

AstraZeneca's continued success depends on focused delivery of our strategy, responding effectively to the challenges of our rapidly changing business environment and successfully identifying and harnessing opportunities to strengthen the value of our contribution to healthcare and society.

This section describes the resources, skills and capabilities that we have in place to drive delivery of our strategic goals and keep AstraZeneca at the forefront of positive change within the industry.

Underpinning all of our activity is our commitment to innovative collaboration, focused on a common goal: better health. This means engaging and working with our stakeholders to gain the insights we need to maintain a flow of new, targeted and valued medicines. It means working in effective teams internally and in external partnerships that complement and strengthen our own capabilities. It also means active participation in the debate on issues that impact our business and shape our operating environment.

MEDICINES

Backed by our 70-year track record of pharmaceutical innovation, we have a broad range of marketed medicines that continue to make a positive difference in important areas of healthcare. We actively and rigorously develop our brands to bring further benefit for patients and maximise their commercial potential.

Our range of medicines is highly competitive and includes 11 products each with annual sales of over \$1 billion. Our business growth in the short to medium term is being driven by *Arimidex*, *Crestor*, *Seroquel* and *Symbicort*. Together with *Nexium*, these five key products provide the platform for our continued success whilst we enhance our pipeline for the future.

Our medicines are testament to the skills of our scientists and our commitment to working closely with physicians, patients and other stakeholders to understand what they need and what they value. Such relationships have helped us develop families of medicines – generation by generation – such as the hormone-based cancer treatments we have discovered since the 1970s, including *Nolvadex* (tamoxifen), *Zoladex*, *Casodex*, *Arimidex* and *Faslodex*. Among other benefits, these have played a part in increasing the five year survival rate for women with breast cancer from under 70% 50 years ago to around 90% today.

We introduced the world's first proton pump inhibitor, *Losec/Prilosec* in 1988 – a breakthrough in the treatment of gastro-oesophageal reflux disease – and we have since developed an improved therapy, *Nexium*, which provides healing and symptom relief in more patients in a shorter time.

Even after a new medicine is launched, we continue to explore all the ways it can be used to maximise patient benefit. We have clearly defined development management programmes for our marketed products designed to optimise both the benefit they bring to patients' lives and their commercial potential within the timeframe that patent protection is available to us.

For example, *Crestor*, our statin for lowering cholesterol levels has been used to treat over 14 million people since its launch in 2003. Studies in recent years have shown that not only does *Crestor* reduce cholesterol, it also slows the progress of atherosclerosis, or "hardening of the arteries". In 2008, a major study reported that *Crestor* significantly reduced major cardiovascular events by 44% in patients with normal cholesterol levels but with other high risk factors.

Similarly, we first introduced *Seroquel* as a treatment for schizophrenia, and our subsequent studies have shown that it is also effective in treating both the manic and depressive dimensions of bipolar disorder. Recent clinical development has also been undertaken for the use of *Seroquel* in treating major depressive disorder and general anxiety disorder. Launched in 1997, *Seroquel* is now the most commonly prescribed atypical anti-psychotic in the US.

We also continue to develop better ways in which our medicines can be used. Our *Symbicort* Maintenance and Reliever Therapy (*Symbicort SMART*) is the first asthma treatment regime to combine both regular maintenance and as-needed reliever therapies – allowing patients to control daily symptoms and reduce asthma attacks using one inhaler, instead of the usual two or more. In another development, *Symbicort* is also now used to treat chronic obstructive pulmonary disease (COPD).

Our acquisition of MedImmune in 2007 brought some significant biological products into our portfolio. *Synagis* is the standard of care for respiratory syncytial virus (RSV) prevention and has been administered to over one million premature babies around the world to help protect them from serious RSV disease.

FluMist, the first intranasal influenza vaccine to be approved in the US, represents the first innovation in flu vaccination in more than 60 years.

Further information about all our major products can be found in the Therapy Area Review on page 53.

ENSURING PATIENT SAFETY

The safety of the patients who take our medicines is a fundamental consideration. All drugs have potential side effects and we aim to minimise the risks and maximise the benefits of each of our medicines, throughout their discovery, development and beyond. After launch, we continually monitor the use of all our medicines to ensure that we become aware of any side effects not identified during the development process and to ensure that accurate, well-informed and up-to-date information concerning the safety profile of our drugs is provided to regulators, physicians, other healthcare professionals and, where appropriate, patients. Clinical trials, although extensive, cannot replicate the complete range of patient circumstances and rare side effects can often only be identified after a medicine has been launched and used in far greater numbers of patients and over longer periods of time. We have comprehensive and rigorous pharmacovigilance systems in place for detecting and rapidly evaluating such effects, including mechanisms for highlighting those that require immediate attention.

We have an experienced, in-house team of around 500 clinical patient safety professionals working around the world who are dedicated to the task of ensuring that we meet our commitment to patient safety. Each of our products (whether in development or on the market) has an assigned Global Safety Physician who, supported by a team of Patient Safety Scientists, is responsible for that product's continuous safety surveillance. Patient Safety Managers in each of our national companies have local responsibility for product safety within their respective countries.

Our Chief Medical Officer (CMO) has overall accountability for the benefit/risk profiles of the products we have in development and those on the market. The CMO provides medical oversight and ensures that appropriate risk assessment processes are in place to enable informed decisions to be made about safety as quickly as possible.

Our commitment to patient safety includes ensuring the security of our medicines throughout their manufacture and supply. We continuously monitor our business environment to identify any new or emerging product security risks and work to ensure that these are managed quickly and effectively. In addition to our internal processes, we also work with regulatory authorities, government agencies, trade associations and law enforcement agencies to combat the growing threat of counterfeiting. Further details of the ways in which we manage the risk of counterfeiting can be found in the Principal Risks and Uncertainties section from page 76.

HOW WE PRICE OUR MEDICINES

Despite significant advances in healthcare in recent decades, many diseases are still under-diagnosed or not well treated, or there is not yet an effective therapy. Continued innovation is required to address these unmet medical needs. At the same time, the growing demand for healthcare, driven by people living longer, increasing populations and the emergence of new economies, means ever greater pressure on the payers' budgets.

At AstraZeneca, our challenge is to balance the associated downward pressure on the price of medicines with the cost of the continued innovation that brings benefit for patients and society.

When setting the price of a medicine, we take into consideration its full value to patients, to those who pay for healthcare and to society in general. Our pricing also takes account of the fact that, as a publicly owned company, we have a duty to ensure that we continue to deliver an appropriate return on investment for our shareholders. We balance many different factors, including ensuring appropriate patient access, in our global pricing policy, which provides the framework for optimising the profitability of our products in a sustainable way.

We continually review our range of medicines (both those on the market and in the pipeline) to identify any that may be regarded as particularly critical to meeting healthcare needs – either because they treat diseases that are (or are becoming) prevalent in developing countries, or because they are potentially a leading or unique therapy addressing an unmet need and offering significant patient benefit in treating a serious or life-threatening condition. In such cases, we aim to provide patient access to these medicines through expanded patient access programmes. We also support the concept of differential

pricing in this context, provided that safeguards are in place to ensure that differentially priced products are not diverted from patients who need them, to be sold and used in more affluent markets.

BRINGING ECONOMIC AS WELL AS THERAPEUTIC BENEFIT

Our medicines play an important role in treating serious disease and in doing so they bring economic as well as therapeutic benefits. Effective treatments can help to save healthcare costs by reducing the need for more expensive care, such as hospital stays or surgery. They also contribute to increased productivity by reducing or preventing the incidence of diseases that keep people away from work.

RESEARCH AND DEVELOPMENT

R&D STRATEGY

Our R&D strategy is geared to maintaining a flow of new products that will deliver sustained business growth in the short, medium and long-term.

In the short-term, we have continued to build on the good growth achieved in 2007. Our overall portfolio volume has grown by 5% and our in-phase distribution of the projects has improved. Phase III volumes have remained constant and our Phase II portfolio has grown by over 50% (20 to 31) during 2008.

Notable successes in the life-cycle management (LCM) of our key marketed products during the year included eight significant submissions and three approvals in the US and/or the EU, which are described in the Therapy Area Review commencing on page 53.

In the medium-term, we will continue to drive our pre-clinical and clinical Phase I and II projects towards proof of concept as rapidly as possible. In line with our ongoing externalisation strategy, we continue to look beyond our own laboratories, and actively seek alliances and acquisitions with external partners to gain access to leading drug projects or technology platforms.

The progress we are making in our drive to increase productivity is reflected in the delivery of projects from discovery and the growth of our early development portfolio. We have introduced a more rigorous and consistent measure for the number of compounds reaching development and now record additions to the pipeline from the first pre-clinical study conducted for regulatory

approval purposes (First Good Laboratory Practice (FGLP)) instead of when a candidate drug is simply nominated for development. During 2008, 32 FGLPs were selected for development (compared with 36 in 2007).

Further details are set out in the Development Pipeline table on pages 22 to 24.

DISEASE AREA STRATEGIES

Our disease area strategies are established using a regular review process that centres on the evaluation of research opportunities against a set of consistent criteria, including unmet medical need, commercial and scientific opportunity, competitive position and alignment with our capabilities. Our R&D Executive Committee (further details of which are set out on page 21) uses the reviews to determine the levels of investment we will make in different disease areas. The process also enables us to deploy our resources in the best way to meet our commercial and scientific objectives.

Our New Opportunities Team, operating from pre-clinical through development, generates more value from disease mechanisms and compounds through both internal efforts and external alliances with the aim to transform them into profitable, innovative therapies. In addition, the New Opportunities Team will consider a broad range of pre-clinical to late stage development opportunities. This includes identification of compounds that help address side effects and complications in disease areas we have prioritised, and of opportunities that enable rapid entry into breaking new disease areas via strategic alliances, in order to provide additional assets for our pipeline and the delivery of profitable growth.

OUR RESOURCES

AstraZeneca's research effort spans a range of different disciplines and locations, but our scientific community shares a common goal: to deliver new and innovative medicines to patients as quickly, efficiently and safely as possible. They work together across national boundaries and sites to exchange ideas, promote best practice and maximise the scientific potential offered by our size and global reach.

We have a global R&D organisation, with around 12,000 people at 17 principal centres in eight countries. Our main small molecule facilities are in the UK (Alderley Park, Macclesfield and Charnwood); Sweden (Lund, Mölndal and Södertälje); and the US (Boston, Massachusetts and Wilmington, Delaware). Other sites which have a focus on discovery



"2008 has been a milestone year for our R&D organisation. We are discovering and developing effective medicines faster than ever before and the considerable progress we have made in reducing development cycle times and costs has been achieved without compromising on quality.

Our review of our disease area strategies and deployment of resources to the best opportunities led us to modify our therapeutic area strategy during the year and to stop discovery work in osteoarthritis to allow us to increase our commitment to biologics. Coupled with a productive licensing activity, we have now created a more balanced portfolio of high quality small molecule and biologics projects that present a strong platform for continued success in important areas of unmet medical need.

During 2008, we delivered eight significant regulatory packages in several jurisdictions to broaden the use of our marketed products, *Seroquel*, *Symbicort*, *Iressa* and *FluMist*;

as well as two new product submissions for motavizumab and Onglyza™. We have strengthened our mid-stage pipeline and maintained 10 projects in Phase III development. 32 projects entered the pipeline during the year and 44 projects were progressed to their next phase of development. We have a total of 144 projects in the pipeline – an increase of seven compared with 2007.

I believe that AstraZeneca is well placed to maintain this rate of progress, backed by our clear strategy for R&D, our drive for continuous improvement, and an R&D leadership committed to delivery of our scientific and commercial objectives."

JOHN PATTERSON CBE FRCP
Executive Director, Development

research are in Canada (Montreal, Quebec); France (Reims); India (Bangalore); China (Shanghai); and the UK (KuDOS and Arrow Therapeutics' sites). We have a clinical development facility in Osaka, Japan. Our principal sites for biologics and vaccines are in the US (Gaithersburg, Maryland and Mountain View, California) and the UK (Cambridge). Substantially all of our properties are held freehold, free of material encumbrances and we believe such properties are fit for their purposes.

In 2008, we invested \$5.2 billion in R&D (2007: \$5.2 billion; 2006: \$3.9 billion), \$101 million on externalisation and approved \$308 million of R&D capital investment to strengthen our resources in line with our strategic objectives. Major capital commitments made in previous years continue to progress as planned. In Boston (US), we have continued to enhance our infection research capability, and at Macclesfield (UK) ongoing work is focused on expanding and improving our Process R&D laboratories. New investments in 2008 included the replacement and consolidation of Pharmaceutical & Analytical R&D's high potents manufacturing facilities at Charnwood (UK), and a major construction project to provide a new biologics services facility at Alderley Park (UK).

As part of our strategic expansion in important emerging markets, we continue to strengthen our research capabilities in Asia. Investment continued during 2008 at our 'Innovation Centre China' research facility in Shanghai,

which opened in 2007. The Centre is focused on translational medicine in cancer, a major cause of death in China. In addition, Process R&D has further expanded its capability in Bangalore as it moves to optimise the capital investment at this site in recent years.

DISCOVERY RESEARCH

In discovery research, we analyse many thousands of compounds for their potential to become a new medicine. Only a few make it through the various, increasingly demanding, stages of discovery research through which we identify the most promising candidates for clinical development. Our discovery teams work closely with clinical and development teams to prioritise their activities in line with our disease area strategies.

We continue to improve the quality of chemical leads and biological targets so that we can eliminate, at an early stage, those compounds that are unlikely to make it through development. We have invested in a number of key academic collaborations to identify potential new targets, disease mechanisms and technology platforms. For example, collaborations with Melior Discovery (Exton, Philadelphia, US) and Graffinity Pharmaceuticals (Heidelberg, Germany) help us to identify more rapidly those high quality, novel compounds which have the potential to proceed rapidly through discovery into clinical development. In addition we have continued to increase the speed and efficiency of our drug discovery processes using Lean Sigma™ approaches.

We believe that one of the reasons for our productivity success in Discovery over the past five years is because we have taken a long-term view and maintained consistency of focus over time on our strategic objectives. Latest industry benchmarks indicate that our speed and cost-effectiveness in Discovery have moved into the top quartile, while our delivery of candidate drugs this year exceeded our targets despite managing significant change across the organisation.

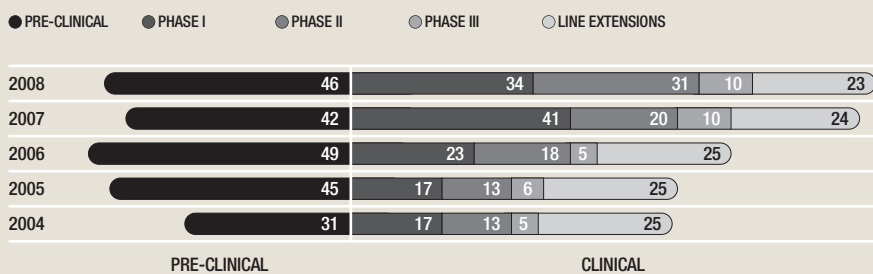
DISCOVERY MEDICINE

Discovery medicine (the collaboration between clinical medicine and basic science) helps us gain a better understanding of human diseases and the suitability of future medicines to treat those diseases, as well as identify and deploy biomarkers (a biological factor or measure that can be used to quantify the progress of a disease and/or the effects of a treatment) which can help us to make early decisions on the effectiveness and safety of our compounds in clinical development. All compounds nominated for development now have a biomarker strategy although it is not always easy to identify a marker for each molecule.

SAFETY ASSESSMENT

Safety assessment is a critical aspect of all our research and we implement high-throughput testing of safety early in the process of prioritising and selecting the best compounds for progression. Recent process improvements have reduced attrition due to safety issues and cut the time taken to deliver key safety studies, without compromising quality – allowing more rapid entry to testing in man.

DEVELOPMENT PROJECTS – NCEs AND LINE EXTENSIONS



DEVELOPMENT

In development, we focus on ensuring that our expanding range of potential medicines is developed effectively to meet the needs of patients and regulators. Project teams bring together all the relevant skills and experience needed for the rapid progress of new medicines, the management of development risks, and ensuring that quality and safety remain fundamental considerations at every stage.

We have a wide range of compounds in early development, and a total of 34 projects in Phase I, 31 projects in Phase II and 10 projects in Phase III development and are running 23 life-cycle management projects.

Throughout 2008, we have continued to focus on improving quality and speeding the progression of early phase projects along the development pipeline to market. Backed by reduced timelines across the whole small molecule development process, Phase I cycle times have halved since 2006 and over the last three years the composite product development cycle time has now been reduced by approximately two years.

With the adoption of Lean Sigma™ methodology and the implementation of best practice solutions, we have eliminated the lost time between key steps in the development process and we again exceeded our targets for development cycle times in 2008 for our small molecules. We believe that we are well placed to achieve our target of median composite development cycle times of eight years by 2010, based on the projects currently in development. Importantly, we have in recent years established a culture of continuous improvement that should sustain the momentum behind our initiatives for increased speed, with better quality, and with improved efficiency.

The initiatives we have in place to deliver significant productivity improvements by 2011 are making excellent progress and all are on track. These include:

- > The change programme that resulted from our disease area strategy review during 2007 was completed in 2008 with anticipated financial benefits of over \$100 million to be delivered by the end of 2009.
- > During 2008, we centralised and outsourced our clinical data handling to our external partner, Cognizant. This has enabled us to simplify our processes, promote consistency and drive resource efficiencies across our data management. These improvements are also helping to speed our internal data interpretation and decision-making.
- > Our re-organisation of the Pharmaceutical and Analytical R&D function aims to improve productivity and meet the demands of an increasingly strengthened pipeline better by changing working processes, while retaining our focus on innovation. For example, we have been able to progress a larger number of early projects by reducing the resource per project by more than 50% since 2004. The function has also downsized by 10% while introducing these productivity improvements.
- > Streamlining of our regulatory function exceeded the target 18% reduction in headcount achieving a 21% reduction by June 2008.

BIOLOGICAL PRODUCTS

We have a significant biologics business with proven end-to-end capabilities from discovery to commercialisation brought together in 2007 under the brand name of MedImmune. As is the case for small molecules, the discovery and development strategy for our biologics business is determined by the R&D Executive Committee, as is the funding allocation from the overall R&D budget.

We have around 30 biological product candidates in our development pipeline, backed by leading-edge technologies and R&D capabilities that cover a broad range of approaches to targeting disease across a range of therapy areas. These include antibodies, antibody derivatives, therapeutic proteins, peptides, RNA interference technologies and various types of live attenuated and sub-unit vaccines.

We also have a world-leading drug discovery platform, based on advanced technology for rapidly isolating human monoclonal antibodies using phage and ribosome display and a significant in-house manufacturing capacity and capability, including expertise in high-yield purification process and analytical development resources.

Our strategic objective is to generate eight compounds entering pre-clinical phase per year, on a steady-state basis, which we anticipate will translate into six new investigational drugs per year.

EXTERNALISATION

Our externalisation strategy continues to focus on enhancing our internal innovation through investment, external partnerships, alliances and acquisitions that further strengthen our pipeline of new products and our Strategic Planning and Business Development (SPBD) team works closely with R&D, global marketing and finance teams to deliver these objectives.

We have completed over 40 major externalisation deals in the last two years, including the acquisitions of MedImmune and Arrow Therapeutics in 2007, as well as numerous smaller deals to enhance and strengthen the overall health of the portfolio.

We believe that every collaboration is unique, and we work with potential partners to structure deals that leverage each party's capabilities and assets. Major transactions in the last two years have included the in-license of rights to Cubicin™ (an antibiotic) from Cubist in certain geographies and a co-development and co-commercialisation agreement with Abbott for a combination of Crestor and Trilipix™. We recently extended our co-development and co-commercialisation agreement with Bristol-Myers Squibb Company regarding saxagliptin (Onglyza™) and dapagliflozin (two products in development for the treatment of Type 2 diabetes) to include dapagliflozin in Japan. We also concluded an exclusive worldwide agreement with MAP Pharmaceuticals to develop and commercialise Unit Dose Budesonide (UDB), MAP Pharmaceuticals' proprietary nebulised formulation of budesonide.

Important early stage collaborations have included deals with Argenta and Silence Therapeutics and more recently with Columbia University in the US regarding both cardiovascular and neurology opportunities. Additionally, we have also formed a significant number of early stage partnerships to ensure that we have access to the latest science and technology.

Our externalisation strategy is not restricted to securing in-licensing deals and research or commercial collaborations. It represents an important component of our efforts to maximise value from our portfolio and incorporates value creation through disposal. To that end, we have completed a number of out-licensing transactions and disposals in 2008, including the transfer out of assets relating to certain gastrointestinal projects to create a new entity, Albireo. We also concluded a fostering agreement with Cancer Research UK under which they will conduct the early development of an Src Kinase Inhibitor at their own cost with AstraZeneca retaining options on the product upon completion of certain development milestones.

We continue to strengthen our biologics capability through externalisation and completed a number of significant transactions during 2008 including deals with Direvo Biotech and SBI Biotech Co.

During 2008 we broadened the scope of activity by MedImmune Ventures, a captive venture capital fund, set up to access leading-edge technology emerging within the biotechnology world. MedImmune Ventures will now seek opportunities on a more global basis to stay at the forefront of novel science accessing the most innovative start-ups in biotechnology.

R&D ETHICS

In our search for new medicines for important areas of healthcare, we are committed to innovative, high quality science, conducted to high ethical standards. Compliance with relevant laws and regulations is a minimum baseline and underpins our own global principles and standards, as outlined in our Bioethics Policy.

Clinical trials

Most of our clinical trials are global in nature because studies conducted across a broad geographic span enable us to represent more fully the diversity of the patient populations for whom the new medicine is intended.

When conducting a trial anywhere in the world, we operate to the highest of the standards required by the external international, regional or local regulations, and our own internal standards. We have strict guidelines to ensure that those taking part are not exposed to unnecessary risks; that they understand the nature and the purpose of the research; that proper procedures for gaining informed consent are followed (including managing any special circumstances such as different levels of literacy); and that appropriate confidentiality rules are applied.

Whilst all AstraZeneca clinical studies are designed and finally interpreted in-house, some of them are run for us by external organisations. The percentage of studies we place with third parties varies, depending on the number of trials we have underway and the amount of internal resource available to do the work. We contractually require all of our suppliers to work to the same standards that we apply in-house. In 2008, around 26% of patients in our global studies were monitored by external contract research organisations on our behalf.

During 2008, we extended the scope of our clinical trials disclosure to include information about the registration and results of all AstraZeneca sponsored clinical trials for all products in all phases, including marketed medicines, drugs in development and drugs whose further development has been discontinued. We make information available, irrespective of whether the results are favourable or unfavourable to AstraZeneca, on public websites including our own dedicated website, astrazenecaclinicaltrials.com. At the end of 2008, we had registered over 800 trials and published the results of more than 500 trials.

Animal research

Our pre-clinical research includes animal studies, which continue to play a vital role. They provide essential information, not available through other methods, about the effects of a potential new therapy on disease and the living body. Regulatory authorities around the world also require safety data from pre-clinical testing in animals before a new medicine can be tested in man.

All our research using animals is carefully considered and justified and, backed by our global policies, we continue to drive the application of the 3Rs (Replacement, Reduction and Refinement of animal studies) across our research activity.

The number of animals we use each year varies according to the amount of pre-clinical research we are doing and the complexity of the diseases under investigation. As we continue to expand our discovery research activity, our ongoing challenge is to ensure that our use of animals is minimised without compromising the quality of the data. We believe that, without our active commitment to the 3Rs, our animal use would be much greater.

We continue to develop our data capture processes to incorporate companies recently acquired by AstraZeneca and our animal numbers for 2008 now include MedImmune, Arrow Therapeutics and KuDOS.

In 2008, AstraZeneca used approximately 347,000¹ animals in-house (2007: 271,000). In addition, approximately 29,000¹ animals were used by external contract research organisations on our behalf (2007: 13,500). Around 93% of the animals used in 2008 were rodents, 4% were fish and amphibians and the remaining 3% included chickens, rabbits, dogs, ferrets, primates, pigs and sheep. We also use genetically modified mice and rats to understand better the genes involved in human disease. In 2008, these accounted for approximately 13% of our total rodent use.

We only use primates in circumstances where no other species or non-animal methods can provide the safety or clinical benefit information that we are seeking in a study, and where the outcomes of the study are likely to bring significant advances for the development of new medicines. Our expanding biologics capability means that we will be increasing our primate use over time, particularly in the development of monoclonal antibodies targeted at important areas such as cancer and respiratory disease. Monoclonal antibodies are highly specific to human physiology, so primates are in most cases the only relevant animal model because of their similarity to humans.

AstraZeneca does not conduct or outsource work using wild caught primates or great ape species. In the future, in the rare case where there is no credible alternative model, exceptions may be considered but this will require rigorous secondary ethical and scientific review – in addition to our normal review processes – to challenge the need for the study, followed by appropriate Board level approval.

¹ Preliminary figures. Final data will be available end March 2009 on our website, astrazeneca.com/responsibility

The welfare of the animals we use continues to be a top priority. Qualified veterinary staff are involved in the development and implementation of our animal welfare programmes and everyone working with laboratory animals is trained and competent in their allocated responsibilities.

As well as mandatory inspections by government authorities, we have a formal programme of internal inspections carried out by our own qualified staff. External contract research organisations that conduct animal studies on AstraZeneca's behalf are also required to comply with our ethical standards, and we conduct regular inspections to ensure our requirements are being met.

Stem cell research

As a company whose success is built on leading-edge science, we continuously monitor and assess new research capabilities to identify opportunities that could help us deliver better medicines for patients worldwide. We believe that human embryonic stem cell research may present such an opportunity.

Because this is a relatively new area for us and because we do not yet have all the necessary skills and technologies in-house, we are working with external partners who have the capabilities and expertise, and an ethical commitment consistent with our own. Some significant progress has been made, with some promising results, but more work is needed to understand the full potential of this type of research.

Our Bioethics Policy demands compliance both with external legislation, regulations and guidelines, and with our own codes of research practice, which include essential criteria that must be met before any such research is undertaken. Similar to those that govern inclusion in public stem cell registries such as the UK Registry and the US National Institute of Health Registry, these criteria require that the stem cells must have been derived from a fertilised egg that was created for reproductive purposes, that the fertilised egg must no longer be needed for these purposes and that fully informed consent (with no financial inducements) must have been obtained for the donation of the fertilised egg for scientific research. These requirements apply to all internal work and external research carried out on our behalf.

AstraZeneca is one of nine partners in a European Framework Research VI programme and is a founding member of the public-private partnership, Stem Cells for Safer Medicines, in the UK, which brings together academia, government and members of the pharmaceutical industry to broaden the approach to understanding this complex area of research.

Further information about our commitment to responsible research is available on our website, astrazeneca.com/responsibility.

R&D EXECUTIVE COMMITTEE, GOVERNANCE AND PORTFOLIO MANAGEMENT

The R&D Executive Committee oversees and prioritises our portfolio of both small molecule and biological discovery and development projects from across the Group (whether originating from our own R&D activities or from external sources). On an annual basis it takes a view across all therapy areas and makes decisions based on unmet therapeutic need, commercial and scientific opportunity, competitive position and capability mix. It is also charged with overseeing a portfolio review process intended to ensure that internal and external opportunities are reviewed using the same criteria and that there is a clear externalisation strategy aligned with the disease area strategies.

The Committee has the following accountabilities:

- > To establish a series of disease area strategies through joint therapy area strategy teams and to bring them together into a single AstraZeneca portfolio across small molecules and biologics.
- > To develop enabling strategies to ensure the optimal delivery of the disease area strategic targets, including technology strategies, capital expenditure, capability mix, shape and size and geographic footprint of the R&D organisation.
- > To work with the Chief Executive Officer and Chief Financial Officer to agree an overall R&D budget for AstraZeneca and, within the R&D Executive Committee, allocate that budget to discovery and development activities across small molecules and biologics.

- > To conduct a portfolio review process to evaluate all potential new medicines within the business to ensure resource prioritisation and delivery in line with that process. In particular, this process is intended to ensure that internal and external opportunities are reviewed using the same criteria and that there is a clear externalisation strategy, aligned with and complementary to, the disease area strategies, the internal portfolio and local market needs.

The R&D Executive Committee currently comprises the Executive Vice-President, Discovery Research; the Executive Vice-President, Development; the Executive Vice-President, Research and Development, MedImmune; the Executive Vice-President, Clinical Research and Chief Medical Officer, MedImmune; the Chief Executive Officer, North America and Executive Vice-President, Global Marketing and the President of MedImmune; the Senior Vice-President, Strategic Planning and Business Development; the Vice-President, R&D Finance; and the Vice-President, Development Projects.

Therapy area	Compound	Mechanism	Areas under investigation	Estimated filing date	
				MAA	NDA
PHASE I NCEs					
Cardiovascular	AZD6482	PI3K-beta inhibitor	thrombosis		
	AZD4017	11BHSD inhibitor	diabetes/obesity		
Gastrointestinal	AZD2066	metabotropic glutamate receptor 5 antagonist	GERD		
	AZD1386	vanilloid receptor antagonist	GERD		
Infection	MEDI-534	RSV/PIV-3 vaccine	intranasal immunisation		
	MEDI-560	PIV-3 vaccine	intranasal immunisation		
	MEDI-566	pandemic influenza virus vaccine	pandemic influenza vaccine		
	AZD9639 (MEDI-564) ¹	RSV F protein inhibitor	RSV treatment		
	CMV Vaccine	CMV vaccine	cytomegalovirus		
	MEDI-557	YTE – extended half-life RSV MAb	RSV prophylaxis		
	MEDI-559	RSV vaccine	RSV treatment		
Neuroscience	AZD5904	myeloperoxidase (MPO) inhibitor	multiple sclerosis		
	AZD3241	myeloperoxidase (MPO) inhibitor	Parkinson's disease		
	AZD2066	metabotropic glutamate receptor 5 antagonist	chronic neuropathic pain		
	AZD6280	GABA receptor subtype partial agonist	anxiety		
	TC-5619 ¹	neuronal nicotinic receptor agonist	cognitive disorders in schizophrenia		
	AZD8529	glutamatergic modulator	schizophrenia		
	AZD2516	metabotropic glutamate receptor 5 antagonist	chronic neuropathic pain		
	AZD1446	neuronal nicotinic receptor agonist	Alzheimer's disease		
AZD7268	enkephalinergic receptor modulator	depression/anxiety			
Oncology	AZD8931	erbB kinase inhibitor	solid tumours		
	AZD7762	CHK1 kinase inhibitor	solid tumours		
	AZD8330 (ARRY-424704) ¹	MEK inhibitor	solid tumours		
	CAT-8015	recombinant immunotoxin	haematological malignancies		
	MEDI-538 ¹	CD19 B cells	leukaemia/lymphoma		
	AZD8055	TOR kinase inhibitor	range of tumours		
	AZD6918	TRK inhibitor	solid tumours		
AZD4769	EGFR tyrosine kinase inhibitor	solid tumours			
Respiratory & Inflammation	Pneumococcal vaccine ¹	pneumococcal vaccine	Streptococcus pneumoniae		
	CAM-3001	anti-GM-CSFR	rheumatoid arthritis		
	AZD8848		asthma		
	AZD8566	CCR5	rheumatoid arthritis		
	AZD8075	CRTh2 antagonist	asthma/COPD		
AZD5985	CRTh2 antagonist	asthma/COPD			

¹ Partnered product.

Therapy area	Compound	Mechanism	Areas under investigation	Estimated filing date	
				MAA	NDA
PHASE II NCEs					
Cardiovascular	AZD0837	direct thrombin inhibitor	thrombosis	2012	2012
	AZD1305	anti-arrhythmic	arrhythmias		
	AZD6370	GK activator	diabetes		
	AZD1656	GK activator	diabetes/obesity		
Gastrointestinal	AZD3355	inhibitor of transient lower oesophageal sphincter relaxations (TLESR)	GERD	2011	2011
Infection	CytoFab™ ¹	anti-TNF-alpha polyclonal antibody	severe sepsis		
	EBV vaccine ¹	Epstein-Barr virus vaccine	post-transplant proliferative disease		
	AZD7295	NS 5a inhibitor	hepatitis C		
Neuroscience	AZD3480 ¹	neuronal nicotinic receptor agonist	Alzheimer's disease		
	AZD6765	NMDA receptor antagonist	depression	2012	2012
	AZD1940	CB1 receptor agonist	nociceptive and neuropathic pain		
	AZD1386	vanilloid receptor antagonist	chronic nociceptive pain		
	AZD2624	NK receptor antagonist	schizophrenia		
	AZD2327	enkephalinergic receptor modulator	anxiety and depression		
	AZD7325	GABA receptor subtype partial agonist	anxiety	2013	2012
Oncology	<i>Recentin</i>	VEGFR tyrosine kinase inhibitor	NSCLC	2013	2013
	AZD6244 ¹ (ARRY-142886)	MEK inhibitor	solid tumours	2014	2014
	AZD2281	PARP inhibitor	breast/ovarian cancer	2012	2012
	AZD0530	SRC kinase inhibitor	solid tumours and haematological malignancies		
	AZD4877	cell cycle agent	haematological malignancies		
	AZD1152	aurora kinase inhibitor	haematological malignancies	2011	2011
Respiratory & Inflammation	AZD9056	ion channel blocker (P2X7)	rheumatoid arthritis	2012	2012
	AZD5672	chemokine receptor antagonist (CCR5)	rheumatoid arthritis	2012	2012
	AZD1981	CRTh2 receptor antagonist	asthma/COPD		
	MEDI-528	anti-IL-9 antibody	asthma		
	CAT-354	anti-IL-13 antibody	asthma		
	AZD9668	neutrophil elastase inhibitor	COPD		
	AZD1236	matrix metallo-proteinase inhibitor	COPD		
	AZD3199	iLABA	asthma/COPD		
	MEDI-563	anti-IL-5R antibody	asthma		
	MEDI-545	anti-IFN-alpha antibody	SLE, myositis		

PHASE II LINE EXTENSIONS

Gastrointestinal	<i>Nexium</i>	proton pump inhibitor	extra-oesophageal reflux disease	3Q 2009 ²	3Q 2009 ²
Infection	Motavizumab	humanised MAb binding to RSV F protein	early and late treatment of RSV in paed >1 yr		

PHASE III/REGISTRATIONS: NCEs

Cardiovascular	Onglyza™ ¹	DPP-4 inhibitor	diabetes	Filed	Filed
	<i>Brilinta</i> (AZD6140)	ADP receptor antagonist	arterial thrombosis	4Q 2009	4Q 2009
	<i>Crestor</i> / <i>Trilipix</i> ™ ¹	statin + fibrate fixed combination	dyslipidaemia		3Q 2009
	Dapagliflozin ¹	SGLT2 inhibitor	diabetes	2H 2010	2H 2010
Infection	Motavizumab	humanised MAb binding to RSV F protein	RSV prevention	TBD	Filed
Neuroscience	PN400 ¹	naproxen + esomeprazole	signs and symptoms of OA, RA and AS	4Q 2009	Mid 2009
Oncology	<i>Zactima</i>	VEGFR/EGFR tyrosine kinase inhibitor with RET kinase activity	NSCLC	2Q 2009	2Q 2009
	<i>Recentin</i>	VEGFR tyrosine kinase inhibitor	CRC	2H 2010	2H 2010
	<i>Recentin</i>	VEGFR tyrosine kinase inhibitor	recurrent glioblastoma	2H 2010	2H 2010
	ZD4054	endothelin A receptor antagonist	hormone resistant prostate cancer	2011	2011

¹ Partnered product.

² Publication only.

Therapy area	Compound	Mechanism	Areas under investigation	Estimated filing date	
				MAA	NDA
PHASE III LINE EXTENSIONS					
Cardiovascular	<i>Atacand</i>	angiotensin II antagonist	diabetic retinopathy	Published ¹	Published ¹
	<i>Atacand Plus</i>	angiotensin II antagonist/thiazide diuretic	32/12.5mg, 32/25mg for hypertension	Filed	
	<i>Crestor</i>	statin	outcomes in subjects with elevated CRP	2Q 2009	2Q 2009
	Onglyza™/Metformin FDC ²	DPP-4 inhibitor + biguanide FDC	diabetes	2H 2010	4Q 2009
	Dapagliflozin/Metformin FDC ²	SGLT2 inhibitor + biguanide FDC	diabetes	2011	2011
Gastrointestinal	<i>Nexium</i>	proton pump inhibitor	peptic ulcer bleeding	Filed	Filed
	<i>Nexium</i> Low Dose <i>Aspirin</i> ™ Combination	proton pump inhibitor	low dose Aspirin™ associated peptic ulcer	3Q 2009	2Q 2009
	<i>Nexium</i>	proton pump inhibitor	extra-oesophageal reflux disease	3Q 2009 ¹	3Q 2009 ¹
Infection	<i>FluMist</i>	live, attenuated, intranasal influenza virus vaccine	influenza	Filed	Launched
Neuroscience	<i>Seroquel</i>	D ₂ /5HT ₂ antagonist	bipolar maintenance	Filed	Launched
	<i>Seroquel</i>	D ₂ /5HT ₂ antagonist	bipolar depression	Approved	Launched
	<i>Seroquel XR</i>	D ₂ /5HT ₂ antagonist	major depressive disorder	Filed	Filed
	<i>Seroquel XR</i>	D ₂ /5HT ₂ antagonist	bipolar mania	Approved	Approved
	<i>Seroquel XR</i>	D ₂ /5HT ₂ antagonist	bipolar depression	Approved	Approved
	<i>Seroquel XR</i>	D ₂ /5HT ₂ antagonist	generalised anxiety disorder	Filed	Filed
Oncology	<i>Iressa</i>	EGFR tyrosine kinase inhibitor	NSCLC	Filed	
	<i>Zactima</i>	VEGFR/EGFR tyrosine kinase inhibitor with RET kinase activity	medullary thyroid cancer	2H 2010	4Q 2009
	<i>Faslodex</i>	oestrogen receptor antagonist	first line advanced breast cancer		
	<i>Faslodex</i>	oestrogen receptor antagonist	adjuvant		
Respiratory & Inflammation	<i>Symbicort pMDI</i>	inhaled steroid/fast onset, long-acting β ₂ agonist	asthma	Filed	Launched ³
	<i>Symbicort pMDI</i>	inhaled steroid/fast onset, long-acting β ₂ agonist	COPD	Filed	Filed
	Unit Dose Budesonide ^{2,4}	inhaled steroid	asthma		

Therapy area	Compound	Areas under investigation
DISCONTINUED NCEs		
Cardiovascular	AZD1175	diabetes/obesity
	AZD2207	diabetes/obesity
Infection	AZD2836	hepatitis C
Neuroscience	AZD3480	cognitive disorders in schizophrenia
	AZD0328	Alzheimer's disease
	AZD1704	analgesia
Oncology	MEDI-561 (IPI-504)	GIST
	MEDI-561 (IPI-504)	solid tumours
	IPI-493	solid tumours
	AZD4877	solid tumours
	AZD1152	solid tumours
Respiratory & Inflammation	AZD4818	COPD

Therapy area	Compound	Areas under investigation
DISCONTINUED LINE EXTENSIONS		
Cardiovascular	<i>Crestor</i> outcomes end stage renal disease ⁵	renal disease

¹ Publication only.

² Partnered product.

³ US approval based on 12 years and above.

⁴ Subject to review under the Hart-Scott-Rodino Act.

⁵ Will proceed to publication.

COMMENTS

As disclosure of compound information is balanced by the business need to maintain confidentiality, information in relation to some compounds listed here has not been disclosed at this time.

Compounds in development are displayed by phase.

SALES AND MARKETING¹

Active in over 100 countries, we have an extensive sales and marketing network focused on growing our business and driving the levels of commercial excellence that will maintain our position among the industry world leaders.

Our Global Marketing (GM) function is responsible for developing and leading our global brand strategy, to ensure strong customer focus and commercial direction in the management of our R&D and brand development activity, across the full range of pipeline and marketed products.

We define at an early stage of the drug discovery process what we believe the profile of a medicine needs to be to work most effectively in combating a particular disease. These disease target product profiles (TPPs) are based on the insights that GM gains through its relationships with healthcare professionals, patients and others for whom the medicine must add value, including regulators and payers. The attitudes and needs of these groups are key drivers of the development of the TPPs which are used throughout the life-cycle of a medicine to guide our R&D activity and help shape the therapy area and marketing strategies. Early in the development of new products, we also consider how best to demonstrate the value of our medicines to payers.

IN THE MARKETPLACE

As well as building on our leading positions in Established Markets such as the US, Japan and Europe, we continue to increase our strength through strategic investment in Emerging Markets, where ongoing GDP growth and changing disease demographics present significant opportunities for our business.

In these markets, we are applying the same strategic approach that has delivered our continued success in Established Markets – a focus on adapting to local customer needs, backed by global capability and scale. As part of this, we are strengthening our in-country sales and marketing presence to support swift and effective response to local customer needs. We continue to deliver strong, profitable growth in our Emerging Markets business, alongside our ongoing investment in these countries.

SALES FORCE EFFECTIVENESS

In the majority of key markets, we sell through wholly-owned local marketing companies. Elsewhere, we sell through distributors or local representative offices. Our products are marketed primarily to physicians (both primary care and specialist) as well as to other healthcare professionals. Marketing efforts are also directed towards explaining the economic as well as the therapeutic benefits of our products to governments and others who pay for healthcare.

Face-to-face contact is still the single most effective marketing method, but increasingly the efforts of our sales forces are being complemented by our use of the internet to facilitate and enhance our commercial activities. For a few products we also use direct-to-consumer advertising campaigns in the US, where it is an approved and accepted practice.

The way in which biologics are marketed and sold is an intensive, personal approach that is more targeted compared with traditional pharmaceuticals, with extensive use of specialty pharmaceutical distributors and little direct-to-consumer advertising.

We continue to evolve our sales and marketing model to ensure we stay at the forefront of best practice in meeting customer needs.

In 2008, we created a cross-commercial strategy team, charged with the development and sharing of new sales and marketing best practice across our marketing companies. Pilot programmes currently being implemented include interactive selling models that are better suited to the time pressures of our customers, and novel approaches to the use of web-based tools that provide customers with information and support for their patients.

In Europe, we have continued to invest significantly in strengthening the skills of our commercial teams. Throughout 2008, several major international training programmes were held to enhance customer interaction skills and build capabilities in collecting and analysing first-hand customer insight. These programmes are being reinforced by in-market follow-up activities to consolidate core segmentation and management skills, and promote high quality customer service.

Our rapid growth in Emerging Markets is driving demand for central commercial support, particularly in respect of sales force effectiveness. Core sales and marketing

training programmes have been adapted for, and deployed in, local environments. The main focus of these programmes is to embed core commercial skills, such as segmentation and targeting, and to strengthen sales managers' coaching and planning skills. Both regional and local senior teams have adopted the same practice of active follow-up and monitoring as applied in our Established Markets.

ADAPTING TO THE CHANGING ENVIRONMENT

We continue to adapt to the changing demands and market conditions. Restructuring of our Established Market sales forces is being made to deliver efficiencies within a challenging business environment alongside the expansion of our Emerging Market teams to ensure we are appropriately resourced to deliver the full potential of the business opportunities in these countries.

Our business in Europe is now delivering improved productivity following our restructuring programme which over the last two years significantly reduced sales force numbers and marketing spend across all our major marketing companies in the region. Productivity benefits are also being seen in Japan, where we continue to reshape our sales and marketing cost base to support existing well performing brands and prepare for potential launches of new products.

In key Emerging Markets, in line with our future growth ambitions, we increased our sales and marketing spending by double-digit growth rates in 2008 and we continue to expand our sales forces to support our strategic expansion in these areas.

SALES AND MARKETING ETHICS

Our global reach, coupled with the broad range of different channels that we use for interacting with our customers, means that we face an increasing level of complexity in the various regulatory and legislative environments in which we operate.

We are committed to ensuring that we manage these complexities consistently and appropriately and deliver ethical sales and marketing practices worldwide that, as a minimum, meet or exceed the standards set by external regulations and codes of practice. To that end, we require all our marketing companies to have codes of practice in place that are in line with our own Code of Conduct and Global Policies, and which are at least as restrictive as all applicable external codes.

¹ For the AstraZeneca definition of markets please see the Glossary on page 199.

During 2008, we updated and further strengthened our existing codes of sales and marketing practice, with a particular focus on interactions with patient groups, the use of the internet for communicating about our products, and anti-bribery and anti-corruption governance. This update was supported by extensive training of all relevant staff in all countries.

Line managers monitor compliance locally within their teams, supported by dedicated compliance professionals, who also work to ensure that appropriate training in sales and marketing practices is provided. We also have a nominated signatory network that focuses specifically on approving promotional materials, to ensure that they meet all applicable internal and external code requirements.

At a global level, our Group Internal Audit teams conduct local audits within our marketing companies and regional offices. Marketing companies outside North America conduct their own local audits under the control of the Local Compliance Officer, reporting to the Regional Compliance Officer.

Information concerning instances where our practices may not be up to the standards we require is collected through our various compliance and continuous assurance reporting routes and reviewed by senior management in local and/or regional compliance committees. As appropriate, serious breaches are reviewed by the AstraZeneca Board and the AstraZeneca Audit Committee. More information about our compliance and assurance processes is contained in the Risk Management and Assurance Processes section on page 74.

The variations between national external frameworks for regulation of sales and marketing practices create a challenge in interpreting the number of cases of confirmed breaches of codes or regulations ruled by external bodies (our key performance indicator (KPI)). Nevertheless, this KPI provides a benchmark against which to measure our performance over time.

In 2008, we identified a total of 15 such cases (32 in 2007), based on information gathered from 63 countries in which we have marketing subsidiaries or branch offices. We believe this significant decrease reflects our continuing commitment in this area and arises primarily from our strengthened internal procedures. The decrease should also be seen in the context of the continuing rise in strict standards from national and international codes.

We take all breaches very seriously and take appropriate action to prevent repeat occurrences. This may include re-training, discipline, or other corrective action up to and including dismissal, depending on the circumstances.

Further information about our commitment to responsible business practice is available on our website, astrazeneca.com/responsibility.

INTELLECTUAL PROPERTY

Patents are important incentives for the continued innovation that drives society's progress. We continue to commit significant resources to establishing effective patent protection for our intellectual property, and to vigorously defending our patents if they are challenged.

The discovery and development of a new medicine requires a significant investment of time, resource and money by research-based pharmaceutical companies over a period of 10 or more years. For this to be a viable investment, the results – new medicines – must be safeguarded from copying with a reasonable amount of certainty for a reasonable period of time. The principal safeguard in our industry is a well-functioning patent system that recognises our effort and rewards our innovation with appropriate protection allowing time to generate the revenue we need to re-invest in new pharmaceutical innovation.

Our first level of protection is typically the patent to the new molecular entity, either a new chemical entity or a biological product. However, further innovations such as new medical uses or different ways of taking the treatment are often made during the R&D process and beyond. Each of these developments also requires significant resource investment to obtain marketing approval from regulatory authorities around the world. Our policy is to protect all the innovations that result from the investment we make in leading-edge science to deliver new and improved medicines.

We apply for patent protection relatively early in the R&D process to safeguard our increasing investment. We pursue these patents as appropriate through patent offices around the world, responding to questions and challenges from patent office examiners. In some countries, our competitors can challenge our patents in the patent offices, and in all countries competitors can challenge

our patents in the courts. We can face challenges early in the patent process and throughout the life of the patent, until the patent expires some 20 to 25 years later (patent expiry is typically ten to 15 years after the first marketing approval is granted). These challenges can be to the validity of a patent and/or to the effective scope of a patent and are based on ever-evolving legal precedents. There can be no guarantee of success for either party in patent proceedings taking place in patent offices or the courts.

Worldwide experience of biotechnology patent procurement and enforcement is, like the technology itself, relatively young and still developing. As a result, there can be some uncertainty about the validity and effective scope of biotechnology patent claims in the biotechnology arena. The investment in bringing biotechnology innovations to the market is huge and a well-functioning, predictable patent system is vital.

The generic industry is increasingly challenging innovators' patents, and almost all leading pharmaceutical products in the US have faced or are facing patent challenges from generic manufacturers. The research-based industry is also experiencing increased challenges elsewhere in the world, for example in Europe, Canada, Asia and Latin America. We are confident of the value of our innovations and, through close collaboration between our intellectual property experts and R&D scientists, we will continue to seek to obtain patents and defend them vigorously, if challenged. Further information about the risk of the early loss and expiry of patents is contained in the Risk section from page 74.

Compulsory licensing (the over-ruling of patent rights to allow patented medicines to be manufactured by other parties) is increasingly being included in the access to medicines debate. AstraZeneca recognises the right of developing countries to use the flexibilities in the World Trade Organization's TRIPS (Trade-Related Aspects of Intellectual Property Rights) Agreement (including the Doha amendment) in certain limited circumstances, such as a public health emergency. We believe that this should apply only when all other ways of meeting the emergency needs have been considered and where healthcare frameworks and safeguards to prevent diversion are in place to ensure that the medicines reach those who need them.

SUPPLY AND MANUFACTURING

Core to our continued business success is our ability to provide a secure, high quality, cost-effective supply of our products worldwide.

We continue to drive operational excellence, make adjustments to our manufacturing base and make effective use of strategic outsourcing to maximise the efficiency of our supply chain whilst maintaining the highest standards of quality and security of supply at every stage.

Our supply chains are structured to be flexible and responsive to the changing needs in our local markets. During 2008 we maintained our focus on driving continuous improvement to our supply system, as part of a wide-ranging cost and efficiency programme. This has delivered significant benefits in recent years, including reduced manufacturing lead times and lower stock levels, which have been achieved without compromising high levels of customer service and quality. Further improvements are planned using principles that focus on what adds value for our customers and patients, whilst also eliminating waste. In line with our commitment to strategic outsourcing to maximise supply chain efficiency, we plan to outsource all of our active pharmaceutical ingredient (API) manufacturing within five to 10 years.

We continuously review our manufacturing assets to make sure that they are being used in the most effective way, whilst preserving the flexibility we need to respond to fluctuations in demand. During 2008, we completed the sale of facilities in Germany and we closed our packaging site in Canada. Capital expenditure on supply and manufacturing facilities totalled approximately \$179 million in 2008 (2007: \$191 million; 2006: \$201 million) across a range of projects. We also recently announced the establishment of regional offices to optimise further our supply chain activity. This includes sourcing centres in Shanghai, China and Bangalore, India, established to identify high quality suppliers in those regions to support the growing market demand there. We will also establish a regional packing strategy, to improve our ability to respond to customer requirements, while equipping the business for Emerging Markets growth.

The introduction of new manufacturing processes has brought further opportunities to drive efficiencies across the global supply chain.

Our drive for efficiency and effectiveness resulted in announcements in 2008 of planned workforce reductions in our Supply organisation, which includes the closure of three sites, Porriño in Spain, Destelbergen in Belgium and Umeå in Sweden. Our facilities in Macclesfield (UK) and Södertälje (Sweden) will also be affected. Subject to local consultation, we expect these moves to result in headcount reductions of approximately 1,400 across the business by 2013. We recognise the impact that significant business change can have on our employees' morale and productivity and the increased risk of industrial action. We aim to manage these risks by ensuring that throughout the implementation of these changes we continue to consult fully with staff representatives and act in line with local labour laws. Our Human Resources policies and processes are also focused on ensuring that the people affected are treated with respect, sensitivity, fairness and integrity at all times, and you can read more about this commitment in the People section from page 28 onwards.

SUPPLY CAPABILITY

We have approximately 10,800 people at 26 manufacturing sites in 18 countries working on the supply of our products.

Our principal small molecule manufacturing facilities are in the UK (Avlon and Macclesfield); Sweden (Snäckviken and Gärtuna, Södertälje); the US (Newark, Delaware and Westborough, Massachusetts); Australia (North Ryde, New South Wales); France (Dunkirk and Reims); Italy (Caponago); Japan (Maihara); China (Wuxi) and Puerto Rico (Canovanas). Approximately 1,400 people work in active pharmaceutical ingredient supply and 8,800 in formulation and packaging. We operate a small number of sites for the manufacture of active ingredients in the UK, Sweden and France, complemented by efficient use of outsourcing. Our principal tablet and capsule formulation sites are in the UK, Sweden, Puerto Rico, France and the US, and we also have major formulation sites for the global supply of parenteral and/or inhalation products in Sweden, France, Italy and the UK.

Packaging is undertaken in a large number of locations, both at our own sites and at contractors' facilities, which are situated close to our marketing companies to ensure rapid and responsive product supply.

Some 600 people are employed at our five principal biologics commercial manufacturing and distribution facilities in the US (Frederick, Maryland; Philadelphia, Pennsylvania and Louisville, Kentucky); the UK (Speke); and The Netherlands (Nijmegen) with capabilities in process development, manufacturing and distribution of biologics, including worldwide supply of monoclonal antibodies and influenza vaccines. In addition to our own capabilities, Boehringer Ingelheim in Biberach, Germany serves as our manufacturing partner for certain monoclonal antibodies. Our biologics production capabilities are scalable, which enables efficient management of our combined small and large molecule pipeline. Substantially all of our properties are held freehold, free of material encumbrances and we believe such properties are fit for their purposes.

As part of our overall risk management, we carefully consider the timing of investment to ensure that secure supply chains are in place for our products. We have a programme in place to provide appropriate supply capabilities for our new products, including an assessment of new technology needs.

ENSURING PRODUCT QUALITY

We are committed to delivering assured product quality that underpins both the safety and efficacy of our medicines.

The manufacturing processes for chemical products and biologics can be very complex and must be conducted under rigorous standards of quality. Manufacturing plants and processes are subject to periodic inspections by regulators to ensure that manufacturers are complying with prescribed standards of operation. Regulators have the power to require, if they believe action is warranted, changes and improvements, to halt production and impose conditions that must be satisfied before production can resume. Regulatory standards also evolve over time as the industry develops new manufacturing techniques, so a process that may have been acceptable at one time may subsequently require changes.

The outcomes of our own routine internal inspections, as well as those conducted by regulatory authorities, are rigorously reviewed and, if required, actions are taken to improve quality and compliance consistently across the organisation. The results of all external inspections carried out during 2008 were generally satisfactory. All regulatory compliance observations that were raised during

inspections at our sites and at our partners' sites were resolved satisfactorily. Where appropriate, the experience and knowledge obtained as a result of these inspections is shared with other sites across the Group.

In March 2008, AstraZeneca Australia undertook a voluntary recall of four batches of Heparinised Saline 50IU/5ml because of the detection of a contaminant in the heparin raw material used in the manufacture of these batches. The heparin raw material was manufactured by a number of independent companies in China and sourced by AstraZeneca from an independent supplier. We communicated with all relevant stakeholders at the time of the recall. No adverse events were reported as a result of patients taking our heparinised saline product. As a result of this incident, we have taken steps to reinforce the security of our incoming materials supply chain, including strengthening our audit programme.

We continue to be actively involved through our membership in industry associations in influencing new product manufacturing regulations, both at national and international levels, primarily in Europe, the US and Japan.

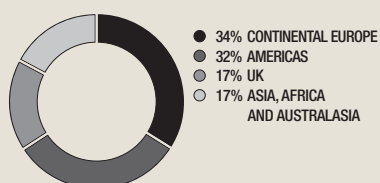
MANAGEMENT OF OUTSOURCING RISK

Our global procurement policies and integrated risk management processes are aimed at ensuring uninterrupted supply of sufficiently high quality raw materials and other key supplies, all of which are purchased from a range of suppliers. We focus on a range of risks to global supply, such as disasters that remove supply capability or the unavailability of key raw materials and work to ensure that these risks are effectively mitigated. Contingency plans include the appropriate use of dual or multiple suppliers and maintenance of appropriate stock levels. Although the price of raw materials may fluctuate from time to time, our global purchasing policies seek to avoid such fluctuations becoming material to our business.

Our risk management also includes mitigating any reputational risk associated with the use of third parties. As stated in our Code of Conduct, we are committed to working only with suppliers that embrace standards of ethical behaviour that are consistent with our own. See the Working with Suppliers section for more on this commitment on page 75.

PEOPLE

EMPLOYEES BY GEOGRAPHICAL LOCATION



With over 65,000 employees worldwide, we value the diverse skills and capabilities that a global workforce brings to our business. Aligning these skills and capabilities with strategic and operational needs, improving leadership capability, optimising performance and maintaining high levels of employee engagement are top priorities, alongside the integration of responsible business thinking across all our activities.

SETTING THE TARGETS

Clear targets and accountabilities are essential for ensuring that people understand what is expected of them as we work to deliver our business strategy. The AstraZeneca Board and Senior Executive Team are responsible for setting our high level strategic objectives and managing performance against these (see the Chief Executive Officer, Delegation of Authority and Senior Executive Team section on page 86). Managers across AstraZeneca are accountable for working with their teams to develop individual and team performance targets that are aligned to our high level objectives and against which individual and team contributions are measured and rewarded.

Our focus on optimising performance is reinforced by performance-related bonus and incentive plans. AstraZeneca also encourages employee share ownership by offering employees the opportunity to participate in various employee share plans, some of which are described in the Directors' Remuneration Report from page 174 and also in Note 24 to the Financial Statements on page 139.

LEARNING AND DEVELOPMENT

We encourage and support all our people in achieving their full potential with a range of high quality learning and development (L&D) opportunities around the world.

We are also in the process of adopting a new global approach, backed by the creation of a new global L&D organisation in 2008, which aims to ensure that standards of best L&D

practice are consistently applied in the most efficient way. During 2008, we also introduced an online resource that will, in time, make L&D tools and programmes available to all employees, creating a common platform that increases access to learning and supports self-development across the organisation. Implementation of further online L&D resources will continue during 2009.

Our leadership development frameworks are focused on six core capabilities which we believe are essential for strong and effective leadership: passion for customers; strategic thinking; acting decisively; driving performance; working collaboratively; and developing people and the organisation. These capabilities apply to all employees and are used in performance management, talent management, staffing and selection at all levels.

To ensure we maintain a flow of effective leaders, we work to identify individuals with the potential for increasingly more senior and complex roles. These talent pools provide succession candidates for a range of leadership roles across the Company that are critical to our continued business success.

COMMUNICATION AND DIALOGUE

We aim to provide an inclusive environment that encourages open discussion and debate at all levels across the Company. As well as line manager briefings and team meetings, we use a wide range of media to communicate with our employees around the world.

We also use a global employee survey (FOCUS) to track employee opinion across a range of key topic areas. The results, which are communicated to all employees, provide valuable insights that inform strategic planning across the business. To support our goal of promoting high levels of employee engagement, in 2008, our SET took the decision to run FOCUS annually, rather than every two years.

86% of our employees participated in the FOCUS 2008 survey – reflecting their continued confidence in this feedback mechanism. Results showed that employee engagement scores were very strong and we continue to outperform other pharmaceutical companies in this area. The results also indicated that people were seeing increased levels of cooperation between senior leaders, enabling more effective global and cross-functional working. The survey also identified some key areas that continue to require attention, in particular the need for improved communication from leaders about

AstraZeneca's strategic direction and the need to strengthen further our change management capabilities whilst continuing to invest in the development of our people. Our leaders take this feedback very seriously. New targets that address these issues have been included in the SET business performance management framework for 2009, and are focused on maintaining the already high levels of employee engagement, and improvements to the clarity of direction by senior leaders.

Our goal of creating a culture of open discussion and debate is supported by our well-developed arrangements for interactions with trade unions, elected employee representatives and local worker councils. A challenge for us is ensuring a level of global consistency whilst allowing enough flexibility to support the local markets in building good relations with their workforces that take account of local laws and circumstances – which vary from country to country. To that end, relations with trade unions are nationally determined and managed locally in line with the applicable legal framework and standards of good practice. We provide training at a local level for managers in consultation requirements as well as relevant labour law, and we have a range of Human Resources (HR) and line manager networks for sharing experience and good practice, and promoting alignment across the organisation. At a global level, we have a Group Employee Relations Director who supports national managers in ensuring that their local activities are consistent with our high level principles.

As we continue to develop our global platform for managing HR going forward, we are working to ensure that the strength of our local management approaches is not undermined. This is particularly critical to the effective management of the impact of our current business changes.

Our continuing strategic drive to improve efficiency and effectiveness resulted in further planned reductions of the workforce in some areas of our business during 2008. New business reshaping activities, combined with revised estimates for the original 2007 programme (7,600 job reductions), will result in the overall programme delivering a reduction of approximately 15,000 positions by 2013. All reductions in positions are subject to consultations with works councils, trade unions and other employee representatives and in accordance with local labour laws.

To ensure that a consistent approach continues to be adopted throughout the programme, specific guidance is provided for the HR teams and line managers throughout the organisation. Our challenge is that there are differences in the legal frameworks and the customary practice in the different geographies which are most affected by the business changes, but the global guidance provided aims to ensure that the same or similar elements are included in local implementation, for example, open communication and consultation with employees, re-deployment support and appropriate financial arrangements. In line with our core values, we expect the people affected to be treated with respect, sensitivity, fairness and integrity at all times.

Our long-standing arrangements for interactions with trade unions, elected employee representatives and worker councils in the UK and Sweden provide the forum for productive discussion and collaboration with regard to our workforce reduction activity. Elsewhere, our processes follow the nationally determined arrangements.

HUMAN RIGHTS

We are fully supportive of the principles set out in the UN Declaration of Human Rights, and our Code of Conduct and supporting policies outline the high standards of employment practice with which everyone in AstraZeneca is expected to comply, both in spirit and letter. This includes, as a minimum, compliance with national legal requirements regarding wages and working hours. We also support the International Labour Organisation's standards regarding child labour and minimum working age.

We believe that every employee should be treated with the same respect and dignity. All judgements about people for the purposes of recruitment, hiring, compensation, development and promotion are made solely on the basis of a person's ability, experience, behaviour, work performance and demonstrated potential. As part of this, we are committed to complying with the provisions of all equality legislation including the UK Disability Discrimination Act 1995.

We continue to work to ensure that diversity is appropriately supported in our workforce, reflected in our leadership and integrated into business and people strategies. Diversity is included in our Talent Management SET objectives and we have a set of minimum standards that support global alignment in the integration of diversity and inclusion into our

human resources processes. As an indicator, 21% of the 82 senior managers reporting to the SET are women. The change from 2007 (26% of 81 senior managers) is not a result of reduced commitment to diversity, but is a consequence of our continued re-organisation of the Company at all levels, which continues to impact SET reporting lines.

We have made significant investment in improving our human resources information technology and are in the process of implementing a global system that will drive consistent people management and data capture worldwide. Launched in the UK, Sweden and China in 2006, the system is now in use in 16 countries which means we have consistent, detailed and integrated people information available at a global level covering over 40,000 employees.

SAFETY, HEALTH AND WELLBEING

Providing a safe workplace and promoting the health and wellbeing of all our people remains a core priority. A safe, healthy working environment not only benefits employees, it supports our business through improved employee engagement, retention and productivity.

We are committed to ensuring that safety and health risks are understood and managed responsibly. We continue to build on our traditional safety and health programmes, which focus on workplace behaviours and attitudes, whilst developing new approaches to managing stress and helping employees understand their personal health risks.

Wellbeing programmes vary according to health risk profile, function and local culture, and include general health initiatives aimed at increasing exercise levels, reducing smoking, improving nutrition and managing stress. We also have plans in place to deal with the potential threat of pandemic flu, including the provision of anti-virals for employees based in areas where adequate supplies may not be available through national treatment regimes.

Our key performance indicator (KPI) for safety, health and wellbeing combines the frequency rates for accidents resulting in fatal and serious injuries and new cases of occupational illness into one KPI, with an overall target of a 50% reduction in the combined rates by 2010, compared with a 2001/2002 reference point. The overall fatal and serious injury accident rate for AstraZeneca employees decreased by 14% to 2.28 per million hours worked in 2008, whilst the occupational illness rate increased by 5% to 1.04.

This equates to a combined reduction of 9% compared to 2007, and we are on track to achieve the targeted reduction by 2010.

We regret that during 2008 there were six fatal accidents, resulting in the deaths of three employees, two sub-contractors and five members of the public. Five of these accidents were vehicle related. Three people were killed in a single vehicle accident in China, two in a single vehicle accident in Saudi Arabia and one person killed in vehicle accidents in the US, Thailand and Egypt. The sixth accident occurred at one of our US sites where two sub-contractors were killed whilst engaged in construction work. Full investigations into the circumstances surrounding these accidents are being carried out.

We work hard to identify the root causes of any serious accident and use a range of investigation procedures to help us avoid repetition. Learning is shared with management and staff, and our conclusions about underlying causes are used to improve our management systems.

With the support of the Executive Vice-President of Operations, a global initiative to share learning from recent accidents and fatalities was implemented during 2008. A learning package was rolled out to employees in Operations and relevant areas of R&D, which focused on involving them in discussions about the root causes of these incidents, and on emphasising the need for everyone to challenge unsafe acts or working conditions.

We remain dissatisfied with our driver safety record and we are determined to improve our performance in this area. Our commitment centres on the promotion of driver safety across our sales forces worldwide, taking into account local conditions and opportunities for improvement.

In the US, where we have a sales force of around 6,500 people, our "Road Scholars" driver safety programme has been in place since 2005 and continues to be a valuable channel for building awareness and improving driver skills. During 2008, we further strengthened commitment and accountability in this area with the inclusion of a driver safety objective in the US performance management framework.

Outside the US, in our International Sales and Marketing Organisation (ISMO), where we have around 17,000 representatives across 61 countries, we are implementing a new driver safety programme, "DriveSuccess". Whilst taking account of the different driving environments across the various ISMO countries, "DriveSuccess" provides a high-level framework of common standards to be adopted by each country. The framework was rolled out across Europe, Central Eastern Europe, Middle East and Africa and Latin America during the last quarter of 2008, and Asia Pacific, including Japan, will follow in 2009.