combined with patent protection and other types of marketing exclusivity, products protected by a valid trademark usually generate higher revenues than those without a trademark. We believe that we have robust trademark protection for our products but cannot be certain that we would be able to defend any challenge successfully.

Expiration or earlier loss of patents covering competing products

The expiration or earlier loss of patents covering others' branded products may lead to the availability of generic products earlier than anticipated, which could have a materially adverse effect on our financial condition and results of operations. For example, the loss/expiry of patent rights covering major products in the US, such as *Lipitor*™ or *Advair Diskus*™ after 2012 may adversely affect growth of our still patented products in that market.

Failure to obtain patent protection

Our policy is to protect our investment in R&D by applying for appropriate intellectual property protection in respect of our inventions and innovations; this is a key business priority. Our ability to obtain patents and other proprietary rights in relation to our products is, therefore, an important element of our ability to create long-term value for the business.

Many of the different countries in which we operate are developing their patent laws for pharmaceuticals and there is more uncertainty regarding the patent protection available now and in the future than in countries with well developed intellectual property regimes. Limitations on the availability of patent protection in certain developing countries could have an adverse effect on the pricing and sales of our products and, consequently, could adversely affect our revenues from them. More information about protecting our intellectual property is contained in the Intellectual Property section on page 26.

Impact of fluctuations in exchange rates

As a global business, currency fluctuations can significantly affect our results of operations, which are accounted for in US dollars. Approximately 47% of our 2008 sales were in North America (US and Canada) with a significant proportion of that figure being in respect of US sales, which is expected to remain our largest single market. Sales in certain other countries are also in US dollars, or in currencies whose exchange rates are linked to the US dollar. Major components of

our cost base are, however, located in Europe, where an aggregate of approximately 51% of our employees are based. Movements in the exchange rates used to translate foreign currencies into US dollars may, therefore, have a materially adverse effect on our financial condition and results of operations.

Certain of our subsidiaries import and export goods and services in currencies other than their own working currency. The results of such subsidiaries could, therefore, be affected by currency fluctuations arising between the transaction dates and the settlement dates for those transactions. We hedge these exposures through financial instruments. The fair value of financial instruments used to hedge these exposures, principally forward foreign exchange contracts, at 31 December 2008 was \$95 million.

We have policies that seek to mitigate the effect of exchange rate fluctuations on the value of foreign currency cash flows and in turn their effects on the results of the Group, but we do not seek to remove all such risks. Further information is contained in Financial Risk Management Policies on pages 120 to 121. In general, a unilateral strengthening of the US dollar adversely affects our reported results whereas a weakening of the US dollar is generally favourable.

Debt-funding arrangements

We incurred substantial debt in connection with the acquisition of MedImmune, Inc.. Our debt could affect our business flexibility and requires us to devote cash resources to service interest and principal payments. Our current debt level could limit our ability to engage in additional transactions or incur additional indebtedness and could potentially affect our investment grade credit rating. Further information is contained in Financial Risk Management Policies on pages 41 to 42.

Bad debts

The Group sells to a large number of customers, across many countries, ranging from government backed agencies and large private wholesalers to privately owned pharmacies. An economic slowdown may impact the ability of some of these customers to continue to trade, which in turn may result in losses from writing these debts off. Although risk management processes are in place to manage this risk, and provisions are established for debts that may not be recoverable we cannot be certain that there will not be further losses above those already provided for. Further information is contained in the Financial Review on page 42.

Adverse impact of a sustained economic downturn

A variety of significant risks may arise from a sustained global economic downturn including those referred to here. Additional pressure from governments and other healthcare payers on medicine prices and volume of sales in response to recessionary pressures on budgets may cause a slow down or decline in growth in some markets. In addition, suppliers of some of the key goods and services we rely upon may cease to trade. The consequence of this may be significant delays and/or difficulties obtaining goods and services on commercially acceptable terms or even at all. We seek to mitigate these risks as described in the Supply and Manufacturing section on page 27.

Moreover, the high fixed costs of operating a global research-based pharmaceuticals business and the long and uncertain development cycles for our products mean that we are highly dependant on being able to access a sustainable flow of liquid funds. In a sustained and/or severe economic downturn financial institutions who hold our cash and other short-term deposits may cease to trade and there can be no guarantee that depositors/investors will be able to access their assets without a protracted, expensive and uncertain process, if at all. Although we have adopted conservative cash management and treasury policies to mitigate this risk (further information of which is contained in Financial Risk Management Policies on pages 41 to 42) we cannot be certain that these will be completely effective should a number of major financial institutions cease to trade. Additionally, if we need access to external sources of financing to sustain and/or grow our business, such as may be available via the debt or capital financial markets, this may not be available on commercially acceptable terms, or at all, in the event of a severe and/or sustained economic downturn.

A particular risk relates to the Group's pension obligations, the single largest of which is the UK Pension Fund. The obligations are backed by assets invested across the broad investment market. Sustained falls in these assets will put a strain on funding resulting in requirements for additional cash, which may restrict our ability to grow the business in line with our strategic objectives. Similarly, if the liabilities rise, for example due to continued, sustained improvements in longevity, or falls in the corporate bond spreads that drive discount rates for accounting valuations, there will be a strain on funding. The likely increase in the IAS19 accounting deficit generated by any of these may cause the

ratings agencies to review our credit rating, with the potential to impact our ability to raise debt to fund further externalisation.

Owning and operating a biologics and vaccines business

As we continue to expand our biologics capabilities, the risks related to owning and operating a biological products business are becoming more important to the Group. Some of the more significant of these risks are described below:

- > We may have limited access to and/or supply of biological materials, such as cells or animal products or by-products. In addition, government regulations in multiple jurisdictions could result in restricted access to, use or transport of such materials. Loss of access to sufficient sources of such materials, or tighter restrictions on the use of such materials may interrupt or prevent our research activities as planned and/or increase our costs.
- > The development, manufacturing and marketing of biological products are often subject to more complex and stringent regulations than those applicable to other pharmaceutical products. As a result, the production and release schedules for biological products may be more significantly affected by the regulatory process than for other products. In addition, various legislative and regulatory authorities are considering whether an abbreviated approval process is appropriate for biosimilars or follow-on biological products (similar versions of existing biological products). It is uncertain as to when, or if, any such process may be adopted or how such a process would relate to intellectual property rights in connection with marketed or pipeline biological products, but any such process could have a material effect on the future commercial prospects for patented biological products.
- > Manufacturing biological products, especially in large quantities, is often complex and may require the use of innovative technologies to handle living micro-organisms. Manufacturing biological products requires facilities specifically designed and validated for this purpose, with sophisticated quality assurance and quality control procedures. Slight deviations in any part of the manufacturing process may result in lot failure, product recalls or spoilage, for example due to contamination.

> The methods of distributing and marketing biological products could have a material impact on the revenue we are able to generate from the sales of products such as *Synagis* and *FluMist*.

The commercialisation of biologic products is often more complex than for traditional pharmaceutical products. This is primarily due to differences in mode of administration, technical aspects of the product, and the rapidly changing distribution and reimbursement environments. The tools available to the commercial team can be more limited and time-consuming in that the target physicians who prescribe biologics are often hospital-based specialists who treat patients with rare diseases. Biologics sales forces are usually smaller, more targeted and typically are required to make a more detailed, data-driven sales call. Patient education and awareness also requires a more personalised approach in that broad-based awareness campaigns, such as direct-to-consumer advertising in the US, is often not an efficient means by which to reach a smaller target population.

Competition, price controls and price reductions

Some of our most valuable products compete directly with other products marketed either by major R&D based prescription pharmaceutical companies or by generic pharmaceutical manufacturers. These competitors may invest greater resources to 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 because they do not have to recoup the significant cost of R&D investment, nor do they generally invest the same amounts in education services for healthcare professionals. Industry consolidation has resulted in a small number of very large companies, some of which have acquired generic businesses. This trend, if it continued, could adversely affect our competitive position, whilst consolidation among our customers may increase price pressures. Some of our patented products, including *Nexium*, *Crestor*, *Seroquel* and *Symbicort* are subject to price pressure from competition from generic products in the same product class.

In most of our key markets there is continued economic, regulatory and political pressure to limit or reduce the cost of pharmaceutical products. 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 Geographical Review from page 48.

In the US realised prices are being depressed through limited lists, or formularies, that may force manufacturers either to reduce prices or be excluded from the list, and as a consequence lose sales revenue from patients covered by that formulary. In addition, private health insurance companies and employers that self-insure increasingly require co-payments from beneficiaries, particularly for branded pharmaceuticals and biotechnology products, among other reasons, to encourage beneficiaries to use generic products. The increased use of strict formularies by institutional customers in response to the current cost-containment environment and increasingly restrictive reimbursement policies could result in a materially adverse effect on our financial condition and results of operations.

In the EU, efforts by the European Commission to reduce inconsistencies and improve standards and best practice in the disparate national regulatory systems have met with little immediate success. The industry is, therefore, exposed to greater application of reference pricing mechanisms and ad hoc national cost-containment measures on prices and the consequent cross-border movement of products. 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, may increase. The accession of additional countries from Central and Eastern Europe to the EU as well as economic changes within EU countries may result in significant increases in the parallel trading of pharmaceutical products. In the US, new legislation is possible that may allow the commercial importation of drugs into the US from selected countries. The adoption of such legislation could result in an increase in volume of cross-border product movements which could result in a materially adverse effect on our financial condition and results of operations.

We expect that pressures on pricing will continue and may increase. Because of these 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 investment in that product.

Taxation

The integrated nature of our worldwide operations can produce conflicting claims from revenue authorities as to the profits to be taxed in individual territories. 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 earnings per share. Claims, regardless of their merits or their outcome, are costly, divert management attention, and may adversely affect our reputation.

The majority of the jurisdictions in which we operate have double tax treaties with other foreign jurisdictions, which enable us to ensure that our revenues and capital gains do not incur a double tax charge. 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 have a materially adverse effect on our financial condition and results of operations, as could a negative outcome of a tax dispute or failure of tax authorities to agree through competent authority proceedings. See the Financial Risk Management Policies on pages 41 to 42 for further details of risk mitigation. The Group is currently managing a number of tax disputes detailed in Note 25 to the Financial Statements.

Substantial product liability claims

Given the widespread impact that prescription drugs may have on the health of large patient populations, pharmaceutical, biopharmaceutical and medical device companies have, historically, been subject to large product liability damages claims, settlements and awards for injuries allegedly caused by the use of their products. Product liability claims, regardless of their merits or their outcome, are costly, divert management attention, and may adversely affect our reputation and demand for our products. Adverse publicity relating to the safety of a product or of other competing products may increase the risk of product liability claims. Litigation, particularly in the US, is inherently unpredictable and verdicts and/or unexpectedly high awards of damages can result. Substantial product liability claims that result in court decisions against us or in the settlement of proceedings could have a materially adverse effect on our financial condition and results of operations, particularly where such circumstances are not covered by insurance. We are currently subject to extensive product liability litigation in relation to *Seroquel*, and further details about this and all material legal proceedings in which we are involved are set out in Note 25 to the Financial Statements. Information about our approach to patient safety is set out in the Medicines section on page 16.

Performance of new products

Although we carry out numerous and extensive clinical trials on all our products before they are launched, for a new product it can be difficult, for a period following its launch, to establish from available data a complete assessment of its eventual efficacy and/or safety in broader clinical use on the market. Due to the relatively short time that a product has been tested and the relatively small number of patients who have taken the product, the available data may be immature. Simple extrapolation of the data may not be accurate and could lead to a misleading interpretation of a new product's likely future commercial performance.

The successful launch of a new pharmaceutical product involves a substantial investment in sales and marketing costs, launch stocks and other items. The commercial success of our new medicines is of particular importance to us in order to replace sales lost as and when patent protection ceases in established markets. If a new product does not succeed as anticipated or its rate of sales growth is slower than anticipated, there is a risk that the costs incurred in launching it could have a materially adverse effect on our financial condition and results of operations. In addition, for launch of products that are seasonal in nature, delays for regulatory approval or manufacturing difficulties can have the effect of delaying launch to the next season and significantly reduce the value of costs spent in preparing for the launch for that season.

Environmental/occupational/health and safety liabilities

We have environmental liabilities at some currently or formerly owned, leased and third party sites, as described in more detail in Note 25 to the Financial Statements. These liabilities are carefully managed by designated technical, legal and business personnel and there is no reason for us to believe that associated current and expected expenditure and/or risks are likely to have a materially adverse effect on our financial condition and results of operations as a general matter, although they could, to the extent that they exceed applicable provisions, have a materially adverse effect on our financial condition and results of operations for the relevant period. In addition, a change in circumstances (including a change in applicable laws or regulations) may result in such an effect.

Nonetheless, a significant non-compliance or incident for which we were responsible could result in us being liable to pay compensation, fines or remediation costs. In some circumstances, such liability could have a materially adverse effect on our financial condition, reputation and results of operations. In addition, our financial provisions for any obligations that we may have relating to environmental liabilities may be insufficient if the assumptions underlying the provisions – including 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.

Developing our business in emerging markets

The development of our business in emerging markets may be a critical factor in determining our future ability to sustain or increase the level of our global product revenues. Challenges that arise in relation to the development of the business in emerging markets include, but are not limited to, more volatile economic conditions, competition from companies that are already present in the market, the need to identify correctly and leverage appropriate opportunities for sales and marketing, poor protection of intellectual property, inadequate protection against crime (including counterfeiting, corruption and fraud) (further details of which can be found below), inadvertent breaches of local law/regulation and not being able to recruit sufficient personnel with appropriate skills and experience. The failure to exploit potential opportunities appropriately in emerging markets may have a materially adverse effect on our financial condition and results of operations. Information on the risks associated with the failure to obtain patent protection can be found above.

Product counterfeiting

Counterfeit medicines may contain harmful substances, the wrong dose of the active pharmaceutical ingredient (API) or no API at all. Counterfeit medicines are a danger to patients in all parts of the world; the International Medical Products Anti-Counterfeiting Taskforce (IMPACT) of the World Health Organization (WHO) estimates that approximately 10% to 30% of medicines in emerging economies are counterfeit, with parts of Latin America, Asia and Africa having a greater percentage than that. By contrast, in developed countries with effective regulatory systems, counterfeits represent less than 1% of the market.

Public loss of confidence in the integrity of pharmaceutical products as a result of counterfeiting could adversely affect our reputation and financial performance. In addition, undue or misplaced concern about the issue might induce some patients to stop taking their medicines, with consequential risks to their health.

We use a range of measures against counterfeit medicines, and continue to develop our capabilities in this area. These include introducing technologies that make it more difficult for counterfeiters to copy our products; conducting market surveillance and monitoring the supply chain to identify potential counterfeiting operations; and responding rapidly to any reports of counterfeit AstraZeneca medicines, working with regulators, healthcare professionals, distributors, law enforcement agencies and other organisations to protect patient interests. We also participate in a variety of anti-counterfeiting forums in the public and private sector, including the WHO's IMPACT working group and the Pharmaceutical Security Institute.

LEGAL/COMPLIANCE/REGULATORY RISKS

Adverse outcome of litigation and/or government investigations and insufficient insurance coverage

Note 25 to the Financial Statements includes information about legal proceedings in which we are currently involved. Unfavourable resolution of these and similar future proceedings, including government investigations, competition and anti-trust enquiries, investigations and litigation, product liability litigation and securities class action law suits, may have a materially adverse effect on our financial condition and results of operations, not least because we may be required to make significant provisions in our accounts related to legal proceedings and/or governmental investigations, which would reduce earnings. In many cases, particularly in the US, the practice of the plaintiff bar is to claim damages – compensatory, punitive and statutory – in extremely high amounts. Accordingly, it is difficult to quantify the potential exposure to claims in proceedings of the type referred to in Note 25 to the Financial Statements.

Recent insurance loss experience in the pharmaceutical industry, including product liability exposures, has increased the cost of, and narrowed the coverage afforded by, pharmaceutical companies' product liability insurance. In order 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 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. If such denial of coverage is ultimately upheld, this could result in material additional charges to our earnings.

Difficulties of obtaining and maintaining regulatory approvals for new products

We are subject to strict controls on the manufacture, labelling, distribution and marketing of pharmaceutical products. The requirement to obtain regulatory approval based on a product's safety, efficacy and quality before it may be marketed for a specified therapeutic indication or indications in a particular country, and to maintain and to comply with licences and other regulations relating to its manufacture, are particularly important. The submission of an application to regulatory authorities (which are different, with different requirements, in each region or country) may or may not lead to approval to market the product. 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 parts of the world. The countries that constitute key markets for our pharmaceutical products include the US, the countries of the EU and Japan. The approval of a product is required by the relevant regulatory authority in each country, although a single pan-EU marketing authorisation approval can be obtained through a centralised procedure.

In recent years, regulatory authorities and sponsor companies have been under increased public pressure to apply more conservative benefit/risk criteria before a pharmaceutical product is approved. In addition, third party interpretation of publicly available data on our marketed products has the potential to influence the approval status or labelling of a currently approved and marketed product. Further, predicting when a product will be approved for marketing remains challenging. For example, a review of the FDA performance data indicates that for new drug and biologic applications approved in 2008, the average review time (ie the time from submission to approval) increased markedly from 2007, in part due to the FDA failing to meet the review time targets for new drug applications specified under the Prescription Drug User Fee Act IV. Delays in regulatory reviews could impact the timing of new product launch.

Failure to observe continuing regulatory oversight

Once a product has been approved for marketing by regulatory authorities, it is subject to continuing control and regulation, such as the manner of its manufacture, distribution, marketing and safety surveillance. In addition, the facilities in which products are produced are subject to continuing inspections, and minor changes in manufacturing processes may require additional regulatory approvals, either of which could result in us having to incur significant additional costs. 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 third parties with which we have relationships). These powers include withdrawal of a marketing approval previously granted, product recalls, seizure of products, closure of manufacturing sites and other sanctions for non-compliance. Regulatory sanction, following a failure to comply with such continuing regulatory oversight, could have a materially adverse effect on the conduct of our business, our financial condition and results of operations. In addition, because our products are intended to promote the health of patients, any supply interruption could lead to allegations that public health has been endangered, and could lead to legal proceedings being filed against us, damage to our reputation and loss of confidence in our products.

BUSINESS EXECUTION RISKS

Challenges to achieving commercial success of new products

The development of new products is complex and involves the commitment of substantial effort, funds and other R&D resources. It involves a high degree of risk and uncertainty and can take many years. New products are important to replace the declining sales of older products following expiry of intellectual property protection. Our development of any product candidate may fail at any stage of the process, and we may ultimately be unable to achieve commercial success for any number of reasons, including:

- > Failure to obtain the required regulatory approvals for the product candidate or the facilities in which it is manufactured.
- > Adverse reactions to the product candidate or indications of other safety concerns.

- > Inability to manufacture sufficient quantities of the product candidate for development or commercialisation activities in a timely and cost-efficient manner.
- > Unfavourable data from key studies.
- > Excessive costs of, or difficulty in, manufacturing.
- > Erosion of patent term and other intellectual property rights, and infringement of those rights and the intellectual property rights owned by third parties.
- > Failure to show value or a differentiated profile for our products.

As a result, we cannot be certain that compounds currently under development will achieve success. There can also be no guarantee that new products in the pipeline will achieve market success or come to market before the expiration of our patents or the erosion of our current product brands. Furthermore, a succession of negative drug project results and a failure to reduce development timelines effectively could adversely affect the reputation of our R&D capabilities. The failure of R&D to yield new products that achieve commercial success may have a materially adverse effect on our financial condition and results of operations.

Acquisitions and strategic alliances formed as part of our externalisation strategy may be unsuccessful

We seek acquisitions of complementary businesses, technology licensing arrangements, strategic alliances and collaborations to expand our product portfolio and geographical presence as part of our business strategy. Examples of such recent strategic acquisitions, arrangements, collaborations and alliances include:

- > Acquisition of MedImmune to accelerate our biologics capability.
- > Collaboration with Bristol-Myers Squibb Company to develop and commercialise two investigational compounds being studied for the treatment of Type 2 diabetes, saxagliptin and dapagliflozin.
- > Collaboration with POZEN Inc. to develop a fixed dose combination of enteric coated naproxen and immediate release esomeprazole for chronic pain (PN400), utilising POZEN's proprietary technology.

- > Agreement with Abbott for the development of Abbott's next-generation fenofibrate (ABT-335) and *Crestor* in a single pill, fixed-dose combination treatment to target all three major blood lipids – LDL-C 'bad cholesterol', HDL-C 'good cholesterol' and triglycerides.
- > Collaboration deals with Columbia University and Newcastle University to support our early stage discovery activities.

We may not complete these types of transactions or collaborative projects in a timely manner, on a cost-effective basis, or at all, and may not realise the expected benefits of any acquisition, licensing arrangement or strategic alliance. Other companies may also compete with us for these opportunities. The success of such current and future arrangements is largely dependent on the technology and other intellectual property we acquire and the resources, efforts and skills of our partners. Disputes and difficulties in such relationships may arise, often due to conflicting priorities or conflicts of interest which may erode or eliminate the benefits of these alliances if, for example, the agreements are terminated; insufficient financial or other resources are made available to the alliances; intellectual property is negatively impacted; obligations are not performed as expected; controls and commercial limitations are imposed over the marketing and promotion of products to be co-developed; or challenges in achieving commercial success of the product are encountered during the development process. Also, under many of our strategic alliances, we make milestone payments well in advance of commercialisation of products, with no assurance that we will ever recoup those payments. If these types of transactions are unsuccessful, this may have an adverse effect on our financial condition and results of operations.

In addition, 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 impairment of long-term assets. These effects, individually or in combination, could cause a deterioration of our credit rating, increased borrowing costs and interest expense. We could also experience difficulties in integrating geographically separated organisations,

systems and facilities, and personnel with different organisational cultures. Integration of an acquired business may also divert management resources that would otherwise be available for continuing development of our existing business. The integration process may result in business disruption, the loss of key employees, slower execution of various work processes, compliance failures due to a change in applicable regulatory requirements and other issues such as a failure to integrate information technology and other systems (further details of the risks associated with information technology and outsourcing can be found below).

Reliance on third parties for supplies of materials and services

Like most, if not all, major research-based pharmaceutical companies we increasingly rely on third parties for the timely supply of specified raw materials, equipment, contract manufacturing, formulation or packaging services and maintenance services that are key to our operations. We actively manage these third party relationships to ensure continuity of supplies on time and to our required specifications. However, events beyond our control could result in the delayed, incomplete or failure of supplies, which could have a materially adverse effect on our financial condition and results of operations. Recently, we have established sourcing centres in China and India to identify high quality suppliers in those regions. Further information is contained in the Working with Suppliers section on page 75.

Failure to manage a crisis

We handle chemical and biological materials, operate research and manufacturing plants and distribute products worldwide. Major disruption to our business and damage to our reputation may be triggered by an operational incident or actions by third parties. In these circumstances, a plan for addressing operational and other issues should ensure a timely response and the ability to resume business as usual. Failure to institute proper communication to internal and external stakeholders and mobilise a rapid operational response could have a materially adverse effect on our financial condition and results of operations. Further information about our business resilience plans and processes are contained in the Business Resilience Plans section on page 75.

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 trials, the manufacture of pre-launch stocks of the products, investment in marketing materials ahead of a product launch, sales force training and the timing of anticipated future revenue streams from commercial sales of new products. 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 negotiation in some countries. Delays in anticipated launch dates can arise as a result of adverse findings in pre-clinical or clinical studies, regulatory demands, competitor activity and technology transfer. Any delay to the anticipated launch dates may therefore impact our business and operations in a number of ways. Significant delay to the anticipated launch dates of new products could have a materially adverse effect on our financial condition and results of operations.

Failure of information technology and outsourcing

We are dependent on effective information technology (IT) systems. These systems support key business functions such as our R&D and manufacturing capabilities, and are an important means of internal communication and communication with customers and suppliers. Any significant disruption of these IT systems or the failure of new IT systems to integrate with existing IT systems could materially and adversely affect our operations. We also have a number of outsourcing arrangements in respect of critical processes, services and the support of our IT infrastructure and our increasing dependency on these outsource providers could impact on our ability to deliver on business targets and to maintain our compliance status and reputation. Risk associated with outsource providers is mitigated by our contracting approach which enables us to monitor closely any degradation in services and enact staged remedies. Our engagement of multiple outsource providers mitigates against risk of over-reliance on any one outsource provider.

Productivity initiatives

We are implementing various productivity initiatives and restructuring programmes, with the aim of enhancing the long-term efficiency of the business. However, the anticipated cost savings and other benefits are based on preliminary estimates and the actual savings may vary significantly. In particular, these cost reduction measures are based on current conditions and do not take into account any future changes to the pharmaceutical industry or our operations, including new business developments, wage and price increases and other factors. If inappropriately managed the expected value of the initiative can be lost through low employee morale and hence productivity, increased absence levels and industrial action. Our failure to implement successfully these planned cost reduction measures, either through the successful conclusion of employee relations processes (including consultation and engagement, talent management and recruitment and retention), or the possibility that these efforts do not generate the level of cost savings we anticipate, could have a materially adverse effect on our financial condition, results of operations and reputation. See the People section on page 28 for information about mitigating the risk of significant business change.