ASTRAZENECA PLC
Form 6-K
February 26, 2004

FORM 6-K

SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549
Report of Foreign Issuer

Pursuant to Rule 13a-16 or 15d-16 of
the Securities Exchange Act of 1934
For February 2004

Commission File Number: 001-11960

AstraZeneca PLC

15 Stanhope Gate, London W1K 1LN, England

Indicate by check mark whether the registrant files or will file annual reports under cover of Form 20-F or Form 40-F.

Form 20-F _X_ Form 40-F ___

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(1): _____

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(7): _____

Indicate by check mark whether the registrant by furnishing the information contained in this Form is also thereby furnishing the information to the Commission pursuant to Rule 12g3-2(b) under the Securities Exchange Act of 1934.

Yes ___ No _X_

If Yes is marked, indicate below the file number assigned to the Registrant in connection with Rule 12g3-2(b): 82-_____

The following information has been given to The Stock Exchange, London and is furnished pursuant to General Instruction B to the General Instructions to Form 6-K:

AstraZeneca PLC Annual Report and Form 20-F Information 2003

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Annual Report and Form 20-F Information 2003

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Trade marks

Trade marks of the AstraZeneca group of companies appear throughout this document in italics. AstraZeneca, the AstraZeneca logotype and the AstraZeneca symbol are all trade marks of the AstraZeneca group of companies.

Use of terms

In this Annual Report and Form 20-F Information 2003, unless the context otherwise requires, □AstraZeneca□, □the Group□, □the Company□, □we□, □us□ and □our□ refer to AstraZeneca PLC and its consolidated entities.

Statements of competitive position

Except as otherwise stated, market information in this Annual Report and Form 20-F Information 2003 regarding the position of our business or products relative to its or their competition is based upon published statistical data for the 12 months ended 30 September 2003, or the month of November 2003, obtained from IMS Health, a leading supplier of statistical data to the pharmaceutical industry. Except as otherwise stated, this market share and industry data from IMS Health has been derived by comparing

our sales revenue to competitors□ and total market sales revenues for that period.

Statements of growth rates

Except as otherwise stated, growth rates in this Annual Report and Form 20-F Information 2003 are given at constant exchange rates (CER).

AstraZeneca website

Information on our website, astrazeneca.com, does not form part of this document.

Cautionary statement regarding forward-looking statements

In order to utilise the □safe harbour□ provisions of the US Private Securities Litigation Reform Act 1995, we are providing the following cautionary statement: This Annual Report and Form 20-F Information 2003 contains certain forward-looking statements about AstraZeneca. Although we believe our expectations are based on reasonable assumptions, any forward-looking statements may be influenced by factors that could cause actual outcomes and results to be materially different from those predicted. We identify

the forward-looking statements by using the words anticipates, believes, expects, intends and similar expressions in such statements. These forward-looking statements are subject to numerous risks and uncertainties. Important factors that could cause actual results to differ materially from those contained in forward-looking statements, certain of which are beyond our control, include, among other things: the loss or expiration of patents, marketing exclusivity or trade marks; exchange rate fluctuations; the risk that R&D will not yield new products that achieve commercial success; the impact of competition, price controls and price reductions; taxation risks; the risk of substantial product liability claims; the impact of any failure by third parties to supply materials or services; the risk of delay to new product launches; the difficulties of obtaining and maintaining governmental approvals for products; and the risk of environmental liabilities.

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Key Achievements

- At constant exchange rates, total sales for the year were unchanged whilst absorbing the loss of $2.6 billion in US sales of *Losec*/*Prilosec*, *Zestril* and *Nolvadex* following anticipated patent expiries.
- Operating profit was down 11% due to planned investments in R&D and SG&A required to launch new products and complete the product portfolio transformation.
- Dividend increased by 13.6% to 79.5 cents for the full year.
- Sales for key growth and launch products increased by 45% to $8.2 billion and now represent 44% of total sales.
- *Nexium* sales reached $3.3 billion, up 62%.
- *Seroquel* sales reached $1.5 billion, up 27%. Approvals for use of *Seroquel* in the treatment of acute bipolar mania were received in the US and Europe.
- *Symbicort* sales reached $549 million, up 61%. *Symbicort* also gained first approval in Europe for use in the treatment of chronic obstructive pulmonary disease.
- *Arimidex* is moving rapidly towards replacing tamoxifen as the standard of care in breast cancer. Sales up 46% to $519 million.
- Rapid uptake of *Iressa* since first launch in Japan in 2002 and in the US in 2003, with over 100,000 patients treated since launch. 2003 sales reached $228 million.
- *Crestor* sales reached $129 million. We estimate that more than 1.5 million prescriptions had been written for, and over 750,000 patients had been treated with, *Crestor* by the end of January 2004.
- *Exanta* received its first regulatory approval (in France) in December 2003. Regulatory submissions were made in the US and Europe for key chronic indications, including prevention of stroke associated with atrial fibrillation.
- R&D investment totalled $3.5 billion. We now have 12 projects in phase 2 development and 28 projects in phase 3.
- Continued enhancement of supply and manufacturing processes led to improved customer service levels and reduced manufacturing lead times which consequently reduced the requirement for stock build-up.

Continuing Operations before Exceptional Items

	2003	2002	% growth CER
Sales $m	**18,849**	17,841	
Operating profit $m	**4,111**	4,356	11
Earnings per share $	**1.78**	1.84	9
Group earnings per share $ (statutory FRS 3)	**1.78**	1.64	+3

Dividend for 2003

	$	Pence	SEK	Payment date
First interim dividend	0.255	15.9	2.07	6 October 2003
Second interim dividend	0.540	29.4	3.91	6 April 2004
Total dividend	**0.795**	**45.3**	**5.98**	

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Chairman's Statement

Five years ago, on the completion of the merger of the Astra and Zeneca businesses, the new Board had a clear vision. AstraZeneca was to be a creative, fast and effective, research-based pharmaceutical company. Its increased global marketing strength provided the platform to realise the full potential of its productive R&D and deliver sustainable value to all its stakeholders.

Back in 1999, there were some substantial hurdles to overcome before this vision could be turned into reality. The first of these was to rapidly complete the merger, build on the strengths of the two partners to create a single unified culture and realise the merger cost benefits without significantly disturbing our day-to-day operations. This was achieved in the first two years.

Our focus was then on another major challenge; the transformation of our product portfolio from its historic reliance on successful but maturing products, such as *Losec*/*Prilosec* and *Zestril*, into a range of newer high potential medicines. Many commentators predicted a steep decline in sales and profit during this period.

By the end of 2003, this transformation had largely been achieved. There have been some delays in new product launches but also some of the more mature brands have not declined as fast as expected.
AstraZeneca is now facing an exciting period of expansion with few patent expiries and growth driven by the recently introduced products and by further new product launches. Recent investments in developing countries also add to the potential for growth.

Taking a wider perspective, the pharmaceutical sector continued to experience pricing pressures in major markets during 2003 and the AstraZeneca Board reviewed the Company's approach to product pricing and market access for our products. We support the World Trade Organisation (WTO) resolution of outstanding

issues relating to the Doha Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPs) and the public health benefits that will flow from this resolution.

In the context of this business environment and recognising the specific challenges faced by the Company, AstraZeneca's financial performance in 2003 has been excellent and the Board has recommended a second interim dividend of $0.54; 29.4 pence; SEK 3.91 per Ordinary Share bringing the total dividend for the year to $0.795; 45.3 pence; SEK 5.98, an increase of 13.6% in dollar terms. The share repurchase programme continued in 2003 with 27.2 million shares re-purchased for cancellation at a total cost of $1,154 million. The Board is proposing a further share repurchase programme of $4 billion to be completed by the end of 2005, subject to shareholders renewing the Company's authority to re-purchase its own shares at the Annual General Meeting in April.

The AstraZeneca share price performed well in 2003 in both absolute terms and when compared with an international group of leading pharmaceutical companies, reflecting the market's positive view of the Company's future growth prospects.

During a busy year, the Board analysed trends in the pharmaceutical environment and reviewed the Company's overall strategy and performance. I am happy to report good progress in the productivity increase programmes that cover all parts of the Company. In line with this culture of continuous improvement, the performance of the Board, its committees and all individual members were reviewed in a constructive discussion that identified areas for further improvement.

During the year the Board has reviewed its already demanding compliance procedures to respond to new laws and regulations in the US, Sweden and the UK. This Annual Report and Form 20-F Information, our Annual Review and Corporate Responsibility Summary Report have all been prepared in accordance with the new requirements. We have also reviewed and strengthened the Company's Code of Conduct. In the US we have undertaken significant compliance training with our sales and other relevant personnel pursuant to the Corporate Integrity Agreement

with the Office of Inspector General of the Department of Health and Human Services.

We welcome Michele Hooper and Joe Jimenez, who joined the Board in July as Non-Executive Directors. Michele's experience at Caremark International and Baxter Healthcare in the US and Joe's background as President and CEO of Heinz Europe and earlier positions in the US bring additional strengths to the Board. Håkan Mogren stepped down as Executive Deputy Chairman in August 2003 and continues as Non-Executive Deputy Chairman. In his executive capacity, Håkan Mogren served both Astra AB and AstraZeneca PLC with distinction and I am delighted that the Board will continue to benefit from his wise counsel.

I am grateful to my colleagues on the Board for their support, to the Senior Executive Team and to all our employees worldwide for their impressive contributions to the Company's success. On behalf of the Board, I would like to thank them most warmly.

In 2004, we aim to deliver strong sales growth from our portfolio of important medicines while, at the same time, progressing the next wave of novel products. We will continue our investment strategy in developing regions to complement our strong presence in the major established markets.

Through strong sales growth coupled with productivity improvements across all our activities, we expect to deliver top tier financial performance in the years ahead.

Percy Barnevik
Chairman

*Abbott Labs, AHP, Aventis, BMS, Eli Lilly, GSK, JNJ, Merck, Novartis, Pfizer, Pharmacia, Roche, Sanofi-Synthelabo, Schering and Schering-Plough
Source: Thomson Financial Datastream

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Global Market Overview

World markets

In 2003, worldwide sales of pharmaceutical products totalled $430 billion, representing an 8% growth (at constant exchange rates), compared to 10% in 2002. This lower growth is largely due to the performance of the US market, which accounts for around half of the world's pharmaceutical expenditure. Whilst the US had a market growth rate of around 10%, this represented a decrease from 2002 (14%). A lower number of new product launches, patent expiries for several high sales products, together with pricing pressure have contributed to this decrease.

In Japan, the world's second largest pharmaceutical market with 12% of world revenues, sales grew 2% reflecting the increasingly tough pricing environment in that country.

In Europe (27% of world revenues, 8% growth), the variations in regulatory frameworks were reflected in the considerably varied growth rates within the region including France with growth of 5%, Germany 6%, Italy 5%, Spain 12%, Turkey 37% and UK 10%.

China, which delivered 20% pharmaceutical market growth in 2003, Korea, Mexico and India are increasing in importance for the future.

Pharmaceuticals as part of healthcare

Expenditure on healthcare typically represents between 6% and 14% of a country's gross domestic product (GDP), with developed nations towards the top end and developing nations spending less. Pharmaceuticals as a proportion of this expenditure is usually between 10% and 20% and therefore, is in most cases still less than 2% of GDP even in developed nations. Pharmaceuticals offer many advantages over other forms of treatment for illness and are progressively replacing in-patient care, particularly for cardiovascular and central nervous system conditions, and they are the principal treatment for illnesses such as diabetes, asthma, gastric ulcers, skin complaints and many infectious diseases.

Doctors are still the key decision makers in relation to which treatments should be prescribed for their patients. As the economic burden of funding therapies increases, payers, including governments, health insurers, managed care organisations and employers are increasing their influence over the choices doctors make and health economics are an increasingly important element in prescribing patterns.

Growth drivers and limiters

Increasing populations and the rising percentage of elderly people are strong growth drivers for the pharmaceutical industry. In addition there are still major areas of unmet medical need since many diseases, such as Alzheimer's Disease and many cancers have no effective therapies, or are under diagnosed or sub-optimally treated. Scientific advances and new forms of communication, such as the internet, are also growth drivers.

Limiting the industry's growth is the increasing pressure to contain healthcare costs from governments and other payers, which affects the pricing and/or the willingness to pay for certain therapies. This has led to a rise in the requirement for 'co-pay' arrangements where patients contribute towards the cost of their therapies. Cost pressure is also driven by governments worldwide facing the challenge of providing more funding for the healthcare of the elderly. A significant example of a response to this challenge is the enactment of the Medicare Prescription Drug, Improvement, and Modernization Act in the US in 2003. Also in the US, the high costs of pharmaceuticals for uninsured senior citizens have led to increased cross border movement of products from Canada where prices are lower. Differential pricing across the world has long been a feature of the pharmaceutical industry but is now particularly evident in the US, especially for the uninsured who have to pay the full cost for their medicines, and this increased awareness of different pricing structures is contributing to a growing resentment of the industry.

Across the industry there has been a reduction in the number of new chemical entities (NCEs) being developed, in part as a result of investment in new technologies taking longer than anticipated to deliver new medicines, although there is evidence of an increase in NCEs entering development in 2003. The increased cost of providing more demanding safety and efficacy studies required by regulators and the effect of patent expiries for a significant number of companies products have also been contributory factors to limited growth.

The industry also faces issues that may curtail its ability to generate attractive return on investment from the growing obligations of corporate social and environmental responsibility and the threat of weakening intellectual property rights.

Future pharmaceuticals market

There are early signs of increasing numbers of potential products coming into development and despite the cost containment pressures, dip in R&D productivity and imminent patent expiries of some major products, the pharmaceutical market overall is forecast to grow by around 7% per annum to 2007. The companies that do best in this difficult environment will be those that combine real innovation with optimum operating efficiency.

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Chief Executive's Review

In 2003, AstraZeneca made excellent progress establishing itself as a world leading pharmaceutical company focused on the research, development, manufacture and marketing of valuable prescription medicines and creating the platform for top tier financial performance in the coming years. First launches of *Crestor*, the further development of marketed products such as *Iressa, Nexium* and *Seroquel*, and the first approval for the revolutionary anticoagulant, *Exanta*, herald the passage into an exciting new era for the Company.

Our sales and marketing teams around the world now have the opportunity to realise the full potential of our successful research and development and, through wise investment and a continuing drive for improved productivity, deliver enduring growth of shareholder value.

In addition to good progress with the new products, we have also expanded our global presence with investments in research, development, manufacturing and marketing in important emerging markets. As a result of these and other initiatives, AstraZeneca has become one of the fastest growing pharmaceutical companies in, among others, Japan, China and Mexico.

During 2003 the performance of the new and growth products in the Company's revitalised portfolio ($8.2 billion) largely offset the decline in global sales of *Losec/Prilosec*, *Zestril* and *Nolvadex* ($3 billion). This transformation, achieved without a decline in top-line sales, from a company that faced the biggest threat from patent expiries in the industry's history, into the one with perhaps the best growth portfolio, is something of which our employees are justifiably proud.

Nexium, for gastrointestinal disorders, has maintained strong momentum despite an increasingly competitive market place. In the US alone, *Nexium* achieved sales of

$2.5 billion in the year. Globally annual sales reached $3.3 billion, less than three years after its first introduction in the US, making it one of the most successful launches ever of a new medicine.

Seroquel continues to grow strongly in the anti-psychotic market where its attractive profile makes it the agent of choice for increasing numbers of physicians and patients. Sales in 2003 were $1.5 billion and now, with the approval of a major new indication, the treatment of mania associated with bipolar disease, *Seroquel* looks set to play a key part in our future growth.

AstraZeneca's cancer portfolio also made strong progress during the year with excellent data supporting the use of *Arimidex* (2003 sales $519 million) in the adjuvant treatment of breast cancer, strong sales for *Faslodex* ($77 million) which was launched in 2002 in the US, and the successful US launch of *Iressa* (2003 global sales $228 million) for the treatment of late stage non-small cell lung cancer.

The year also saw significant developments in AstraZeneca's cardiovascular business including the launch in the US and 20 other markets of the lipid-lowering drug *Crestor* (2003 sales $129 million). The treatment of lipid disorders is a major priority for healthcare systems around the world and the profile of *Crestor*, which allows physicians and patients to achieve guideline lipid levels quickly and easily, gives us an opportunity to build a major new franchise in one of the largest sectors of medicine. Following successful introduction into a number of other markets, launch in the very important US market has gone well and early sales progress is encouraging. An important new study (CHARM) supporting the use of *Atacand* (2003 sales $750 million) in heart failure and the continued growth of *Seloken/Toprol-XL* (2003 sales $1.3 billion) have also helped to reinforce a leading position in cardiovascular medicine.

After a lengthy development programme involving more than 30,000 patients, I am pleased to report that the oral anticoagulant *Exanta* met important milestones at the end of 2003. In December we gained our first approval in France for this breakthrough medicine in the prevention of blood clots following orthopaedic surgery. As scheduled, in December we also filed in the US, Canada and Europe our largest ever

regulatory submission, this time for long term uses of *Exanta* in conditions such as the prevention of stroke in patients with atrial fibrillation.

In summary, 2003 has been an exciting year of great achievement. I would like to acknowledge the tremendous support I have received from my executive team and to recognise the immense contribution made by our creative, hardworking and committed employees around the world. Their combined efforts have already achieved a great deal. There is now much to do to realise the potential for outstanding growth and financial performance from this strong base.

The external environment is changing and our industry has to change with it.

Demographics and technology continue to drive demand for healthcare and for our products with the result that governments and payers face increasing pressure to control costs. At the same time the disparity of healthcare between the developed and the least developed nations continues to grow and the industry finds itself at the centre of much of this debate. It is in this environment that AstraZeneca has to succeed if it is to create value for all its stakeholders. The hard work of the last five years has positioned us well. We recognise and understand the challenges the future holds and we look forward to meeting those challenges in 2004 and beyond.

Sir Tom McKillop
Chief Executive

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Financial Highlights

Key growth and launch products

Atacand, Arimidex, Casodex, Crestor, Faslodex, Iressa, Nexium, Seroquel, Symbicort, Zomig

*Sales growth in the key product sales table sets out underlying performance which shows growth at constant exchange rates to reflect the volume and price changes of the individual products by excluding the effects of exchange.

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Board of Directors at 31 December 2003

Percy Barnevik
Non-Executive Chairman

Håkan Mogren
Non-Executive Deputy Chairman

Jane Henney
Non-Executive Director

Karl von der Heyden
Non-Executive Director

Sir Tom McKillop
Executive Director
Chief Executive

Sir Peter Bonfield
Senior Non-Executive Director

Marcus Wallenberg
Non-Executive Director

John Buchanan
Non-Executive Director

Erna Möller
Non-Executive Director

Jonathan Symonds
Executive Director
Chief Financial Officer

Dame Bridget Ogilvie
Non-Executive Director

Michele Hooper
Non-Executive Director

Joe Jimenez
Non-Executive Director

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Percy Barnevik (62)
Non-Executive Chairman
Chairman of the Nomination Committee

Appointed as a Director 6 April 1999. Honorary Chairman of Sandvik AB. Non-Executive Director of General Motors Corporation. Member of the Academies of Engineering Sciences in Sweden and Finland and Honorary Member of the Royal Academy of Engineering, UK. Member of Advisory Councils in Korea, India and the Investment Council advising the South African Government. Member of the Business Council of American CEOs.

Member of the Advisory Board, Centre for European Reform, UK.

Håkan Mogren (59)
Non-Executive Deputy Chairman
Member of the Nomination Committee

Appointed as a Director 6 April 1999. Formerly CEO and a Director of Astra AB (appointed 18 May 1988). Chairman of Affibody AB and the Sweden-America Foundation. Vice-Chairman of Gambro AB. Member of the Board of Directors of Investor AB, Rémy Cointreau S.A., Groupe Danone and Norsk Hydro ASA. Director of the Marianne and Marcus Wallenberg Foundation.

Jane Henney (56)
Non-Executive Director
Member of the Audit Committee, the Nomination Committee and the Science Committee

Appointed as a Director 24

Sir Tom McKillop (60)
Executive Director and Chief Executive

Appointed as a Director 1 January 1996. Non-Executive Director of Lloyds TSB Group plc. President of the European Federation of Pharmaceutical Industries and Associations. Pro-Chancellor of the University of Leicester. Chairman of the British Pharma Group and the North West Science Council.

Sir Peter Bonfield CBE, FREng (59)
Senior Non-Executive Director
Chairman of the Remuneration Committee and Member of the Nomination Committee

Appointed as a Director 1 January 1995. Fellow of the Royal Academy of Engineering. Non-Executive Director of Telefonaktiebolaget LM Ericsson, Mentor Graphics Corporation and Taiwan Semiconductor Manufacturing Company, Ltd. Vice-President of The British Quality Foundation. Member of Citigroup International Advisory Board.

Marcus Wallenberg (47)
Non-Executive Director
Member of the Audit Committee

Appointed as a Director 6 April 1999. Formerly a Director of Astra AB (appointed 18 May 1989). President and Chief Executive Officer of Investor AB. Non-Executive Vice-Chairman of Saab AB, Skandinaviska Enskilda Banken AB and Telefonaktiebolaget LM Ericsson. Non-Executive Director of Scania AB, Stora Enso Oyj and the Knut and Alice Wallenberg Foundation.

Jonathan Symonds (44)
Executive Director and Chief Financial Officer

Appointed as a Director 1 October 1997. Also has overall responsibility for Information Services. Non-Executive Director of QinetiQ Group plc. Member of the UK Accounting Standards Board. Chairman of The Hundred Group of Finance Directors in the UK.

Dame Bridget Ogilvie (65)
Non-Executive Director
Member of the Audit Committee and the Science Committee

Appointed as a Director 1 January 1997. Also has responsibility for overseeing corporate responsibility. Non-Executive Director of the Manchester Technology Fund Limited. Chairman of the Medicines for Malaria Venture and the Association of Medical Research Charities. Trustee of Cancer Research UK. Chairman of the Trustees of the AstraZeneca Science Teaching Trust.

Michele Hooper (52)
Non-Executive Director

Appointed as a Director 1 July 2003. President and Chief Executive Officer of Stadtlander Drug Company 1998-1999. Corporate Vice-President and President, International Businesses of Caremark International Inc. 1992-1998. Non-Executive Director of PPG Industries, Inc., Target Corporation and Davita Inc.

September 2001. Senior Vice-President & Provost for Health Affairs, University of Cincinnati Medical Center. Commissioner of Food and Drugs 1998-2001 and Deputy Commissioner for Operations 1992-1994, US Food and Drug Administration. Deputy Director, US National Cancer Institute 1980-1995. Non-Executive Director of AmerisourceBergen Corporation. Member of the Board of Trustees of the Commonwealth Fund and the Scripps Research Institute. Member of the Medical & Scientific Advisory Board of MPM Capital.

Karl von der Heyden (67)
Non-Executive Director
Chairman of the Audit Committee

Appointed as a Director 1 October 1998. Executive Vice-President 1989-1992 and Co-Chairman and Chief Executive Officer 1993 of RJR Nabisco. President and Chief Executive Officer of Metallgesellschaft Corp. 1993-1994. Vice-Chairman of PepsiCo, Inc. 1996-2001. Non-Executive Director of Federated Department Stores Inc., ARAMARK Inc. and Exult, Inc.

John Buchanan (60)
Non-Executive Director
Member of the Audit Committee and the Remuneration Committee

Appointed as a Director 25 April 2002. Executive Director and Group Chief Financial Officer of BP p.l.c. 1996-2002. Member of the UK Accounting Standards Board 1997-2001. Senior Independent Non-Executive Director of BHP Billiton Plc and Non-Executive Director of Vodafone Group Plc.

Erna Möller (63)
Non-Executive Director
Member of the Remuneration Committee and the Science Committee

Appointed as a Director 6 April 1999. Formerly a Director of Astra AB (appointed 15 May 1995). Executive Director of the Knut and Alice Wallenberg Foundation. Professor of Clinical Immunology and Member of the Nobel Assembly and of the Nobel Committee, Karolinska Institutet. Member of the Royal Swedish Academy of Engineering Sciences and the Royal Swedish Academy of Science.

Joe Jimenez (44)
Non-Executive Director
Member of the Nomination Committee

Appointed as a Director 1 July 2003. Executive Vice-President of H J Heinz Company and President and Chief Executive Officer of Heinz Europe since 2002. Corporate Vice-President then Senior Vice-President and President of Heinz North America 1998-2002. Non-Executive Director of Hain Celestial Group, Inc.

Other officers of the Company at 31 December 2003 included members of the Senior Executive Team, as set out on page 45, and:

Graeme Musker
Group Secretary and Solicitor

Appointed as Company Secretary 6 June 1993.

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Strategy

We aspire to be the best in all areas of our business within a culture based on innovation combined with the disciplined and responsible approach required to achieve industry leading productivity.

By discovering, developing, manufacturing and marketing differentiated medicines that make a real contribution to human health, AstraZeneca aims to create enduring value for shareholders and society, and deliver a sustained financial performance that will match the best in the industry.

Our strategy for sustainable growth is:

- Expansion of the development pipeline through continuously improved in-house discovery processes complemented by external collaborations and partnerships
- Successful delivery to market of the next wave of differentiated products currently in late stage development
- Realising the full potential of our therapies through investment in projects that will extend their use and bring benefits to new patient populations
- Further strengthening our commercial skills to drive success in our key markets
- Enhancing our presence in important new, emerging markets through organic growth and strategic regional investments
- Pursuing value creating investment in significant targeted licensing and acquisition opportunities
- Continuing to improve productivity in pursuit of operational excellence in all our activities
- Delivering our core values through a responsible approach to business

Key Products

Cardiovascular
Atacand[1] (candesartan cilexetil) angiotensin II antagonist for hypertension

Gastrointestinal
Losec/Prilosec (omeprazole) proton pump inhibitor for acid related diseases

Oncology
Arimidex (anastrozole) aromatase inhibitor for breast cancer

Casodex(bicalutamide) anti-androgen for prostate cancer

Crestor[2] (rosuvastatin) HMG-CoA reductase inhibitor (□statin□) for dyslipidaemia

Exanta (ximelagatran) oral direct thrombin inhibitor for prevention of thrombosis in association with major orthopaedic surgery

Plendil (felodipine) calcium antagonist for hypertension and angina

Seloken/Toprol-XL (metoprolol) beta blocker for hypertension, angina, heart failure and other uses

Zestril[3] (lisinopril) angiotensin converting enzyme inhibitor for hypertension, heart failure and diabetic nephropathy

Losec MUPS omeprazole in tablet form

Nexium (esomeprazole) proton pump inhibitor for acid related diseases

Faslodex (fulvestrant) oestrogen receptor antagonist with no agonist effects for breast cancer

Iressa (gefitinib) signal transduction inhibitor for non-small cell lung cancer

Nolvadex (tamoxifen) anti-oestrogen for breast cancer

Zoladex(goserelin) LHRH agonist for prostate and pre-menopausal breast cancer, certain benign gynaecological disorders and assisted reproduction

Respiratory and Inflammation

Accolate (zafirlukast) oral leukotriene receptor antagonist for control of asthma

Oxis (formoterol) inhaled fast onset long-acting bronchodilator for relief of asthma symptoms

Pulmicort (budesonide) inhaled anti-inflammatory for asthma control

Rhinocort (budesonide) topical nasal anti-inflammatory for control of rhinitis

Symbicort (budesonide/formoterol) inhaled combination of anti-inflammatory and fast onset long-acting bronchodilator in a single inhaler

Neuroscience

Diprivan (propofol) intravenous general anaesthetic for induction/maintenance of anaesthesia and sedation of intensive care patients

Naropin (ropivacaine) local anaesthetic for surgical anaesthesia and acute pain management

Seroquel (quetiapine) atypical anti-psychotic for schizophrenia and other psychotic disorders

Xylocaine (lidocaine) local anaesthetic for use in surgery and dentistry

Zomig (zolmitriptan) for the treatment of acute migraine with or without aura

Infection

Merrem/Meronem[4] (meropenem) ultra broad spectrum injectable antibiotic for serious bacterial infection

[1] Licensed from Takeda Chemical Industries Ltd. [2] Licensed from Shionogi & Co., Ltd. [3] Licensed from Merck & Co., Inc. [4] Licensed from Sumitomo Pharmaceuticals Co., Ltd.

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Operational Review

The growing demand for new medicines is driven by increasing populations and improved life expectancy as modern medicine supports an ageing population. According to the latest information available from the World Health Organisation (www.WHO.int), the greatest burden of disease is in the non-communicable disease sector where diseases such as unipolar depression, schizophrenia, diabetes, ischaemic heart disease, cerebrovascular disease and asthma have all increased over the last five years. Communicable diseases are also increasing due primarily to HIV/AIDS and tuberculosis.

AstraZeneca focuses its skills, experience and resources on six therapy areas: Cardiovascular, Gastrointestinal, Neuroscience, Oncology, Respiratory and Inflammation, and Infection which represent the majority of the worldwide burden of disease. We have a powerful range of products that meet patient needs in our chosen areas of activity including some significant areas of hitherto unmet medical need. We are committed to delivering new, medically important and commercially successful products to the market every year.

This Operational Review (pages 9 to 30) provides detailed information about our research, development, manufacturing and marketing activities worldwide and our performance in 2003.

AstraZeneca in brief

- We spend around $14 million each working day on research and development (total R&D spend in 2003: $3.5 billion)
- We employ 11,600 people in research and development at 11 R&D centres in seven countries: Sweden, the UK, the US, Canada, France, India and Japan
- Our strong R&D pipeline includes a number of significant innovations
- We have 12 projects in phase 2 and 28 projects in phase 3 development, as shown on page 24
- Collaborations with leading academic centres and biotechnology companies and the in-licensing of innovative products and technologies complement our in-house capabilities and play a key role in strengthening our portfolio
- We have 31 manufacturing sites in 20 countries
- Around 16,000 people worldwide work in supply and manufacturing, including some 13,000 people in formulation and packaging, and 1,750 in active pharmaceutical ingredient supply
- We have over 60,000 employees worldwide:
  - 35,000 in Europe
  - 18,000 in the Americas
  - 8,000 in Asia, Africa and Australasia
- We sell in over 100 countries
- Along with our commitment to competitiveness and high performance, we will continue to be led by our core values to achieve sustainable success

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Cardiovascular (CV)

We are a world leader in CV medicines, backed by over 40 years experience. We aim to build on our strong position, focusing in the short to medium term on the growth segments of hypertension, dyslipidaemia, thrombosis and type 2 diabetes.

Therapy area overview

> CV world market value: $98 billion.

> CV diseases account for 17 million deaths globally each year, making it the greatest risk to life for most adults.

> CV is the single largest therapy area in the global healthcare market.

> The statin market has a world market value of $22 billion.

2003 in brief

> *Crestor* available in 25 markets including the US by the end of January 2004.

> Over 750,000 patients treated with *Crestor* by the end of January 2004.

> *Seloken/Toprol-XL* sales grew by an underlying 38% and exceeded $1 billion.

> First approval for *Exanta* in France. US and EU filings submitted.

> Erosion of *Zestril* sales following patent expiries in 2002.

Products

Crestor (rosuvastatin) is a member of the class of products known as statins. During 2003, *Crestor* gained regulatory approval in more than 40 countries, including 13 European markets, the US and Canada.

In multiple clinical studies, *Crestor* has been shown to be more effective in lowering low density lipoprotein (LDL-C) than other prescribed statins. Additionally, *Crestor* produces a significant increase in high density lipoprotein (HDL-C), an effect that is maintained across the 10-40mg dose range. By the end of January 2004, we estimate that more than 1.5 million prescriptions were written for *Crestor* and over 750,000 patients had taken *Crestor*. Along with the extensive clinical trial database this experience demonstrates that *Crestor* is well tolerated in clinical use, with a safety profile in line with other marketed statins.

Our extensive, long term global clinical research initiative known as the GALAXY programme, including studies which investigate cardiovascular risk reduction and patient outcomes with *Crestor*, is now well underway. More than 30,000 patients are involved, two studies have been completed and 14 studies are ongoing in important medical areas including heart failure, end stage renal disease, acute coronary syndrome and regression of atherosclerosis.

By the end of January 2004, *Crestor* was launched in 25 countries including the US, Canada, the UK and the Netherlands. Further launches are planned throughout 2004 including in Japan, Italy and France.

Atacand (candesartan cilexetil) is an angiotensin II antagonist for the first line treatment of hypertension. The *Atacand* family of products shows a strong market acceptance and competes in the fastest growing sector of the global hypertension market (angiotensin II antagonists plain and combinations with diuretic). During 2003, the CHARM programme, a comprehensive clinical study programme in heart failure, was published, showing significant reduction in cardiovascular mortality and hospitalisation for heart failure in patients treated with *Atacand*. The beneficial effect was regardless of age, sex and background treatment (also additive to the effect seen with angiotensin converting enzyme (ACE) inhibition). Initial regulatory approvals for the new indication of heart failure are currently

anticipated during 2004. The results of the CHARM programme will further differentiate *Atacand* within its drug class. The clinical programme investigating the effect of *Atacand* on retinopathy in diabetic patients (DIRECT) continued during 2003.

Seloken ZOK/Toprol-XL (metoprolol), a once daily tablet for 24 hour control of blood pressure and for use in heart failure, is the world s leading product by sales in the beta blocker (plain and combinations with diuretic) class.

Plendil (felodipine) is a calcium antagonist for the treatment of hypertension and angina.

Zestril (lisinopril dihydrate), an ACE inhibitor, is used for the treatment of a wide range of CV diseases, including hypertension.

Information regarding patent challenges for Seloken/Toprol-XL and *Plendil* is set out on page 104.

Pipeline

We aim to broaden our CV portfolio into the areas of thromboembolism, dyslipidaemia, type 2 diabetes/metabolic syndrome, atrial fibrillation and vascular disease prevention.

Exanta, the first new oral anti-coagulant in almost 60 years, is a novel oral direct thrombin inhibitor targeted to prevent and treat the formation of blood clots (thrombosis). *Exanta* has been subject to the largest clinical study development programme in anti-coagulation to date, involving around 30,000 patients, and providing extensive outcome data. Several clinical studies with *Exanta* in prevention of stroke in patients with atrial fibrillation (SPORTIF III and SPORTIF V) and treatment of venous thromboembolism (VTE) (THRIVE Treatment) were presented during 2003. Liver enzyme elevations have been seen in a small proportion of patients treated with *Exanta* in chronic studies and are typically transient (occurring within the first two to six months), not associated with specific symptoms and tend to return towards normal whether or not treatment is continued. All data from the

extensive clinical study programme has been shared with regulatory authorities to support a full evaluation of the benefit-risk profile for *Exanta*. The practical benefits of *Exanta* include fixed oral administration, rapid onset of action, low potential for drug/food and drug/drug interactions and no need for routine blood coagulation monitoring. A

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Sales growth is shown in both reported and underlying performance. Reported performance takes into account all the factors (including those which we cannot influence, principally currency exchange rates) that have affected the results of our business. Underlying performance shows sales growth at constant exchange rates (CER) to reflect the volume and price changes of the geographic and therapy areas and individual products by excluding the effects of exchange. A description of the calculation of this measure is set out in the Financial Review on page 31, together with the reasons for its use.

Key product performance

	2003			2002			2001	2003 compared to 2002		2002 compared to 2001	
	Sales $m	Growth underlying $m	Growth due to exchange effects $m	Sales $m	Growth underlying $m	Growth due to exchange effects $m	Sales $m	Growth underlying %	Growth reported %	Growth underlying %	Growth reported %
Seloken	1,280	340	39	901	187	3	711	38	42	27	27
Atacand	750	121	60	569	148	11	410	21	32	36	39
Plendil	540	25	26	489	21	5	463	5	10	5	6
Zestril	478	(446)	47	877	(195)	5	1,067	(50)	(45)	(18)	(18)
Tenormin	342	(53)	25	370	(28)	(6)	404	(15)	(8)	(7)	(8)
Crestor	129	122	7	□	□	□	□	n/m	n/m	□	□
Other	391	(17)	45	363	(79)	14	428	(4)	8	(18)	(15)
Total	**3,910**	**92**	**249**	**3,569**	**54**	**32**	**3,483**	**3**	**10**	**1**	**2**

phase 2 study (ESTEEM) also indicates that *Exanta* provides additional benefits when added to standard therapy (including aspirin) in prevention of major CV events in patients following a heart attack.

Exanta received its first regulatory approval for the prevention of VTE in major elective orthopaedic (hip or knee replacement) surgery in December 2003 in France. First regulatory submissions for the chronic indications in the US, Canada and Europe were made in December 2003. The filing in the US also includes prevention of VTE in major elective orthopaedic (knee replacement) surgery.

Galida is a treatment for insulin resistance related glucose and lipid abnormalities associated with type 2 diabetes/metabolic syndrome. It is in phase 3 development for the treatment of diabetes.

Our further research in thrombosis includes **AZD6140**, an oral anti-platelet therapy which is in phase 2. Novel research in atrial fibrillation includes **AZD7009**, an atrial repolarisation delaying agent, which is in phase 2 and **AZD0837** and **AZD0303** (both for thrombosis) which are in phase 1 and in pre-clinical development respectively. **AZD9684** (a carboxy peptidase-U inhibitor for thrombosis) is in phase 1. **AZD7806** and **AZD8294** (in the dyslipidaemia area) and **AZD4619** and **AZD6610**, for the treatment of metabolic disorders (diabetes mellitus and dyslipidaemia), are all in pre-clinical development.

Performance 2003

Reported performance

Reported growth for CV was 10% with sales of $3,910 million, an increase of $341 million from $3,569 million, notwithstanding the anticipated erosion of *Zestril* sales

following patent expiry.

Underlying performance

Excluding exchange effects of $249 million, CV underlying sales growth was $92 million or 3%. Sales in the US exceeded $1.6 billion.

Global sales of *Seloken/Toprol-XL* exceeded $1 billion for the first time, on continued strong growth in the US (up 47%), where total prescriptions increased by 25%, and market share of total beta blocker prescriptions of *Seloken/Toprol-XL* reached 26.2% in December, up 2.6 percentage points compared to 2002. Despite destocking in the last quarter, wholesaler inventories remained higher than normal at the year end.

Atacand sales increased by 28% in the US, and by 18% in the markets outside the US, which account for nearly two-thirds of global *Atacand* sales. US sales growth exceeded growth in total prescriptions, indicating some increase in wholesaler inventories.

Crestor sales were $129 million, including $62 million in the US. The early launch markets for *Crestor* included the Netherlands, Canada and the UK. Based on recent market research data, *Crestor* share of total prescriptions in these markets has reached 8.2% (the Netherlands), 6.9% (Canada), and 2.9% (UK) respectively, with shares of the dynamic segment (new and switch therapies only) considerably higher. In the US, *Crestor* was launched in mid-September. In the week ending 16 January 2004, *Crestor* share of new prescriptions in the US statin market was 4.6%, a good start in a highly competitive market. *Crestor* dynamic share of new statin treatments (new and switch therapy only) in the US is 13.7%.

Lisinopril, the active ingredient in *Zestril*, lost patent protection in most major markets during 2002. The major part of anticipated sales erosion has taken place during 2003, with sales falling by 50% to $478 million from $877 million. In the US, generic lisinopril held an 80% share of sales by the end of 2003.

Plendil sales rose by 5%, to $540 million. Continuing the trend of the last two years, growth in the US, where sales were up 13% to $237 million, was offset by lower sales in the rest of the world.

Performance 2002

Reported performance

CV sales grew by 2% to $3.6 billion in 2002, an increase of $86 million compared to 2001.

Underlying performance

CV sales growth included $32 million of exchange effects. Underlying sales increased by 1%.

Atacand sales grew by 36% to $569 million with an increase in the US of 37% to $206 million.

Prescriptions grew strongly for*Seloken/Toprol-XL* in the US generating sales of $617 million, an increase of 43% and a market share of 25%. Worldwide sales grew by 27% from $711 million to $901 million.

Erosion of *Zestril* sales commenced during the second half following patent expiry in the US, the UK and Japan, falling by 18% from $1,067 million to $877 million.

Plendil sales rose by 5% to $489 million. As in 2001, growth in the US (up 6% to $209 million) was offset by falling sales in the rest of the world.

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Gastrointestinal (GI)

We aim to maintain our number one position in GI treatments through continued market penetration for *Nexium* worldwide, coupled with high quality innovation and productivity in the research and development of new GI therapies.

Therapy area overview

- World market value: PPI: $19.1 billion.
- 40% of adults in the western world regularly experience heartburn and 10% have gastro-oesophageal reflux disease (GERD).
- Helicobacter pylori (H.pylori) is the major cause of peptic ulcer disease and is a risk factor for gastric cancer. Prevalence rate of H.pylori infection in the population is 40%.
- Irritable bowel syndrome (IBS) is an increasingly common complaint which is inadequately treated. Prevalence rate in the population is 20%.
- Inflammatory bowel disease (IBD) is another area of significant unmet medical need.

2003 in brief

- *Nexium* launch in the US is one of the most successful pharmaceutical launches ever.
- Global sales of *Nexium* exceeded $3 billion (62% underlying growth).
- US court judgement in *Losec/Prilosec* litigation challenges confirmed by the US Appeals Court.

Products

Nexium (esomeprazole) is the first proton pump inhibitor (PPI) to offer significant clinical improvements over *Losec/Prilosec* and its main competitors, lansoprazole and pantoprazole. *Nexium* has been evaluated in clinical studies involving over 68,000 patients in 57 countries. It offers more effective acid inhibition than all other PPIs and, in the treatment of reflux oesophagitis, provides healing and symptom relief in more patients and in a shorter period of time than *Losec/Prilosec*, lansoprazole or pantoprazole. It is an effective, long term therapy for patients with GERD, with or without oesophagitis. For the treatment of active duodenal ulcer disease, seven day *Nexium*

triple therapy (in combination with two antibiotics for the eradication of H.pylori) heals most patients without the need for follow up anti-secretory monotherapy.

Nexium is used to treat a wide range of patients, including both newly diagnosed and also patients switched from other therapies such as omeprazole, other PPIs and H2-receptor antagonists.

Nexium continues to establish a new improved treatment standard. It was first launched in Sweden in August 2000 and it is now available in 100 markets, including the US, Canada and all European countries. It has been well received by patients and physicians alike and over 145 million patient treatments had been administered by the end of 2003.

Regulatory filings for *Nexium* for the treatment (symptom resolution) of side effects from non-steroidal anti-inflammatory drugs (NSAID) and a parenteral formulation were made in 2003. First regulatory approval and launch of parenteral *Nexium* were achieved in 2003. The parenteral form of *Nexium* was approved in Europe in late 2003 as a dosage form when oral administration is not applicable for the treatment of GERD and it was confirmed that the side effect NSAID indication is within the existing treatment usage.

Losec/Prilosec (omeprazole), the first PPI, set a new global standard in the short and long term treatment of acid-related diseases in the 1980s and 1990s. Patients have benefited from over 720 million treatments with *Losec/Prilosec* since launch. *Losec* MUPS, a tablet formulation, has been launched in 57 markets.

Patent protection for omeprazole, the active ingredient in *Losec/Prilosec*, has expired. In a small number of countries, including some major markets, patent term extensions or supplementary protection certificates have been granted for the active ingredient.

In October 2002, the US Court for the Southern District of New York ruled that three out of four generic manufacturers sued by AstraZeneca infringed certain patents, including formulation patents for omeprazole, the active ingredient in *Losec/Prilosec*. This decision was upheld by the US Appeals Court in late 2003. The first US generic omeprazole product was launched in December 2002. Three further generic versions were launched in the US during 2003. Further information about the status of omeprazole patents and patent litigation is set out on pages 102 and 103.

In July 2003, the European Commission served a Statement of Objections on the Company, referring to alleged infringements of European competition law relating to certain omeprazole intellectual property rights and associated litigation, details of which are set out on page 103.

Entocort (budesonide) is a locally acting corticosteroid for the treatment of IBD with better tolerability than other corticosteroids and greater efficacy than aminosalicylic acid medicines.

Pipeline

In addition to exploring new areas of clinical use for *Nexium* and further strengthening the scope of its use in current areas, we focus on developing novel approaches to treating GERD, H.pylori, peptic ulcer disease, IBD and other gastrointestinal diseases, such as functional dyspepsia and IBS.

AZD0865 is a compound in a new class, potassium-competitive acid blockers, that has potential to provide faster, more effective and reliable inhibition of gastric acid secretion than PPIs in the treatment of acid-related diseases, such as GERD. It is now in phase 2.

AZD3355 and **AZD9343**, which are in pre-clinical development, are reflux inhibitors offering a potential breakthrough in the treatment of GERD through a new, targeted approach (other than inhibition of acid secretion) by inhibition of transient relaxations of the lower oesophageal sphincter.

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Key product performance

	2003			2002			2001	2003 compared to 2002		2002 compared to 2001	
	Sales $m	Growth underlying $m	Growth due to exchange effects $m	Sales $m	Growth underlying $m	Growth due to exchange effects $m	Sales $m	Growth underlying %	Growth reported %	Growth underlying %	Growth reported %
Nexium	3,302	1,225	99	1,978	1,395	15	568	62	67	n/m	n/m
Losec/Prilosec	2,565	(2,259)	201	4,623	(985)	30	5,578	(49)	(45)	(18)	(17)
Other	76	8	5	63	17	2	44	13	21	38	43
Total	**5,943**	**(1,026)**	**305**	**6,664**	**427**	**47**	**6,190**	**(16)**	**(11)**	**7**	**8**

AZD7371 is being evaluated in clinical studies for the treatment of functional GI disorders in phase 1.

Performance 2003

Reported performance

Reported sales in the GI therapy area fell by 11%, $721 million, to $5,943 million as increases in *Nexium* sales were offset by declines in *Losec*/*Prilosec* sales following patent expiries. Our world leading position in GI was nevertheless maintained.

Underlying performance

Exchange effects on sales in 2003 amounted to $305 million. As a consequence, the underlying sales decline at 16%, was higher than reported.

Global sales performance for *Nexium* was strong, particularly in the US where total prescriptions for *Nexium* overtook those for *Losec*/*Prilosec* during the year. Sales of *Nexium* in the US for the full year increased by 62% to $2,477 million. Total prescriptions for *Nexium* were up 46% and its share of total prescriptions in the US PPI market grew by nearly five percentage points over the course of the year, to 25.3%. It is the most prescribed PPI among gastro-enterologists in the US and overall the second most prescribed PPI in the US market. It is the leading product to which patients switch from other treatments in the anti-secretory category. This performance in the US was attributed to the strong clinical data available to support the sales force, Managed Care Access and a nationwide, direct-to-consumer advertising programme.

Sales of *Nexium* outside the US increased by 60% for the full year, with excellent growth in the major markets in Europe, particularly France, Germany and the UK, and a strong performance in Australia. On 14 January 2004 the Company announced that the European Mutual Recognition Procedure for the intravenous formulation of

Nexium had been successfully completed. An application for approval in the US is under review by the US Food and Drug Administration (FDA). The global PPI market continues to grow strongly (around 15% per annum). *Nexium* share of the PPI market across major markets was 24% in November 2003.

Losec/Prilosec sales were down by 49% for the year. The 70% decline in the US was broadly in line with the prescription trend. At the end of the year *Losec/Prilosec* brand share of total omeprazole prescriptions in the US was 27.4% as four more generic versions of omeprazole entered the market and Proctor & Gamble launched the first over-the-counter (OTC) version of the brand *Losec/Prilosec* OTC. Outside the US sales fell by 16%, although there was strong growth in Japan where sales increased by 39% from $92 million to $138 million.

Performance 2002

Reported performance

GI sales grew by 8% from $6,190 million in 2001 to $6,664 million in 2002.

Underlying performance

Excluding exchange effects, GI growth was 7%.

Nexium sales in the US totalled $1.5 billion and in December 2002 accounted for a 21% share of new prescriptions in the US PPI market. In the rest of the world, sales were $453 million by the end of the year *Nexium* had been launched in 76 countries. *Losec/Prilosec* sales fell by 18% to $4.6 billion. The US decline of 21% was broadly in line with the prescription trend. Generic competition entered the US market in December 2002. Outside the US sales fell by 12%, despite strong growth in Japan (up 40% to $92 million) and Australia (up 25% to $95 million).

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Neuroscience

We aim to be a leader in neuroscience, by continuing to deliver a range of life changing medicines in the three key areas of psychiatry, analgesia and neurology and by maintaining our world leading position in anaesthesia.

Therapy area overview

> Neuroscience world market value: over $85 billion.

Psychiatry (market value: $37 billion)
> More than six million people suffer from schizophrenia and 17 million suffer from bipolar disorder in the major markets.

Neurology (market value: $20 billion)
> Migraine is one of the 20 leading causes of disability in the world. Stroke is the third leading cause of death and one of the major causes of serious long term disability among adults in the US.

Analgesia (market value: $25 billion)
> Over 46% of adults in the western world suffer from chronic pain. Pain management is the most common reason for seeking medical care.

Anaesthesia (market value: $3 billion)
> Each year more than 26 million people in the US undergo medical treatment requiring anaesthesia.

2003 in brief

> *Seroquel* sales grew by an underlying 27% to $1.5 billion.

> *Seroquel* widely approved in Europe and the US for the treatment of bipolar mania.

> *Zomig Nasal Spray* launched in the US and Europe.

Products

Seroquel (quetiapine) is an atypical anti-psychotic for the treatment of schizophrenia as an established first line, first choice treatment for a broad range of symptoms. It combines excellent efficacy with unique patient tolerability in terms of dose independent low level of extrapyramidal symptoms providing schizophrenia patients with benefits in mood symptoms.

This profile has led to the increased usage of *Seroquel*, substantially exceeding market growth across the globe. *Seroquel* is the only leading atypical to be gaining market share. In January 2004, the weekly new US prescriptions for *Seroquel* exceeded those written for olanzapine for the first time.

Seroquel is now widely approved in Europe and the US for the treatment of bipolar mania offering clinicians rapid control of their patients manic symptoms including psychosis, aggression/agitation with no emergent depression and a superior side effect profile.

Zomig (zolmitriptan) is indicated for the treatment of migraine with or without aura which offers migraine sufferers rapid, reliable relief of headache pain and other migraine symptoms and is well tolerated. Available in over 80 countries, it is the leading second-generation triptan with a unique range of formulations to provide rapid migraine relief.

Zomig Nasal Spray is a new formulation in a convenient device, which delivers fast pain relief. The nasal spray has been successfully launched in Europe and the US. Launch in Japan is expected in 2004.

Zomig Rapimelt is a rapidly dispersible formulation offering patients a convenient, orange flavoured melt-in-the-mouth tablet that now accounts for more than 30% of *Zomig* sales.

Diprivan (propofol), the world s largest selling general anaesthetic, is used in the induction and maintenance of anaesthesia and for intensive care sedation. More than 90% of total *Diprivan* sales consist of *Diprivan EDTA*, a microbial resistant formulation, which is approved in the majority of markets.

Naropin (ropivacaine) is the best selling, long-acting local anaesthetic. With its improved safety and mobility profile, it is

replacing the previous standard treatment of bupivacaine in major markets.

Xylocaine (lidocaine) continues to be the world s most widely used local anaesthetic after 50 years on the market.

Information regarding legal proceedings in relation to *Seroquel* is set out on page 104.

Pipeline

We are focused on unmet medical needs in three key areas.

Psychiatry

Further developments of *Seroquel* are planned to show the full spectrum of clinical benefit in those suffering from mood disorders. In addition, new formulations are being developed to expand the treatment options available for patients.

AR-A2 is a novel $5HT_{1B}$ autoreceptor antagonist in phase 2 for the treatment of depression and anxiety and **AZD5455** is a pre-clinical candidate drug with a novel mechanism of action for treating anxiety.

We have discontinued the development of **AZD1134** as a result of its failure to meet the target profile.

The collaboration with Shanghai Jiaotong University on neurogenetics, established in 2001, continues to progress well.

Analgesia

In pain control, our research focus is nociceptive pain (caused by tissue damage) and neuropathic pain (caused by nerve damage). Our pipeline includes **AZD4282** in phase 1 for the treatment of neuropathic pain.

We have discontinued the development of **AZD3582** and **AZD4717** as a result of their failure to meet our target profile and have returned all rights to these compounds to NicOx.

Neurology

Cerovive (previously known as NXY059) is a nitrone with free radical trapping properties under development for the treatment of acute ischaemic stroke, a disease with substantial unmet need for new effective therapies. Pre-clinical data show that *Cerovive* preserves function and brain tissue, otherwise irreversibly damaged, when administered after the onset of permanent ischaemia in a model of

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Key product performance

	2003			2002			2001	2003 compared to 2002		2002 compared to 2001	
	Sales $m	Growth underlying $m	Growth due to exchange effects $m	Sales $m	Growth underlying $m	Growth due to exchange effects $m	Sales $m	Growth underlying %	Growth reported %	Growth underlying %	Growth reported %
Seroquel	1,487	304	38	1,145	457	3	685	27	30	67	67
Local anaesthetics	466	&#150	34	432	&#150	(2)	434	&#150	8	&#150	&#150
Diprivan	458	(7)	22	443	(12)	(1)	456	(2)	3	(3)	(3)
Zomig	349	(3)	24	328	52	3	273	(1)	6	19	20
Other	73	(5)	8	70	(80)	1	149	(7)	4	(54)	(54)
Total	**2,833**	**289**	**126**	**2,418**	**417**	**4**	**1,997**	**12**	**17**	**21**	**21**

acute stroke. We have commenced two major phase 3 trials known as the SAINT (Stroke Acute Ischaemic NXY Treatment) trials, which will compare the efficacy and safety of a 72 hour intravenous infusion of *Cerovive* given within six hours of the onset of symptoms versus placebo.

ZD0947, a novel non-muscarinic approach to overactive bladder, which is a common condition, is currently in phase 2.

AZD0328, AZD2858 and **AZD3102** are new candidate drugs with novel mechanisms of action for the treatment of Alzheimer's disease, a core strategic focus of our research. Alzheimer's disease, the most common cause of dementia, affects more than 45 million people in the US.

Our collaboration with NPS
Pharmaceuticals continues to progress well with early and late phase pre-clinical projects on metabotropic glutamate receptors covering all major neuroscience disease indications.

We have discontinued the development of **AZD5106** as a result of its failure to meet the target profile.

Performance 2003

Reported performance

Reported growth for Neuroscience was 17%, with sales up $415 million from $2,418 million in 2002 to $2,833 million in 2003. The performance of *Seroquel* accounted for the majority of this increase.

Underlying performance

In the US, sales grew strongly by 14% to $1.7 billion. In the rest of the world sales also grew strongly by 10% to deliver global sales of $2.8 billion, a combined growth of 12% worldwide.

In the US, *Seroquel* sales reached $1,134 million for the full year, an increase of 22%. Total prescriptions for *Seroquel* in the US were up 34% for the year. The share of total prescriptions for *Seroquel* in the US anti-psychotic market reached a new high at 21.2% in December, up 3.4 percentage points compared to 2002. *Seroquel* was the only product among the three leading brands to increase its market share in 2003. Sales growth in the last quarter of the year was lower than the underlying prescription trend implying some reduction in wholesaler stocking.

Sales of *Seroquel* in markets outside the US increased 45% for the full year. Sales in Europe were up 40%, and sales in Japan rose 67%. Japan is now the second largest market for *Seroquel* where it is sold by Fujisawa and continued growth is anticipated through the development of new claims, new indications, new formulations and increasing penetration of a growing schizophrenia market.

Zomig sales for the full year fell by 1% to $349 million (global market share remains at 16%); growth was 7% outside the US, whilst sales were down 8% in the US. *Rapimelt* continued to grow strongly in southern Europe and Japan and now contributes more than half of brand sales in these markets. *Zomig Nasal Spray* launches continue and the introduction of this formulation in the US helped drive sales in the last quarter.

Sales of *Diprivan* worldwide, at $458 million, fell by 2%. The rate of decline since patent expiry has slowed.

Performance 2002

Reported performance

Neuroscience sales increased by 21% to $2,418 million in 2002, an overall increase of $421 million.

Underlying performance

Underlying sales growth was also 21%, with minimal exchange effects.

Seroquel sales grew strongly by 67% to $1.1 billion. US sales also grew by 67% to $927 million. Market share of new prescriptions in the US market was 19.2% by the end of the year, up 3.7 percentage points in the year making it the only major anti-psychotic with increasing share in this key market.

Zomig sales grew by 19% to $328 million (a global market share of 16%) with the bulk of the increase arising in Japan (up 67% to $14 million), France (up 29% to $60 million) and the US (up 20% to $177 million).

The sales increase for *Diprivan* in the US (up 3% to $216 million) was the result of growth in the underlying demand for propofol. However, global sales fell by 3% to $443 million.

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Oncology

We aim to maintain our position as a world leader in cancer treatment through continued growth for *Casodex*, *Arimidex* and *Zoladex*, further launches of newer products, *Faslodex* and *Iressa* and the successful introduction of novel approaches currently in the pipeline.

Therapy area overview

> World market value: cancer therapies: $18 billion.

> Globally, over 12 million people are diagnosed with cancer each year.

> Cancer is predicted to be the leading cause of death in the US by 2005.

2003 in brief

> Rapid uptake of *Iressa* since first launch in Japan in 2002 and the US in 2003. Over 100,000 patients treated since launch.

> Positive opinion on approvability of *Faslodex* from the CPMP in 2003.

> *Arimidex* rapidly moving towards replacing tamoxifen as the standard of care in breast cancer.

> Anticipated erosion of *Nolvadex* sales following expiration of US marketing exclusivity in early 2003.

Products

Casodex (bicalutamide) is the world's leading anti-androgen therapy for the treatment of prostate cancer. Recent growth of *Casodex* has largely been driven by its use to treat early stage prostate cancer (EPC). *Casodex* 150mg has received regulatory approval for the treatment of EPC in over 50 markets to date. In the US, in 2002 the FDA did not approve this new indication. It is under review in several other markets. Elsewhere, the rapid uptake of *Casodex* in EPC as a favoured therapy is a demonstration of physicians' growing confidence in the efficacy and tolerability profile of *Casodex* as a treatment in all stages of prostate cancer.

Zoladex (goserelin acetate) is one of the world's best selling luteinising-hormone releasing hormone (LHRH) agonists for the treatment of prostate cancer, breast cancer and gynaecological disorders. It has been approved in

24 countries for the adjuvant treatment of early stage pre-menopausal breast cancer, as an alternative to and/or in addition to chemotherapy. *Zoladex* offers the proven disease free survival benefits of cytotoxics but with improved patient tolerability. In prostate cancer, *Zoladex* in the adjuvant setting is the only LHRH agonist shown to improve overall survival following radical prostatectomy or radiotherapy.

Iressa (gefitinib) is a novel anti-cancer agent that acts to block signals for cancer cell growth and survival. Clinical trials with *Iressa* as monotherapy for non-small cell lung cancer (NSCLC) showed response rates and disease control in approximately half of patients and symptomatic benefit in over 40% of patients treated. Regulatory filings based on monotherapy began in December 2001. Since first launch in Japan in 2002, uptake of *Iressa* has been rapid, reflecting the high unmet need in NSCLC and the significant benefit seen with *Iressa*. In the US, the FDA granted *Iressa* approval in May 2003, conditional upon conduct of further specified studies, and it is now approved in more than 15 countries. We are pursuing monotherapy submissions for *Iressa* in all other major markets, including Europe where filing was submitted in the first quarter of 2003 and definitive clinical studies are underway to secure unconditional approval in the US. To date, over 100,000 patients have been treated with *Iressa*. In Japan, reporting of interstitial lung disease associated with *Iressa* has

stabilised at 3%, a rate comparable to other therapies. By contrast, the reported rate is below 0.5% outside Japan.

Arimidex (anastrozole) is the world□s leading aromatase inhibitor. The ATAC study in breast cancer, first reported in December 2001 and then subsequently updated in December 2002, showed that *Arimidex* is significantly more effective in prolonging disease-free survival and has important tolerability benefits compared with tamoxifen. Based on the ATAC study, *Arimidex* is rapidly moving towards replacing tamoxifen as the standard of care in breast cancer. Regulatory approvals for *Arimidex* in the adjuvant treatment of early breast cancer in post-menopausal women have been granted in 57 markets including the US, Europe and Japan. Early breast cancer represents a major new market for *Arimidex* and is driving significant growth. Recent data from a major trial has shown significant improvements in efficacy and tolerability for women who switch therapy from tamoxifen to *Arimidex* before their standard five year course is complete. *Arimidex* is also approved for the treatment of advanced breast cancer in post-menopausal women based on demonstrated advantages over tamoxifen and megestrol acetate.

Faslodex (fulvestrant) is a new type of endocrine therapy, an oestrogen receptor antagonist, with no agonist effects, that down regulates the oestrogen receptor. It was launched in the US in May 2002 and subsequently in Brazil in July 2003, for the second line treatment of hormone receptor positive advanced breast cancer in post-menopausal women. Due to its novel mode of action, *Faslodex* offers an effective, well tolerated treatment option for patients, with the compliance and convenience benefits of a once monthly injection. In November 2003, the Committee for Proprietary Medicinal Products (CPMP) gave a positive opinion on the approvability of *Faslodex* in Europe. We currently expect to receive European approval in early 2004.

Nolvadex (tamoxifen citrate) remains the world□s most commonly prescribed breast cancer therapy and the first medication approved in the US for reducing the incidence of breast cancer in women at high risk of developing the disease. US marketing exclusivity for tamoxifen expired during 2003.

Sales growth is shown in both reported and underlying performance. Reported performance takes into account all the factors (including those which we cannot influence, principally currency exchange rates) that have affected the results of our business. Underlying performance shows sales growth at constant exchange rates (CER) to reflect the volume and price changes of the geographic and therapy areas and individual products by excluding the effects of exchange. A description of the calculation of this measure is set out in the Financial Review on page 31, together with the reasons for its use.

Key product performance

	2003			2002			2001	2003 compared to 2002		2002 compared to 2001	
	Sales $m	Growth underlying $m	Growth due to exchange effects $m	Sales $m	Growth underlying $m	Growth due to exchange effects $m	Sales $m	Growth underlying %	Growth reported %	Growth underlying %	Growth reported %
Zoladex	869	6	69	794	80	(4)	718	9	9	12	11
Casodex	854	140	70	644	81	2	561	22	33	15	15
Arimidex	519	152	36	331	141	2	188	46	57	75	76
Iressa	228	152	9	67	69	(2)		227	240	n/m	n/m
Nolvadex	178	(314)	12	480	(134)	(4)	618	(66)	(63)	(21)	(22)
Faslodex	77	42		35	35			120	120	n/m	n/m
Other	18	(1)	1	18	(8)		26	(6)		(31)	(31)
Total	**2,743**	**177**	**197**	**2,369**	**264**	**(6)**	**2,111**	**8**	**16**	**12**	**12**

Pipeline

We focus on the development of new agents and novel approaches across a wide range of cancers that include targeting tumour vasculature to control tumour growth, invasion and spread. The potential of *Iressa* to show benefits in a number of tumours in addition to expanding use of *Iressa* in NSCLC is being investigated with particular focus on head and neck, breast and colorectal cancers.

ZD6474 and **AZD2171** are anti-angiogenics in phase 2 and phase 1 respectively which target the growth of blood vessels of tumours. **AZD9935** is another anti-angiogenic in pre-clinical development.

ZD6126 is a vascular targeting agent in phase 2 which targets and destroys the vasculature of tumours, working to destroy the tumour from within. **AZD4440**, another vascular targeting agent, is in pre-clinical development. **ZD4054** is an endothelin antagonist in phase 2 that works by targeting the endothelin A receptor, inhibiting tumour cell proliferation.

AZD0530 and **AZD0424**, anti-invasives in phase 1 and pre-clinical respectively, are designed to prevent tumours from spreading. **AZD3409** is a prenylation inhibitor in phase 1 designed to inhibit the proliferation of cancer cells. **AZD5438** is a novel selective cyclin dependent kinase inhibitor in phase 1 targeted at proliferating tumour cells. **AZD1152,** an aurora kinase inhibitor designed to target cell division in proliferating tumours, is now in pre-clinical development. **AZD6244**, also in pre-clinical development, is a selective MEK inhibitor targeting proliferating tumour cells.

Performance 2003

Reported performance

Oncology□s reported sales growth was 16% as revenues grew by $374 million from $2,369 million to $2,743 million.

Underlying performance

Oncology sales grew by 8% to $2,743 million with growth from *Casodex*, *Arimidex* and *Iressa* offsetting the decline in *Nolvadex*.

Casodex sales outside the US increased by 23%, driven by good growth in Europe (up 20%) and Japan (up 28%). Growth in Europe and Japan is driven by the expanding use of *Casodex* in early stage disease. In the US (where the market for anti-androgen therapy of advanced prostate cancer is maturing) the underlying demand is broadly unchanged with *Casodex* share of total prescriptions in this market being 83% in December. US sales growth of 18% is principally a reflection of wholesaler destocking in 2002.

Sales of *Arimidex* increased by 47% in the US and by 45% in the rest of the world, including a 61% increase in Japan.

Sales of *Iressa* reached $228 million during the year including sales in Japan of $101 million. *Iressa* sales in the US since launch in May 2003 totalled $102 million. In December, more than 7,300 retail prescriptions were dispensed in the US, bringing the total for the year to over 42,000.

Faslodex sales of $77 million reflect a steady increase in usage for the treatment of advanced breast cancer in the US market.

Underlying sales of *Zoladex* were maintained at $869 million. US sales of *Nolvadex* declined by $296 million to

$41 million following patent expiry in February 2003. Sales of *Nolvadex* elsewhere were $137 million.

Performance 2002

Reported performance

Sales grew by $258 million to $2,369 million in 2002, an increase of 12%.

Underlying performance

Minimal exchange effects meant that underlying sales growth was unchanged from reported performance at 12%.

Sales of *Casodex* outside the US increased by 42% to $464 million in 2002. Prescriptions for *Casodex* grew by some 5% in the US market. The reported sales decline in the US of 23% to $180 million reflected an adverse comparison against wholesaler stockbuilding which occurred at the end of 2001.

Arimidex enhanced its leading position in the aromatase inhibitor market. Monthly prescriptions in the US doubled since December 2001, driving the 127% increase in US sales for the year to $134 million. Sales outside the US increased by 51%.

Sales of *Faslodex* reached $35 million after eight months in the US, representing the most successful US launch of a hormonal agent for breast cancer in the last 20 years.

Sales of *Iressa* for the treatment of inoperable or recurrent NSCLC reached $67 million. *Zoladex* was the leading oncology product with $794 million sales and growth of 12%. US revenues for *Nolvadex* fell 27% to $337 million, as sales of our tamoxifen products fell as a result of the expiry of our distribution agreement with Barr Laboratories.

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Respiratory and Inflammation (R&I)

We aim to build on our leading position in asthma treatment through the growth of key products, particularly *Symbicort*, new indications and market launches and the successful introduction of novel approaches to other areas of inflammatory disease such as chronic obstructive pulmonary disease (COPD) and rheumatoid arthritis.

Therapy area overview

> R&I world market value: over $30 billion.

> The World Health Organisation estimates that 100 million people worldwide suffer from asthma and that COPD is the fourth greatest cause of death globally.

2003 in brief

> Clinical data confirm efficacy and safety of *Symbicort* as an adjustable maintenance treatment for asthma.

> Filing submitted in Europe for *Symbicort* as a single inhaler treatment of asthma.

>

First approval for *Symbicort* for COPD in Europe.

Products

Symbicort (budesonide/formoterol) is an innovative and effective asthma treatment that offers easily adjustable dosing. This will enable doctors to tailor a patient□s treatment of this variable disease with a single inhaler for all situations; for baseline therapy for increasing the dose during worsening attacks as well as for acute situations, thereby achieving greater efficacy than with fixed doses. It is a combination of the inhaled corticosteroid, budesonide, and the fast onset, long-acting bronchodilator, formoterol, in the *Turbuhaler* dry powder inhaler. *Symbicort Turbuhaler* is approved in 85 countries and launched in 62 countries. Encouraging clinical results confirm the efficacy and safety of *Symbicort* as an adjustable maintenance treatment for asthma providing superior asthma control compared to traditional fixed dose treatment. Phase 3 trials in asthma are progressing in the US. In 2003 *Symbicort* became the first fixed combination of inhaled corticosteroid and fast onset, long-acting bronchodilator approved for COPD in Europe.

In November 2003 a regulatory application in Europe was submitted for the new asthma treatment concept *Symbicort* Single inhaler Therapy (SiT), which is a further development of *Symbicort* adjustable maintenance dosing.

Pulmicort (budesonide) is a corticosteroid anti-inflammatory inhalation drug that helps prevent symptoms and improves the control of asthma. *Pulmicort* remains one of the world□s leading asthma medicines and is available in several forms, including the *Turbuhaler* dry powder inhaler, a pressurised metered dose inhaler and the *Respules* suspension for the treatment of children. The START study is a five year global trial and the largest of its kind involving more than 6,000 patients in 31 countries, with the objective of evaluating whether early intervention with inhaled glucocorticosteroids will affect the evolution of newly diagnosed asthma. The first three year clinical results of the study demonstrate the benefits of *Pulmicort* showing high efficacy and a good safety profile in the early treatment of asthma in adults and children preventing serious attacks.

Pulmicort Respules is the first and only nebulised corticosteroid in the US for children as young as 12 months. It has

grown strongly as a result of its beneficial profile and it has strengthened its position as the inhaled corticosteroid of choice for the treatment of children under five with asthma.

Oxis (formoterol) is a beta-agonist asthma therapy with a fast onset and long-acting clinical effect for the relief of asthma symptoms when corticosteroid treatment is not adequate. The RELIEF study, comparing *Oxis* to salbutamol/albuterol for exacerbation and asthma symptom control, was published in November 2003. Encompassing more than 18,000 patients, the study showed that *Oxis* is a more effective reliever therapy and at least as safe as salbutamol/albuterol.

Rhinocort (budesonide) is a nasal steroid treatment for allergic rhinitis (hay fever), perennial rhinitis and nasal polyps. It combines powerful efficacy with rapid onset of action and minimal side effects and is available as a once daily treatment in the *Rhinocort Aqua* pressurised metered dose inhaler and the *Turbuhaler* dry powder inhaler forms.

Accolate (zafirlukast) is an oral leukotriene receptor antagonist for the treatment of asthma available in most markets.

Pipeline

Symbicort phase 3 development is progressing in the US in the pressurised metered dose inhaler for asthma and COPD.

Development of *Symbicort* to further enhance its competitive differentiation in asthma is underway.

Four new compounds have entered pre-clinical development. They are targeted at asthma (**AZD3778**, **AZD2098, AZD1981**) and COPD (**AZD6067**). Compounds currently in clinical development include **AZD8309** and **AZD9056**, each of which have novel mechanisms of action and are targeted at rheumatoid arthritis. **AZD3342**, **AZD0902**, **AZD8309** and **AZD9056** are all in pre-clinical development for COPD. **AZD0902** for rheumatoid arthritis and **AZD9056** and **AZD8955**, for osteoarthritis are also in pre-clinical development.

We have discontinued the development of **AZD7140** and **AZD0275** as a result of their failure to meet the target profile.

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Sales growth is shown in both reported and underlying performance. Reported performance takes into account all the factors (including those which we cannot influence, principally currency exchange rates) that have affected the results of our business. Underlying performance shows sales growth at constant exchange rates (CER) to reflect the volume and price changes of the geographic and therapy areas and individual products by excluding the effects of exchange. A description of the calculation of this measure is set out in the Financial Review on page 31, together with the reasons for its use.

Key product performance

	2003			2002			2001	2003 compared to 2002		2002 compared to 2001	
	Sales $m	Growth underlying $m	Growth due to exchange effects $m	Sales $m	Growth underlying $m	Growth due to exchange effects $m	Sales $m	Growth underlying %	Growth reported %	Growth underlying %	Growth reported %
Pulmicort	968	101	55	812	36	10	766	12	19	5	6
Symbicort	549	180	70	299	206	10	83	61	84	248	260
Rhinocort	364	56	9	299	33	1	265	19	22	13	13
Oxis	120	(14)	14	120	(11)	4	127	(12)		(9)	(6)
Accolate	107	(40)	3	144	2	(1)	143	(28)	(26)	2	1
Other	153	(8)	17	144	(14)	3	155	(6)	6	(9)	(7)
Total	**2,261**	**275**	**168**	**1,818**	**252**	**27**	**1,539**	**15**	**24**	**16**	**18**

Performance 2003

Reported performance

Reported growth for R&I was 24%. Sales increased from $1,818 million to $2,261 million, with *Pulmicort* and *Symbicort* driving the improvement.

Underlying performance

After excluding exchange effects of $168 million, R&I sales grew by 15% during 2003.

Symbicort sales for the full year increased 61% to $549 million, as the product continues to gain share in the rapidly growing market for fixed combination asthma treatments. Launches for the COPD indication as well as promotion of its specific adjustable maintenance dose regimen for asthma treatment, are fuelling this growth.

Pulmicort sales for the full year increased by 12% as a result of growth in the US market (up 41%). *Pulmicort Respules* accounts for most of this growth, with total prescriptions in the US market up 32% for the year.

Rhinocort sales in the US were up 27%, as growth in *Rhinocort Aqua* (58%) continues to more than offset the sales lost from the discontinuation of the *Rhinocort Nasal Inhaler* formulation.The sales growth in the US accounts for almost all of the global increase of 19% in *Rhinocort* sales.

Performance 2002

Reported performance

Reported sales grew by 18% from $1,539 million in 2001 to $1,818 million in 2002.

Underlying performance

After adjusting for the positive benefits of exchange of $27 million, sales increased by 16%.

Symbicort sales for the year were $299 million, an increase of nearly 250%.

Pulmicort Turbuhaler sales globally reflect the declining inhaled bronchial steroid market in the face of growing acceptance of combination products. However, this was more than offset by the 75% growth of *Pulmicort Respules* in the US, enabling *Pulmicort* to achieve a 5% global sales increase for the full year to $812 million.

Rhinocort sales in the US increased by 19% for the year to $211 million, fuelled chiefly by share gains for *Rhinocort Aqua*, which increased revenue by 39%. Sales were flat in the rest of the world resulting in a global 13% increase in the *Rhinocort* franchise sales to $299 million in 2002.

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Infection

Sales growth is shown in both reported and underlying performance. Reported performance takes into account all the factors (including those which we cannot influence, principally currency exchange rates) that have affected the results of our business. Underlying performance shows sales growth at constant exchange rates (CER) to reflect the volume and price changes of the geographic and therapy areas and individual products by excluding the effects of exchange. A description of the calculation of this measure is set out in the Financial Review on page 31, together with the reasons for its use.

We aim to build a franchise in the treatment of infectious diseases by increasing sales of *Merrem* and by exploiting our traditional, structural and genomic-based technologies.

Key product performance

	2003			2002			2001	2003 compared to 2002		2002 compared to 2001	
	Sales $m	Growth underlying $m	Growth due to exchange effects $m	Sales $m	Growth underlying $m	Growth due to exchange effects $m	Sales $m	Growth underlying %	Growth reported %	Growth underlying %	Growth reported %
Merrem	346	46	15	285	59	(1)	227	16	21	26	26
Other	130	(36)	11	155	(17)	1	171	(24)	(17)	(9)	(9)
Total	**476**	**10**	**26**	**440**	**42**	□	**398**	**2**	**8**	**11**	**11**

Therapy area overview

> Infection world market value: $46 billion.

> Infectious diseases cause more than 11 million deaths each year.

> World demand for antibiotics remains high due to escalating resistance and the increased risk of serious infections.

2003 in brief

> Steady underlying growth for *Merrem* in the US (7%) and globally (16%).

> New laboratories opened in Bangalore, India, dedicated to finding a new treatment for tuberculosis.

Products

Merrem/Meronem (meropenem) is an intravenous carbapenem antibiotic for the treatment of serious hospital acquired infections. Clinical studies are in place to support a supplementary new drug application in the US in 2004 aimed at securing an indication for skin and skin structure infections in 2005.

Pipeline

Our R&D facility in Boston, US is progressing a range of projects using traditional, structural and genomic based technologies to deliver innovative antibacterial agents to the infection pipeline.

In June 2003, our new R&D facility opened in Bangalore, India. Work there is dedicated to finding a new treatment for tuberculosis, an infectious disease that is newly diagnosed in approximately two million people every year in India and over eight million people worldwide.

Performance 2003

Reported performance

Sales grew by 8% on a reported basis, rising by $36 million from $440 million to $476 million.

Underlying performance

Sales of *Merrem* grew steadily by a further 16% for the year to $346 million. Growth was largely attributable to sales outside the US, which were up 19% to $283 million. In the US sales grew by 7% to $63 million.

Performance 2002

Reported performance

Infection sales rose from $398 million in 2001 to $440 million in 2002, a reported increase of 11%.

Underlying performance

The underlying performance of 11% growth was driven by sales of *Merrem* which grew by 26% for the full year to $285 million, chiefly on the 31% increase in sales outside the US. In the US sales grew by 9% to $59 million. Other infection products declined by 9%.

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Geographic Review

Sales growth is shown in both reported and underlying performance. Reported performance takes into account all the factors (including those which we cannot influence, principally currency exchange rates) that have affected the results of our business. Underlying performance shows sales growth at constant exchange rates (CER) to reflect the volume and price changes of the geographic and therapy areas and individual products by excluding the effects of exchange. A description of the calculation of this measure is set out in the Financial Review on page 31, together with the reasons for its use.

Geographic sales performance

	2003			2002			2001	2003 compared to 2002		2002 compared to 2001	
	Sales $m	Growth underlying $m	Growth due to exchange effects $m	Sales $m	Growth underlying $m	Growth due to exchange effects $m	Sales $m	Growth underlying %	Growth reported %	Growth underlying %	Growth reported %
US	8,747	(608)	4	9,351	868	□	8,483	(6)	(6)	10	10
Europe	6,709	75	939	5,695	244	213	5,238	2	18	5	9
Japan	1,189	129	83	977	181	(55)	851	14	22	21	15
ROW	2,204	294	92	1,818	215	(47)	1,650	16	21	13	10
Total	**18,849**	**(110)**	**1,118**	**17,841**	**1,508**	**111**	**16,222**	□	**6**	**9**	**10**

North America

US

Sales fell by 6% ($604 million) in 2003 from $9,351 million to $8,747 million following the loss of $2,646 million in sales to generic competition for *Losec/Prilosec*, *Zestril* and *Nolvadex*. The US remains the world□s largest market for pharmaceuticals and US consumers continue to drive demand and reward innovation especially for medicines that prolong, or improve the quality of, life. Our sales in the US of $8.7 billion reflect our commitment to driving growth in this key market. The US represents 46% of our total sales. AstraZeneca is currently the fifth largest pharmaceutical company in the US with our sales representing a 5% share of US prescription pharmaceutical sales. Underpinning our success in the highly competitive US market were the top-tier performances of *Nexium*, *Seroquel* and *Toprol-XL*, with combined sales of $4.5 billion. *Nexium* surpassed the $2 billion sales mark and now holds the position of the fastest growing PPI in terms of total prescriptions in a highly competitive market. Total US sales were $2,477 million for 2003 ($1,525 million for 2002) and total Group sales were $3,302 million for 2003 ($1,978 million for 2002). *Toprol-XL* became the most prescribed anti-hypertensive among cardiologists and *Seroquel* continued to gain share in the atypical anti-psychotic market. Other key growth products, including *Arimidex*, *Pulmicort Respules* and *Rhinocort Aqua*, outperformed the market in both sales and prescriptions. As expected, sales of *Losec/Prilosec* continued to decline as four more generic versions of omeprazole entered the market and Proctor & Gamble launched the first over-the-counter (OTC) version of the brand *Losec/Prilosec* OTC. *Iressa* was launched in May and has become an important medicine in the treatment of non-small cell lung cancer. *Crestor* was launched in September into the intensely competitive

lipid-lowering market and is now already the third largest statin in the US for patients who took statin therapy for the first time or who switched from another statin. We submitted our regulatory package for *Exanta* for chronic indications to the FDA in December 2003.

Our US sales force of 5,700 people is the sixth largest in the US. Investment in technology, strategic realignment and award winning training has significantly increased productivity and customer satisfaction.

During 2003 we entered into an arrangement whereby, from January 2004, a third party will manage the promotion, marketing and distribution of all *Zomig* formulations to provide greater field force coverage in this key market.

In 2003, we settled the investigation into the sales and marketing of *Zoladex* between 1993 and 1996 with the Department of Health & Human Services. This involved the payment of $355 million and, under the terms of the settlement, the Company pleaded guilty to one count of violating the Prescription Drug Marketing Act. In addition, our sales and marketing function and all other relevant employees received additional code of conduct and policy training as part of the Corporate Integrity Agreement with the Office of Inspector General of the US Department of Health & Human Services. Further information is set out on page 104.

Efficiency and effectiveness

In 2003, we undertook and completed a number of projects focused on efficiency and effectiveness.

We restructured our commercial organisation from a therapy area to a brandled structure, adding new business units dedicated to emerging brands and mature

products. We consolidated the number of advertising agencies we use, resulting in substantial cost-savings for the business.

We also established a new External Scientific Affairs function dedicated to enhancing relationships with key opinion leaders, academic and healthcare institutions and importantly, the FDA. Plans are also underway to locate an office close to the FDA to share scientific expertise on areas of common interest to the FDA.

Passage of a Medicare prescription drug benefit

In November 2003, the US Congress passed bipartisan legislation to add a prescription drug benefit to the Medicare programme. This new legislation is the first major change to Medicare in nearly 40 years. The drug benefit programme will take full effect in January 2006 although discount cards will be available in 2004 and 2005. We believe aspects of the law will have a positive incremental impact on patients and the industry in 2004. The final regulations for the law□s implementation in 2006 and market forces will ultimately determine the full effect on our business.

We anticipate that the issue of cross border movement of products into the US and coverage for the uninsured will remain contentious among politicians, the media and special interest groups during 2004. We will continue to provide free and discounted medicines to qualifying patients through our Prescription Partnership Programmes. State Medicaid programmes will continue to be a challenge to the market in the US but innovative partnering opportunities with key states are in development to mitigate downward pressures on reimbursement.

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Geographic Review continued

Canada

In 2003, underlying sales growth in Canada was 14% (reported growth of 25%) with total sales of US$712 million. We rank number three in Canada with a 7% market share. Canada was the first market to launch *Crestor* and it has already achieved 45% of new prescriptions in the private payer market. *Iressa* was also launched in late 2003. *Symbicort* and *Nexium* continued their strong performance as they both built market share. *Atacand* and *Seroquel* continued to enjoy double digit growth with underlying increases of 29% and 42% (reported growth of 44% and 55%) respectively. The oncology group grew 13% due to the continued success of *Casodex* and *Arimidex*. AstraZeneca ranks number one in Canada in oncology with a 21% market share.

Rest of the World

Europe

The market environment in Europe is increasingly challenging with governmental initiatives being taken to cut prices, particularly in Germany, Italy and the Netherlands. Generic substitution in Europe is being encouraged through legislation and in 2003, this has been particularly emphasised in France and the Netherlands. AstraZeneca is ranked fifth in the European pharmaceutical market with a market share of 5%. Sales reached $6.7 billion for the year resulting in an underlying 2% increase in Europe (18% reported growth). Strong sales performance in France (up 9% on an underlying basis and 28% on a reported basis to $1.5 billion) and Spain (up 12% on an underlying basis and 32% on a reported basis to $616 million) offset declining sales in the UK, the Netherlands and Sweden. Our increased focus in central and eastern Europe has resulted in a strong growth (19%) ahead of market growth for 2003.

Our sales growth in Europe was driven particularly by *Nexium* (+55% underlying, +80% reported), *Symbicort* (+53% underlying, +77% reported), *Casodex* (+20% underlying, +40% reported), *Arimidex* (+40% underlying, +63% reported) and *Seroquel* (+40% underlying, +60% reported) which offset the impact of patent expiries, specifically *Losec/Prilosec*, *Plendil* and *Zestril* in the UK, Sweden and the Netherlands. The underlying decrease in sales in Europe of these three products amounted to $390 million of which *Losec/Prilosec* alone accounted for $305 million. This decrease was offset by the

effects of exchange of $210 million and $149 million, respectively.

Crestor has exceeded expectations in most countries where it has been launched. In sales value, *Crestor* is, after seven months, the most successful product launch ever in the UK and the Netherlands. We have also seen strong uptake of market share for total prescriptions, particularly in the Netherlands, Ireland and Finland.

The transformation of our portfolio due to strong contribution of new products and the fast development of central and eastern European markets constitute a solid platform for future growth.

Japan

We continued to be the fastest growing major pharmaceutical company in Japan. AstraZeneca was ranked 14th by sales at the end of 2003. Sales reached $1,189 million, up from $977 million in 2002. A strongly performing product range in oncology including *Arimidex*, *Casodex* and *Iressa*, plus continued strong growth in *Losec/Prilosec* (up 39% on an underlying basis and 50% on a reported basis) drove an underlying 14% sales growth and a reported growth of 22%. After a weak first quarter, *Iressa* sales in Japan grew steadily in 2003. The growth is based on growing experience in Japanese patients and increasing confidence in second line treatment among oncology specialists. We have initiated a number of studies to further investigate the use of *Iressa* in Japan and will continue to work with the Ministry of Health, Labour and Welfare to ensure that *Iressa* is used appropriately in all patients who can be expected to benefit from the drug.

Asia Pacific (excluding Japan)

During 2003 we have achieved continued strong sales growth in the region despite the impact of the SARS outbreak earlier in the year. Sales reached $918 million with an underlying growth rate of 18%. Our continued investment in China, which resulted in above market performance (+37% on both underlying and reported basis), included increased manufacturing and commercial capability. Strong growth also continued in South Korea and India. Across the region the GI portfolio performed strongly. In Australia, *Nexium* sales grew strongly (+229% underlying, +279% reported) and its market share reached 25% in December. *Crestor* and *Iressa* were

successfully launched in a number of markets in Asia Pacific during 2003. This region represents an area of potential continued high growth for the future.

Latin America

The region has during 2003 continued to grow strongly with 17% underlying growth (6% on a reported basis) and sales reaching $515 million. Mexico with 24% underlying growth (12% reported) and Venezuela with 44% underlying growth (15% reported) provided strong sales growth with AstraZeneca being the fastest growing major pharmaceutical company in those countries. In Brazil, Chile, Uruguay and Peru, we grew significantly above market growth.

Crestor was successfully launched in, among others, Mexico, Argentina and Venezuela and it rapidly achieved a 24% volume market share in Mexico six months after its launch.

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Research and Development (R&D)

R&D continues to focus on improving the productivity and efficiency of new drug discovery and development. We are simplifying our processes and continually review our plans and decision-making. We have streamlined portfolio reviews and target our strategic investment on areas directly linked to increased quality and output of new products.

In Discovery, we aim to increase the output of high quality candidate drugs (CDs) with a lower risk of failure in development. In Development, we aim to develop better drugs faster.

During 2003 we significantly increased the number of new Discovery projects, delivered a more consistent flow of good quality CDs, progressed a greater number of products to a robust clinical proof of principle stage and increased the number of drugs reaching human testing.

As described in the Development Pipeline table on pages 24 and 25, we now have 12 projects in phase 2 and 28 projects in phase 3 development.

AstraZeneca employs around 11,600 people in R&D. We have six major joint discovery and development facilities in the UK, the US and Sweden; a further four sites in the US, Canada, India and France which focus only on discovery, and a facility in Japan for development only. These resources are complemented by clinical development at 43 sites around the world. In 2003, our R&D investment totalled $3.5 billion.

R&D remains an integrated, project driven organisation. Our approach is therapy area led with scientific, medical, technical and ethical input and control being provided by large, multi-skilled Discovery and Development organisations. This offers a number of advantages including sharing of best practice in terms of science and technology and efficient use of resources across a multi-site, global organisation.

We remain focused on meeting our objectives of delivering new, medically important and commercially successful products to the market every year.

Discovery

Our Discovery organisation consists of highly skilled scientists working together across boundaries to gain critical mass

efficiencies and exchange of ideas and project opportunities.

Specialised groups in Safety Assessment and Process R&D work across all research areas, starting in Discovery and following projects through to Development and lifecycle management initiatives. Our strategic effort to significantly upgrade the links between clinical medicine and basic science (Discovery-Medicine) is already proving to be valuable to the drug discovery process. Discovery-Medicine helps us gain a better understanding of human diseases and how future drugs will work to prevent and treat those diseases. We also continue to introduce more stringent safety and drug metabolism/pharmacokinetic testing earlier in the process, in order that CDs chosen for development are more likely to succeed.

During 2003, a further 15 CDs were selected (11 in 2002) and, in addition, 10 early development projects reached the stage of human testing (six in 2002).

Our global knowledge exchange system, which serves all Discovery sites maximises the benefits of the latest communication and informatics technologies. Our global Enabling Science and Technology group continues to

support all research areas with skills in compound management, natural product screening, structural chemistry, bio-imaging, genetics, transgenics, protein science and informatics. New enabling technologies for drug searching have been introduced and a global compound collection enhancement project is ongoing.

We continue to invest in R&D facilities in line with our strategy. New or upgraded laboratory facilities were opened in 2003 in Sweden, the UK, the US and India. Recruitment of highly skilled new staff continues alongside the ongoing training and development of existing employees.

Development

Our Development organisation consists of people skilled in clinical research, regulatory affairs and pharmaceutical development. We believe that efficiencies are achieved from global working applied flexibly across the business. Our therapy area led product teams represent a matrix of all relevant functional skills and experience needed for robust, rapid drug development.

Our product focus in 2003 was to complete the development programmes and deliver the regulatory support required for the approval of *Exanta* and approval and launch of *Crestor* and *Iressa*. We also placed high priority on successful delivery of lifecycle management programmes designed to optimise growth of key marketed products including *Nexium*, *Seroquel* and *Symbicort*.

We continue to focus on improving our productivity and speed of product development. Significant e-based clinical and regulatory systems were introduced in 2003 that significantly increase the speed of access to data worldwide and reduce regulatory file preparation and submission timelines. These activities will be continued and extended.

Collaborations

To complement our in-house R&D capabilities, over 200 new collaborations have been entered into in 2003 with leading academic centres and biotechnology companies.

We entered into a collaboration with Abgenix Inc. with the aim of discovering fully humanised monoclonal antibodies for the treatment of cancer. This arrangement is complementary to our major activity in small molecules and will allow us to tackle a broader range of targets. Abgenix will provide antibody expertise and will take projects into clinical trials. We will provide the cancer expertise that will guide the choice of targets, the properties required out of the candidate drugs and clinical development.

Other examples of external collaborations include those with the University of Dundee and the University of Gratz as well as with, among others, Sumitomo Pharmaceuticals Co., Ltd., NeoGenesis Pharmaceuticals, Inc., Cytokinetics, Inc., Biosignal Inc. and Array Biopharma.

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Development Pipeline

Compound	Mechanism	Areas under investigation	Phase				Estimated filing date	
			PC	1	2	3	MAA	NDA
Cardiovascular								
NCEs								
Exanta	thrombin inhibitor	prevention of VTE					Approved*	Filed
Exanta SC formulation	thrombin inhibitor (sc)	prevention of VTE					Approved*	>2006
Galida	PPAR agonist	diabetes /metabolic syndrome					2006	2006
AZD6140	ADP receptor antagonist	arterial thrombosis					>2006	>2006
AZD7009	ARDA	atrial fibrillation					>2006	>2006
AZD9684	CPU inhibitor	thrombosis					>2006	>2006
AZD0837	thrombin inhibitor	thrombosis					>2006	>2006
AZD7806	IBAT inhibitor	dyslipidaemia					>2006	>2006
AZD6610		dyslipidaemia					>2006	>2006
AZD4619		dyslipidaemia					>2006	>2006
AZD0303		thrombosis					>2006	>2006
AZD8294		dyslipidaemia					>2006	>2006
Line Extensions								
Atacand	angiotensin II antagonist	CHF outcomes (CHARM study)					2Q 2004	2Q 2004
		diabetic retinopathy					2006	2006
Crestor	statin	atheroma					2006	2006
		outcomes CHF					>2006	>2006

		outcomes renal		>2006	>2006
Seloken/Toprol-XL	beta blocker	HCTZ combination			1H 2005
Exanta	thrombin inhibitor	prevention of stroke in AF		Filed	Filed
		treatment of VTE		Filed	>2006
		arterial/post MI		>2006	>2006

* France, Reference Member State for the EU Mutual Recognition Procedure.

Gastrointestinal