



"My number one priority is to strengthen the pipeline, drive the pace of innovation and deliver a flow of new medicines that bring benefit for patients and support sustained growth for AstraZeneca in the short, medium and long term.

I am pleased to be able to report that 2007 has been a year of significant progress.

We have continued to put huge effort into our drive for quality and industry-leading speed in our development cycle times, while at the same time creating a leaner, more cost-effective R&D organisation.

The year was also marked by the acquisition of MedImmune – a transformational event for our R&D organisation, which has significantly boosted our pipeline and accelerated our ambition to build a major presence in biopharmaceuticals.

Our pipeline has increased from 71 clinical projects in 2006 to 95 clinical projects in 2007, a 50% increase compared with 2005. In 2006,

12 new molecules entered phase I (first tests in man), a record year for us. In 2007, we doubled the rate with 24 new molecules entering phase I, which puts us on track for a milestone number of phase II progressions in the second half of 2008 and early 2009. We have also doubled our phase III pipeline over the past year, increasing it from five to 10 projects.

I am confident that, with the progress we have made in 2007, and as we continue to introduce further speed and quality initiatives throughout 2008, we will achieve upper quartile industry performance by 2010."

JOHN PATTERSON CBE FRCP
Executive Director, Development

RESEARCH AND DEVELOPMENT

Introduction

We have a global R&D organisation, with around 13,000 people at 17 principal centres in eight countries – the UK, the US, Sweden, France, Japan, China, Canada and India. Of these, 14 sites focus on small molecule R&D and three on biologics and vaccines R&D. These resources are complemented by clinical development capability at 47 sites around the world.

In 2007, we invested \$5.2 billion on R&D (2006 \$3.9 billion, 2005 \$3.38 billion) and approved \$291 million of R&D capital investment. New facilities established or announced in 2007 included an expansion of our facility in Boston, US principally to enhance our infection research capability. We also inaugurated a new state-of-the-art Process and Development R&D (PR&D) facility next to our existing R&D centre in Bangalore, India. With accommodation for up to 75 scientists (supported by office and engineering staff), this laboratory should accelerate the production of our new treatments, and its position alongside our Discovery site will help maximise scientific interactions. Additional investments in PR&D laboratories were also made in Macclesfield, UK, which should accommodate around 170 people and give the flexibility to accommodate a further 50 people within pre-planned expansion areas.

During 2007, we opened our 'Innovation Centre China' research facility in Shanghai, which is focused on translational medicine in cancer, a major cause of death in China. Approximately 40 highly qualified scientists

have been recruited so far. We have also formed a strategic partnership with Peking University Third Hospital, which will focus on phase I clinical research, including clinical pharmacology and safety evaluation.

We want to be among the best in the industry in terms of the quality of our work and the speed with which we get new medicines to market. During 2007 we continued our drive to improve the efficiency of our processes and the effectiveness of our decision-making so that we can quickly eliminate weaker compounds and concentrate on the robust, rapid progress of the ones most likely to succeed as significant advances in healthcare. Further information about our progress to improve the efficiency of our R&D processes can be found later in this section.

We have a clearly defined process to manage our therapy area and disease area (TA/DA) strategies recognising the breadth of our portfolio across therapy areas and treatment modalities. Our TA/DA strategy review process enables us to evaluate key features of each TA/DA including clinical need, commercial opportunity, scientific opportunity, competitive position and resources. The process is managed by the R&D Executive Committee and our regular reviews define which disease areas we will grow, maintain, reduce or exit. The process also enables us to deploy our resources in the best way to meet our commercial and scientific objectives.

In line with our strategy, we also continued to focus on gaining access to external innovation that complements our in-house capabilities. Further information about our externalisation

activities during the year can be found on page 25. By far the most significant transaction in 2007 was the acceleration of our biologics and vaccines strategy through the acquisition of MedImmune, Inc..

Our global R&D organisation is led by the R&D Executive Committee. Further information about the R&D Executive Committee and how we manage our portfolio is given in the R&D Governance and Portfolio Management section on page 27.

In 2007, Alderley Park, one of our major R&D sites, celebrated its fiftieth anniversary. Some of the world's most important medicines have come out of Alderley Park, including the invention of beta-blockers, which revolutionised the treatment of certain heart diseases and a series of inhaled and intravenous anaesthetics. New hormonal treatments for breast and other cancers were also developed there, which have gone on to become market leaders and have played a major role in today's much improved treatment of cancer. We aim to maintain Alderley Park's contribution and we continue to invest in upgrading this site, most recently with the opening of a £60 million dedicated cancer research facility in 2006.

Pipeline progress

Full details of our pipeline are set out in the table on pages 28 to 30. 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.

OUR RESOURCES, SKILLS AND CAPABILITIES CONTINUED

In the short term, we have continued to strengthen our pipeline across all stages of discovery and development and we now have 95 clinical projects. In 2007, significant progress was made in strengthening our late stage development portfolio. We have doubled the size of our phase III portfolio from five to 10 projects (covering nine compounds). We have also had a record year in terms of the number of new molecules entering phase I compared with 2006 (24 in 2007, 12 in 2006) and this puts us on track for a record number of phase II progressions in the second half of 2008 and early 2009.

Notable successes in the life cycle management of our key marketed brands during the year included nine submissions and nine approvals in the US or the EU, which are described in the therapy area reviews on pages 50 to 68.

In the medium term, we will drive our pre-clinical and clinical phase I and II projects towards proof of concept as rapidly as possible, whilst recognising that we need to continue our emphasis on externalisation to complement our internal R&D efforts. Our drug discovery efforts extend beyond our own laboratories, as we actively seek to make 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. As part of our continuing drive for improvement, we have introduced a more rigorous and consistent measure for the number of compounds reaching development. We now record additions to the pipeline from the first pre-clinical study that is required for regulatory approval (First Good Laboratory Practice (FGLP)), instead of when a candidate drug (CD) is simply nominated for development. During 2007, 36 FGLPs were selected (compared with 22 in 2006).

In addition to our current capabilities, we have transformed our R&D capability and pipeline through our strategic move into biologics and vaccines, described in more detail below.

Discovery research

In Discovery, our scientists work together across national boundaries and sites to exchange ideas, to promote best practice and to maximise the scientific potential offered by our size and global reach. We work closely with clinical and development teams to prioritise our activities and to link our research activities to clinical need and patient benefit.

Improving productivity, efficiency and quality remain core priorities and over recent years we have introduced a process improvement system based around the principles of Lean Sigma™ that has significantly reduced project timelines and increased the quality and efficiency of our drug discovery programmes. For example, in lead optimisation in our Cardiovascular and Gastrointestinal therapy areas, we have delivered an improvement in product development cycle times, a reduction in non-core activities and a positive impact on the quality of the science conducted.

Lead generation

Our strategic initiatives are directly aligned to improving the quality of chemical leads and biological targets, so that we can eliminate, at an earlier stage, those compounds that are unlikely to make it through clinical development. Strategic alliances, such as those with WuXi Pharmatech Co., Ltd (China) and ChemBridge (US), supply proprietary compounds that significantly enhance our own compound collection and increase the prospects of us finding compounds that we can quickly develop into new medicines.

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, 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.

Safety assessment

We implement high-throughput testing of safety early in the research process and use this data to prioritise and select the best compounds for progression. We have been able to reduce attrition due to safety issues and the time taken to deliver key safety studies by process improvements, thereby allowing more rapid entry to testing in man.

Development

Our principal focus is ensuring that our growing range of potential medicines are developed effectively to meet the future needs of patients, and in a way that meets the regulatory requirements necessary to gain marketing approval. We have a wide range of compounds in early development, and a total of 41 projects in phase I, 20 projects in phase II and 10 projects in phase III development and are running 24 life cycle management projects.

People in our Development organisation specialise in taking a newly discovered compound from the laboratories, through clinical research, regulatory submissions, continuing pharmaceutical development and life cycle management. Project teams bring together all the relevant skills and experience needed for the rapid progress of new medicines and the management of development risks.

The change programme initiated during 2005 to enhance project delivery and improve R&D performance has continued. Throughout 2007, we have built on the speed and quality improvement projects that were begun in 2006 focusing on speeding the progression of early phase projects along the pipeline and to market. This has resulted in reductions in the average product development cycle time of approximately one and a half years, with reduced timelines across all parts of the development process.

With the implementation of best practice solutions aimed at eliminating the lost time between key steps in the development process and, critically, by changing behaviours across the organisation, we exceeded our 2007 targets for development cycle times. We believe that we are well placed to achieve median cycle times of eight years in 2010 based on the projects currently in development. Importantly, we also put in place the fundamental building blocks for a culture of continuous improvement that should sustain the momentum behind our initiatives for increased speed, with better quality, and at the right cost.

The continued growth in the number of drug projects in our pipeline will require us to reshape our R&D budget to accommodate these increased numbers, both in the next three years and beyond to 2017. We are running a portfolio of programmes aimed at delivering significant productivity improvements

that we expect will yield efficiency gains between 2008 and 2011. Projects currently within this programme are making good progress and are on track. These include:

- > Disease area strategy: As part of a continuing process, a comprehensive review of all disease areas comparing the position of AstraZeneca relative to our competitors was undertaken following the acquisition of MedImmune, Inc. The conclusions have resulted in the prioritisation of key disease areas for growth and decisions to exit other areas, for example, in cancer research we are exiting cell cycle blockade approaches and in the respiratory and inflammation area we are exiting osteoarthritis disease modification.
- > Clinical data management: We have commenced a project to centralise, streamline and outsource clinical data management activity, aimed at delivering savings of \$30 million per year.
- > Re-organisation of the Pharmaceutical and Analytical R&D (PAR&D) function: We aim to improve productivity and better deliver the demands of an increasingly strengthened pipeline. This programme already shows 20% less PAR&D resource per project in 2006 compared with 2004. The organisation has also downsized by 10% while introducing these productivity improvements.
- > A re-organisation of our Regulatory function: Streamlining the organisation, including the withdrawal from Charnwood (UK) and the consolidation onto one site of key teams in Sweden, aimed at delivering an 18% reduction in headcount by June 2008.

Biologics and vaccines

The acquisition of US-based biotechnology company, MedImmune, Inc., in mid-2007 has enabled us to greatly accelerate our biologics and vaccines strategy and build on the expertise of Cambridge Antibody Technology Group plc (CAT) acquired in 2006 and pre-existing biological programmes within AstraZeneca. It has also enabled us to create a significant, world-class, vertically-integrated biologics and vaccines capability through which we have access to cutting-edge technologies, intellectual property, a skilled and dedicated workforce and a large scale manufacturing capability. All of our biologics and vaccines capabilities will be operated under MedImmune's leadership.

Although MedImmune will be operationally independent within our R&D organisation, it will be aligned with our overall R&D strategy and objectives and its scientists will work collaboratively with AstraZeneca scientists. This combination of operational independence, collaboration and strategic alignment will enable us to preserve the agility and entrepreneurialism within MedImmune while allowing it to benefit from the expertise and capabilities of the broader AstraZeneca organisation. David Mott (MedImmune's President and Chief Executive Officer for the past seven years), along with a number of other members of the former MedImmune, Inc. management team have been tasked with leading our new biologics and vaccines capability.

With MedImmune's biologics and vaccines capabilities sitting alongside our existing small molecule resources, our objective is that from 2010 onwards, one in four of our projects eligible for full development will be biological drugs or vaccines.

Our R&D capability in biologics and vaccines now covers a broad range of approaches including antibodies, antibody derivatives, therapeutic proteins, peptides, RNA interference technologies and various types of live attenuated and sub-unit vaccines that can all be used to target diseases across a range of therapy areas. This includes a world-leading drug discovery platform pioneered by CAT, based on advanced technology for rapidly isolating human monoclonal antibodies using phage and ribosome display (extensive antibody libraries incorporate more than 100 billion distinct antibody fragments) and MedImmune's own proven, vertically-integrated, end-to end capabilities from discovery to commercialisation, such as high-yield purification expertise, process and analytical development resources, as well as significant in-house manufacturing capability and capacity.

The MedImmune organisation has nearly 3,000 employees, of which approximately 1,400 are focused on discovery, development, clinical and regulatory activities. Its principal R&D sites are in the US (Gaithersburg, Maryland and Mountain View, California, the latter focusing on vaccines research) and Cambridge, UK. MedImmune's goal is to generate eight potential new biological drugs per year, on a steady-state basis, which we anticipate will translate into six new investigational drugs per year.

MedImmune's heritage includes the development of the technology underpinning the human papilloma virus vaccines to prevent cervical cancer that are marketed by GlaxoSmithKline and Merck, in respect

of which we receive royalty streams, and the discovery by scientists in Cambridge, UK of Humira™, an antibody treatment for rheumatoid arthritis with global sales of over \$3 billion in 2007, marketed by Abbott Laboratories. MedImmune's influenza vaccine, *FluMist*, is the first advance in flu vaccine technology in over 60 years, with demonstrated efficacy against matched and mismatched strains.

Externalisation and new opportunities

In today's world of rapid scientific and technological advances, no single company can rely exclusively on its own R&D capabilities to deliver the next generation of medicines that offer better results for patients. Our Strategic Planning and Business Development (SPBD) team works closely with R&D, global marketing and finance teams to deliver our externalisation strategy, by which we seek to establish collaborations with external partners whose skills and resources complement our own internal capabilities. We have also established a group to focus on potential new opportunities that lie beyond our current therapy areas.

We have completed over 20 major externalisation deals in the last two years, as well as the acquisitions of CAT and MedImmune. We believe that every collaboration is unique, and we work with potential partners to structure deals that leverage each other's unique capabilities and assets. For example, in 2007 we entered into an innovative deal with Bristol-Myers Squibb Company to co-develop and co-commercialise saxagliptin and dapagliflozin (two products in development for the treatment of Type 2 diabetes), a collaboration with Silence Therapeutics plc and we completed the acquisition of Arrow Therapeutics Ltd. (Further information about these transactions can be found in the relevant therapy area section on pages 50 to 68). Furthermore, each year we establish numerous earlier stage partnerships to ensure that we have access to the latest science and technology.

Our biologics and vaccines externalisation activities will be led by MedImmune, which executed almost 40 business development and licensing transactions and acquisitions between 2004 and 2007. The more significant deals in MedImmune's history include its collaborations with Abbott Laboratories for the co-promotion of *Synagis* in the US and distribution outside the US, the licensing of its human papilloma virus vaccine product candidate to GlaxoSmithKline, as well as the acquisitions of US Bioscience, an oncology company, and Aviron, a California-based vaccine company.

OUR RESOURCES, SKILLS AND CAPABILITIES CONTINUED

In 2002, MedImmune launched a captive venture capital fund, MedImmune Ventures, to expand its access to cutting edge technology emerging within the biotechnology world. Since then, MedImmune Ventures has invested in about 25 different companies around the world. MedImmune Ventures will continue to be operated by MedImmune and will broaden its focus to include areas of strategic interest to MedImmune and AstraZeneca, helping both to stay at the forefront of novel science with a direct window to the most innovative start-ups in the biotechnology industry.

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 in all areas of our R&D worldwide. Compliance with relevant laws and regulations is a minimum baseline and underpins our own global principles and standards, as outlined in our Bioethics Policy.

We conduct our clinical trials in accordance with the Declaration of Helsinki. We ensure that those taking part in clinical research anywhere in the world 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 and that appropriate confidentiality rules are applied. Informed consent procedures are specifically included in the audits conducted by our Clinical Quality Assurance teams of our clinical research related activities – whether they are being done in-house or by a Contract Research Organisation (CRO).

Most of our clinical trials are global in nature. By conducting our studies across a broad geographic span, we aim to ensure that those taking part fully represent the diversity of the patient populations around the world for whom the new medicine is intended. This approach also helps to identify those for whom the treatment will be most beneficial. 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, or our own internal standards. The percentage of clinical studies run for us by third parties varies depending on the number of trials we have underway and the amount of internal resource available to do the work. On average, approximately 35% of our studies (which are always designed by AstraZeneca) involve CROs and we contractually require them to operate to the same standards that we apply in-house.

In line with our commitment to providing patients and healthcare professionals with meaningful information about our products, we publish, and provide open access to, the findings of AstraZeneca-sponsored clinical trials, whether favourable or unfavourable, together with the latest information about trials currently underway. This information is available via our dedicated website, astrazenecaclinicaltrials.com.

Animal studies continue to play a vital role in our research. 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 humans. We are committed to applying the principle of the 3Rs (replacement, reduction and refinement of animal studies) across our research activity. In 2007, we used approximately 271,000 animals in-house, a decrease on 2006 (276,000 animals). In addition, approximately 13,500 animals were used by external contractors, an increase on 2006 (12,000). The number of animals involved in our scientific studies reflects the size of the pre-clinical portfolio and the complexity of the diseases under investigation. As we continue to expand our discovery research, our ongoing challenge is to ensure that our animal use is minimised without compromising the quality of the data. The growth of our early development portfolio during 2007 reflects the effort we are putting into improving the quality and productivity of our research, and we believe that, without our active commitment to the 3Rs, our animal use in discovery research would be much greater.

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 highly qualified staff. External organisations that conduct animal studies on AstraZeneca's behalf are also expected to comply with high ethical standards, and our staff conduct inspections of contractors to ensure our expectations are being met.

In biopharmaceutical research, primates are in most cases the only relevant animal model. In anticipation of our increased use of

primates, therefore, during 2006/2007, we developed a specific standard for their use and care globally to ensure consistent practice across our primate research.

In our external partnerships, we are committed to working only with organisations that embrace standards of ethical behaviour that are consistent with our own.

As a company whose success is built on leading-edge science, we continuously monitor new capabilities and opportunities that will help us to develop the next generation of medicines that offers better results for patients. 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 to explore the potential of this type of research.

Our Human Embryonic Stem Cell Research Policy framework demands compliance both with external legislation, regulations and guidelines, and with our own codes of research practice. This framework applies to all internal work and external research on AstraZeneca's behalf and includes 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. The framework is designed to ensure all research effort in this area remains consistent with our strategy of developing more effective, safer medicines for serious disease.

Further information about our commitment to high ethical standards and our performance is available on our website, astrazeneca.com/responsibility.