

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 27 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 and securities class action cover 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.

#### **Risk of 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 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.

#### **BUSINESS EXECUTION RISKS**

##### **Risk that R&D will not yield new products that achieve commercial success**

The development of new pharmaceutical and biological products is complex and involves the commitment of substantial effort, funds and other resources to R&D activities. It also involves a high degree of risk and uncertainty and can take many years. New products are important to replace the sales of older products that decline upon the expiration of exclusive rights. Our product development efforts with respect to 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:

- > Difficulty enrolling patients in clinical trials.
- > Our 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.
- > Our 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.
- > Our 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. For example, in 2007 we discontinued a number of projects as shown in the pipeline table on page 30. 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 affect on our financial condition and results of operations.

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

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

- > Acquisitions of MedImmune, Inc., Cambridge Antibody Technology Group plc, Arrow Therapeutics Ltd and KuDOS Pharmaceuticals Limited.

## RISK CONTINUED

- > 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 naproxen and esomeprazole for chronic pain (PN400), utilising POZEN's proprietary technology.
- > Agreement with Abbott Laboratories 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.

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. For example, in April 2007, we terminated our licensing and collaboration agreement with AtheroGenics, Inc. following the discontinuation of the development of AGI-1067 (an investigational anti-atherosclerotic agent for the potential treatment of patients with coronary artery disease) due to its failure to meet its target product profile. Other companies may also compete with us for these strategic opportunities. When we are able to complete these transactions, the success of these types of arrangements (whether already existing or to be entered into in the future) is largely dependent on the technology and other intellectual property acquired from a business or contributed from our strategic partners and the resources, efforts and skills of our partners. Disputes and difficulties in such relationships are common, often due to conflicting priorities or conflicts of interest. The benefits of these alliances would be reduced or eliminated should strategic partners terminate the agreements; fail to devote sufficient financial or other resources to the alliances; suffer negative outcomes in intellectual property disputes; fail to perform their obligations as expected; or impose controls and commercial limitations over the marketing and promotion of products developed under that collaboration. 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 a materially adverse effect on our financial condition and results of operations.

In addition, integration of an acquired business could result in us 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 and result in increased borrowing costs and interest expense. We could also experience difficulties in integrating geographically separated organisations, systems and facilities, and personnel with diverse backgrounds. Integration of an acquired business may also require management resources that would otherwise be available for continuing development of our existing business. For example, the process of ensuring that our biologics and vaccines business, MedImmune, is operationally independent within our R&D organisation but aligned with our overall R&D strategy and objectives may be time-consuming and hard to achieve. The 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). Furthermore, although the operating model for MedImmune has significant potential benefits, it may not be the most effective way of realising efficiencies. As a result, we cannot be certain that we will not encounter difficulties in aligning MedImmune whilst maintaining its operational independence as contemplated, or that the expected benefits, including anticipated synergies, will be realised.

#### **Risk of reliance on third parties for supplies of materials and services**

Like most, if not all, major prescription pharmaceutical companies, in some of our key business operations, such as the manufacture, formulation and packaging of products, we increasingly rely on third parties for the timely supply of specified raw materials, equipment, contract manufacturing, formulation or packaging services and maintenance services. Although we actively manage these third party relationships to ensure continuity of supplies on time and to our required specifications, some events beyond our control could result in the complete or partial failure of supplies or in supplies not being delivered on time. Any such failure could have a materially

adverse effect on our financial condition and results of operations.

#### **Risk of 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 well tried and tested 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.

#### **Risk of 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.

#### **Information technology and outsourcing**

We are dependent on effective information technology systems. These systems are an important means of internal communication and communication with customers and suppliers, and also play an important role in respect of our R&D capabilities. Any significant disruption of these systems could materially and adversely affect our operations. We also have a number of outsourcing arrangements in respect of critical processes and services and our increasing dependency on these service

providers could impact on our ability to deliver on business targets and to maintain our compliance status and reputation.

**Risks relating to 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. Our failure to successfully implement these planned cost reduction measures, either through the successful conclusion of employee consultation processes or otherwise, or the possibility that these efforts do not generate the level of cost savings we anticipate going forward, could have a materially adverse effect on our financial condition and results of operations.

**REPUTATION**

Some parts of society continue to challenge the pharmaceuticals industry, which is under the close scrutiny of the public, the media and other stakeholders. Rising expectations are especially noteworthy in the areas of improving access to medicines for the underprivileged, both in our established markets and in less-developed nations; business conduct in our supply chain; fair marketing practices; bio-ethical challenges; working conditions; human rights; and animal rights. Although we seek to manage these risks through various proactive measures, there can be no assurance that in the future such risks will not have a materially adverse effect on our financial condition or results of operations.