ASTRAZENECA PLC
Form 6-K
February 25, 2005

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 2005

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-_____

AstraZeneca PLC

INDEX TO EXHIBITS

1. Annual Report and Form 20-F Information 2004.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

AstraZeneca PLC

Date: February 25, 2005

By: /s/ A C N Kemp

Name: A C N Kemp
Title: Assistant Secretary

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The Year in Brief

- Group sales up 9% at constant exchange rates to $21.4 billion strong sales performance from key growth products (up 30% to $11.2 billion)
- Operating profit up 15% at constant exchange rates to $4.8 billion EPS pre-exceptional items up 18%
- Dividend increased by 18% to $0.94 for the full year
- *Nexium* sales reached $3.9 billion, up 15%
- *Seroquel* sales increased by 33% to just over $2 billion
- *Symbicort* sales totalled $797 million, up 32%
- Expanded use of *Arimidex* in the treatment of early stage breast cancer underpinned 48% increase in sales to $811 million
- *Crestor* sales totalled $908 million despite challenging environment. Sales impacted by allegations regarding the product s safety. Clinical trials experience and post-marketing surveillance continue to support our belief that the safety profile is in line with other marketed statins
- FDA decision not to approve *Exanta*. In the EU, where *Exanta* already marketed for acute indications, more data have been requested before approval of use in chronic indication can be considered
- Results of ISEL clinical study for *Iressa* showed no statistically significant increase in survival of overall population. Data suggest survival benefits in patient populations of East Asian origin and non-smokers
- R&D investment totalled $3.8 billion. 40% more projects in clinical development (phases 1 and 2) than in 2003. 31 projects in pre-clinical testing (26 in 2003)
- Important strategic alliance with Cambridge Antibody Technology to discover and develop human antibody therapeutics in inflammatory disorders
- Global clinical trials website on track for launch in the first quarter of 2005. This will provide a detailed, publicly available, scientific, non-promotional summary of clinical trials conducted for products approved since AstraZeneca was formed in 1999
- Appointment of Executive Director for Development as part of accelerated significant programme of change to optimise the contribution of our development and regulatory functions

Continuing Operations before Exceptional Items

			% growth
	2004	2003	CER

Sales $m	**21,426**	18,849	+9
Operating profit $m	**4,770**	4,111	+15
Earnings per share $	**2.11**	1.78	+18
Group earnings per share $ (statutory FRS 3)	**2.28**	1.78	+27

Dividend for 2004

	$	Pence	SEK	Payment date
First interim dividend	0.295	16.0	2.200	20 September 2004
Second interim dividend	0.645	34.3	4.497	21 March 2005
Total dividend	**0.940**	**50.3**	**6.697**	

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Chairman s Statement

Leading the Board during AstraZeneca s formative years has been an exciting journey.

2004 was a year of both performance and challenge for AstraZeneca and the pharmaceutical industry in general. Worldwide demand for modern medicines continued to grow, driven by the availability of innovative new medicines, demographics and emerging market opportunities. At the same time, these global drivers are being offset by increased pricing pressure, escalating costs in the development and commercialisation of medicine, and a generally more risk-averse environment as regulators seek to strike an appropriate balance in weighing the risks and benefits of innovation.

For AstraZeneca, the year was characterised not only by good sales growth, productivity gains and continued investment in innovation but also by the disappointments of the US FDA decision not to approve our novel anti-clotting agent, *Exanta*, the failure to demonstrate an overall survival benefit for the lung cancer product, *Iressa*, and what we consider to be unfounded speculation about the safety of our during the year with the divestment of its joint venture interest in the seed company, Advanta BV. Of all the major pharmaceutical companies, AstraZeneca is probably the most focused on prescription medicines, our only other businesses being Astra Tech, the medical device company, and Salick Health Care, which delivers services to cancer care centres.

In such a rapidly changing environment, the Board has been monitoring developments carefully to ensure the appropriateness of our corporate strategy. Particular attention has been paid to the regulatory progress and sales performance of our newer products, the overall composition of our product portfolio and the various productivity initiatives that have been pursued. Success in Research and Development is essential to our strategy and it is good to see the emergence of an impressive early development portfolio with 40% more projects in phase 2 clinical trials than this time last year. We also have more new development candidates emerging from Discovery than ever before. As well as new investments in R&D facilities in Sweden, the UK and bodies. In preparation for the adoption of new international accounting standards in 2005, AstraZeneca was the first FTSE 100 company to make available to shareholders financial information for 2003 and the first half of 2004 prepared in accordance with the new standards.

AstraZeneca s share price performance, and that of other major pharmaceutical companies, were disappointing in 2004 with the AstraZeneca share price in particular affected by the FDA s non-approval of *Exanta*, the challenges facing *Crestor* and the recent clinical trial results for *Iressa*.

The composition of the Board is also undergoing some change. On my retirement at the end of the year, the Board confirmed the appointment of Louis Schweitzer as my successor as Non-Executive Chairman of AstraZeneca with effect from 1 January 2005, following his appointment to the Board in March 2004. Louis Schweitzer is a distinguished industrialist with wide international experience and I congratulate him most warmly on his appointment.

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

lipid-lowering medicine, *Crestor*.

Growth came from our broad range of products, especially the newer products which are largely free of threat from patent expiry. In addition to strong performances from the established markets, good progress continued to be made in emerging markets such as China and Mexico. Since 2001, we have recruited an additional 2,500 staff to strengthen our presence in emerging markets and AstraZeneca is now one of the fastest growing major pharmaceutical companies in the world s top eight emerging markets: China, Mexico, Brazil, South Korea, India, Poland, Turkey and Taiwan.

AstraZeneca further emphasised its strategic focus on prescription pharmaceuticals

the US, we announced a £75 million equity investment and R&D collaboration with Cambridge Antibody Technology to discover and develop human antibody therapeutics. This strategic alliance complements last year s oncology alliance with Abgenix Inc. and brings to over 1,700 the number of active R&D collaborations and agreements we now have in place.

The Board has also reviewed its corporate governance including individual Directors performance. A great deal of effort has gone into preparing and implementing the numerous changes required to comply with the increasing demands from external

Karl von der Heyden, the Chairman of the Audit Committee, retired at the 2004 AGM after more than five years as a Non-Executive Director. I thank him for his contribution to the Company and, in particular, the role he played in the development of the work of the Audit Committee. John Buchanan succeeded Karl as Chairman of the Audit Committee. Most recently, the Board announced the appointment of Dr John Patterson, with effect from 1 January 2005, to the Board as Executive Director responsible for Development, emphasising the importance we place on this activity.

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I look forward to playing my part in ensuring AstraZeneca s future success.

My six year engagement with AstraZeneca, from the announcement of the proposed merger in December 1998 to my departure as Chairman at the end of 2004, has been an exciting journey. This includes the fast merger with delivery of promised synergies and, not least, the creation of a cross-border, unified culture. The growth of new products and penetration of developing markets helped bridge the inevitable gap caused by patent expirations of mature products. In spite of recent setbacks in product launches, we have a strong product pipeline underpinning further growth ambitions.

I want to thank my Board colleagues for their valuable support and the Company management, spearheaded by Sir Tom McKillop, for their excellent achievements over these years. I also want to thank all employees and wish them and this fine company every success in the future.

Percy Barnevik

I am grateful to the AstraZeneca Board for the confidence they have shown in me by electing me as their Chairman. Percy Barnevik as the first Chairman of AstraZeneca has served the Company with distinction. On behalf of the Board, shareholders and AstraZeneca employees, I would like to thank him most warmly for his wise counsel, influence and leadership of the Board.

Since my appointment to the Board in March 2004, I have had the opportunity to get to know my Board colleagues, to meet senior managers in the Company and to get a clear view of the Company s strong financial performance as well as the strategic opportunities and significant challenges facing AstraZeneca. I have been most impressed with what I have seen of the senior management of the Company led by Sir Tom McKillop. I very much look forward to working closely with him and my Board colleagues and playing my part in ensuring the Company s future.

Following the Company s strong financial performance in 2004, the Board has recommended a second interim dividend of $0.645, 34.3 pence, SEK4.497 per Ordinary Share bringing the total dividend for the year to $0.94, 50.3 pence, SEK6.697 per Ordinary Share, an increase in dollar terms of 18.2%.

In 2005, we aim to deliver strong financial performance, characterised by top-tier earnings growth and improved shareholder returns, while continuing to build an innovative and valuable pipeline capable of driving shareholder value over the long term.

Louis Schweitzer

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Chief Executive s Review

I am confident in the future prospects for AstraZeneca, despite the recent disappointments.

At the start of 2004, the year seemed full of opportunity: AstraZeneca was moving into a new and exciting phase. The excellent foundations created by a successful merger and the subsequent transformation of an ageing product portfolio had set us up for strong growth from our key products. The growth portfolio, including products that were on the range before the merger, such as *Seroquel* and *Arimidex*, and newly introduced products, such as *Nexium*, *Crestor*, *Symbicort* and *Iressa*, provided an excellent opportunity to deliver value to physicians, patients and shareholders alike.

While we made good progress in this respect, building on the success of our gastroenterology, cardiovascular, respiratory, neuroscience and oncology franchises, we also experienced disappointments with *Exanta* and *Iressa* and some difficult market conditions with *Crestor*.

Nexium (2004 sales $3.9 billion) is now recognised as one of the most successful products in our industry and it has continued to grow, both in the important US market and worldwide, despite an increasingly competitive environment. During the year, we added *Nexium Intravenous* to the product range and the recent, well-publicised problems with the new class of anti-inflammatory drugs, such as Vioxx, offers further opportunities for *Nexium,* which is approved for the prevention of the gastrointestinal side effects associated with such anti-inflammatory drugs.

Seroquel ($2.0 billion) continues to grow strongly and is increasingly recognised by patients and doctors for its outstanding safety and efficacy profile. During 2004, *Seroquel* became the leading atypical anti-psychotic therapy in the US market based on monthly new prescriptions and made strong progress in other markets. Important new opportunities to extend the use of *Seroquel* also emerged with the exciting results from clinical studies in the treatment of bipolar depression and the management of agitation in the elderly.

The Company s leading range of anti-hormonal cancer therapies continued to make a major contribution to the business and there is considerable scope for further growth. In particular, positive five-year data from the landmark ATAC study have established *Arimidex* as the agent of choice in the adjuvant treatment of breast cancer replacing *Nolvadex* (tamoxifen) as the new gold standard for treatment.

Sales of *Iressa* ($389 million) grew well in those markets where it is available and, early in the year, exciting science emerged indicating that certain patients with non-small cell lung cancer (NSCLC) carried genetic mutations that appeared to make them particularly sensitive to the beneficial effects of the drug. Disappointingly however, the ISEL study, designed to study the effect of these patients. While sales will continue in all markets where the drug is currently approved, the Company has chosen to suspend promotion in the US until the implications of the ISEL results have been discussed with the regulatory authorities. The application for marketing approval of *Iressa* in the EU has been withdrawn but we will continue to work with opinion leaders and regulators to determine the most appropriate next steps for this innovative medicine. We are also determined to benefit from this experience with *Iressa* and apply the learning to the other exciting novel cancer therapies we have in development.

2004 also proved to be a challenging year for two key products in our cardiovascular range.

Crestor, our new lipid-lowering drug, first launched in 2003, has now been approved in 67 countries (launched in 56) and achieved sales of $908 million in 2004. Its ability to control lipid disorders more effectively than any other available statin has been well recognised by prescribers but, during the year, the product was the subject of speculation that questioned its safety profile. Patient safety is the highest priority for AstraZeneca and the Company has worked diligently and transparently to monitor, communicate and mitigate any risk associated with the use of *Crestor*. We remain confident that the clear benefits of *Crestor* are achieved with a

Iressa compared to placebo on survival in refractory NSCLC, failed to meet its primary endpoint of survival in the overall population, although there were statistically significant differences in survival in favour of *Iressa* in patients of East Asian origin and non-smokers. In the East Asian subgroup there was a near doubling of median survival which is consistent with the positive benefit/risk ratio seen in previous studies in

safety profile in line with that of other marketed members of the class. Our confidence derives from an extensive database involving over 40,000 patients in clinical trials and post-marketing surveillance of more than 15 million prescriptions written and four million patients treated with *Crestor*.

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Exanta, AstraZeneca s innovative oral therapy for the treatment of diseases associated with blood clots, was launched in its first markets in 2004 for the prevention of blood clots following orthopaedic surgery. *Exanta* is the first oral anti-coagulant to be developed for more than 60 years, and its greatest potential is in the chronic prevention of strokes and other events related to blood clots in patients at high risk as a result of the common heart rhythm disorder, atrial fibrillation. During a development programme that involved more than 30,000 patients, we established that the drug had the potential to be an effective alternative to the only existing therapy in this area (warfarin) but also discovered that *Exanta* had an undesirable impact on the livers of a small percentage of treated patients. Following a review at a public Advisory Committee hearing in Washington in September 2004, the US FDA decided that AstraZeneca had not established a favourable benefit/risk profile for the drug and did not approve it for use in the US market. In Europe, *Exanta* is already marketed in many countries for the prevention of clots after orthopaedic surgery, but more clinical data will be required before approval for long term use can be considered.

Despite these setbacks, we remain committed to building our future on science and innovation and believe AstraZeneca has the capacity to succeed in an increasingly competitive healthcare market. We are determined to apply the learning from these recent experiences and ensure that we better manage the risks inherent in this strategy to deliver an innovative and valuable pipeline that will sustain the Company over the long term whilst allowing us to return value to our shareholders in the short term.

The appointment of John Patterson to the Board as Executive Director responsible for Development reflects the importance we attach to our ability to convert science into sales. John has immense experience in drug development and will be working to optimise our capabilities in this critical area.

The Company has, since its creation, placed great emphasis on productivity and this will continue, indeed accelerate, to ensure we are at the forefront of our industry as it goes through a period of considerable change.

The problems encountered in 2004 with *Iressa*, *Crestor* and *Exanta* are, themselves, illustrative of issues that are faced by all who are committed to innovation as a source of progress, the enhancement of quality of life and the creation of value. Innovation, in any field, is associated with risk but in healthcare, in particular, where unmet needs in the developed and developing worlds continue to increase, the innovator s contract with society needs to reflect an appropriate balance of benefit to risk.

I would like to express the Company s condolences to all those affected by the tsunami disaster. I am sad to report that, to date, three of our employees are still missing. Our deepest sympathies go to their families and friends. The Company immediately contributed $600,000 in cash, made our drugs available where appropriate and has created a fund of $1.5 million to help with reconstruction projects being implemented through our local companies in the affected areas.

Finally, I once again thank my colleagues on the Executive Team for their continuing commitment and support throughout the year and also our employees around the world. Their contribution, their skills and their abilities are the building blocks of our future.

Sir Tom McKillop

Chief Executive

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Global Market Overview

World markets

In 2004, the world market for pharmaceuticals, as defined by the 46 countries audited by IMS, was valued at $492 billion. Growth for the total market remained at 8% (the same level for 2003) in constant US dollars terms, despite lower growth (9% as compared to 10%) in the US, which accounts for approximately 47% of world sales. The US, Europe and Japan together represent 88% of the world market.

Over the past five years, the US has increased its share of the world market by 3%, in contrast to Europe, where market share has been static at 29%, and Japan, where market share has declined from 15% to 12%. This changing pattern reflects differences in the respective healthcare systems approaches to drug use and pricing: the US allows free pricing and tends to adopt innovative products more rapidly compared to Europe and Japan which both enforce price control measures.

Several countries experienced above average growth in 2004. In Europe, Turkey (30%), Greece (19%), Ireland (16%), Spain (10%), and Portugal (10%) outgrew the world market. In Asia, China showed continued strong growth in absolute and percentage terms, reaching $7.2 billion (the ninth largest worldwide market), an increase of 26%. China s growth along with that of Thailand (16%), Egypt (15%), the Philippines (14%) and Taiwan (12%) show the potential of the region for future sales. In Latin America, Mexico, the tenth largest worldwide market, and Venezuela delivered growth of 10% and 24%, respectively. However, despite good growth in 2004 of 28% and 19%, respectively, Brazil and Argentina remain below their 1999 sales levels.

Pharmaceuticals as part of healthcare

Expenditure on healthcare typically represents between 6% and 15% of a country's gross domestic product (GDP), with developed nations towards the top end and developing nations spending less. As a proportion of this, pharmaceutical expenditure is usually between 10% and 20% and is therefore still less than 2% of GDP in most cases. Pharmaceuticals offer many advantages over other forms of treatment for illness and they are often particularly cost-effective when compared to in-patient care.

Doctors remain the key decision makers as to which treatments should be prescribed for their patients, but as the economic burden of funding therapies increases, payers, including governments, health insurers, managed care organisations, employers and patients, are increasing their influence over the choices doctors make. Pharmaceutical companies are increasingly having to demonstrate the value of their products in terms of health and economic outcomes to a wide variety of customer groups including payers, patients, physicians, regulators and governments. This requires investment throughout the clinical and commercial development of a product, in studies covering cost-effectiveness, cost-benefit and post-approval outcomes in addition to traditional trials designed to prove safety and efficacy.

Growth drivers and limiters

The continued growth of the pharmaceutical industry indicates that the market for the industry is not mature. There is a strong fundamental demand for healthcare that underwrites the industry s future growth prospects. Specific elements that contribute to this include:

- The growing number of people who expect high standards of healthcare, especially among the elderly, who represent a rising proportion of developed nations populations.
- Many diseases are under diagnosed, sub-optimally treated or do not have effective therapies.

This growing demand will be met not only by existing therapies but also by new ones originating from the advances in the understanding of the biology of disease and the application of new technologies. Innovative new products have been launched in recent years, which are changing therapeutic approaches and are improving quality of life for patients.

Healthcare systems, whether based on public or private funding, have a finite ability to pay for treatments. Cost containment remains an ever-present restraint to growth. During 2004, this has become even more evident with increasing pricing pressures across all major markets, notably the US and Germany. This is felt most within large primary care categories.

Future pharmaceuticals market

Whilst the fundamentals of the world pharmaceuticals market remain robust, the industry is facing real challenges.

Heightened public awareness of drug safety concerns rather than a balanced perspective of benefit/risk, coupled with worries over the cost of medicines, has undermined the reputation of the industry.

Regulators are setting increasingly high hurdles as the industry is working to improve R&D productivity through application of new technologies.

The industry s intellectual property base is being challenged by generic manufacturers looking to make an early entry into large markets with resultant pressure on life cycles.

Successful companies will be required to enhance their productivity in the discovery and development of new products designed to meet the burgeoning needs of the market.

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Financial Highlights

Key growth 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 2004

Percy Barnevik*
Non-Executive Chairman

Håkan Mogren
Non-Executive Deputy Chairman

Louis Schweitzer
Non-Executive Director**

Dame Bridget Ogilvie
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

Jane Henney
Non-Executive Director

Michele Hooper
Non-Executive Director

Joe Jimenez
Non-Executive Director

* Retired from the Board on 31 December 2004
** Appointed Non-Executive Chairman with effect from 1 January 2005

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Percy Barnevik (63)
Non-Executive Chairman
Chairman of the Nomination Committee

Appointed as a Director 6 April 1999. Retired from the Board on 31 December 2004. 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 the International Advisory Council of the Federation of Korean Industries and the Investment Council advising the South African Government. Member of the Business Council of American CEOs. Member of the Advisory Board of the Centre for European Reform, UK.

Håkan Mogren (60)
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 SA, Groupe Danone and Norsk Hydro ASA. Director of the Marianne and Marcus Wallenberg Foundation.

Louis Schweitzer (62)
Non-Executive Director

Appointed as a Director 11 March 2004. Appointed Non-Executive Chairman and Chairman of the Nomination Committee with effect from 1 January 2005. Chairman and Chief Executive Officer of Renault SA since May 1992. President of the Management Board of Renault-Nissan BV since March 2002. Chief Financial Officer and Executive Vice-President 1988-1992 and President and Chief Operating Officer 1990-1992, Renault SA. Non-Executive Director of BNP-Paribas, Electricité de France, Philips Electronics NV, Veolia Environnement and Volvo AB.

Dame Bridget Ogilvie (66)
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. 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.

Sir Tom McKillop (61)
Executive Director and Chief Executive

Appointed as a Director 1 January 1996. Non-Executive Director of BP p.l.c. and (until 31 December 2004) Lloyds TSB Group plc. Vice-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 Northwest Science Council.

Sir Peter Bonfield CBE, FREng (60)
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 the Citigroup International Advisory Board. Member of the Sony Corporation Advisory Board. Non-Executive Director, Corporate Board of the Department for Constitutional Affairs.

Marcus Wallenberg (48)
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.

John Buchanan (61)
Non-Executive Director
Chairman of the Audit Committee and Member of 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 (64)
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.

Jonathan Symonds (45)
Executive Director and Chief Financial
Officer

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

Jane Henney (57)
Non-Executive Director
Member of the Audit Committee, the
Nomination Committee and the Science
Committee

Appointed as a Director 24 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 and CIGNA Corporation. Member of the Board of Trustees of the Commonwealth Fund and the China Medical Board.

Michele Hooper (53)
Non-Executive Director
Member of the Audit Committee

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.

Joe Jimenez (45)
Non-Executive Director
Member of the Remuneration
Committee and 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 Blue Nile, Inc.

Other officers of the Company at 31 December 2004 included members of the Senior Executive Team, as set out on page 54, and:

Graeme Musker
Group Secretary and Solicitor
Appointed as Company Secretary 6 June 1993.

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Strategy

AstraZeneca aims to create enduring value for society and shareholders, by discovering, developing, manufacturing and marketing differentiated medicines that make a real contribution to human health. Our culture is based on innovation, a responsible way of doing business and performance.

In response to an environment that is becoming even more challenging, we aspire to deliver a level of productivity that matches the best among our peers. We are committed to delivering sustained financial performance, through growth and productivity, that will place AstraZeneca among the best in the industry.

This strategy for sustainable, profitable growth is supported by the following core business priorities, paying heed to the setbacks experienced in 2004:

Sales growth

> Release of the full potential of our marketed therapies through resource allocation and 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

Step-change in productivity

> Commitment to vigorously improve productivity in pursuit of operational excellence in all our activities, to be among the most efficient and effective companies in our sector.

> Developing new business approaches that will meet the changing needs and expectations of regulators, payers, prescribers and patients.

Strong pipeline and active risk management

> Successful delivery to market of the next wave of differentiated products currently in development.

> Rigorous management of our portfolio of products in development, to mitigate risks associated with new innovative products and make future growth more robust.

> Expansion of the development pipeline through continuously improved in-house discovery processes, complemented by external collaborations and partnerships.

> Pursuit of value-creating investment in significant targeted licensing and acquisition opportunities.

Corporate responsibility

> Delivery of our core values through a responsible approach to business.

People

> Delivery of optimised performance and sustainable business outcomes through:

- Improved organisational effectiveness.
- Optimised individual and team performance.
- Effective management and development of talent.
- Improved leadership capability.

Key Products

Cardiovascular

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

Crestor[2] (rosuvastatin calcium) 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 succinate) beta blocker for hypertension, angina, heart failure and other uses

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

Gastrointestinal

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

Nexium (esomeprazole magnesium) proton pump inhibitor for acid-related diseases

Oncology

Arimidex (anastrozole) aromatase inhibitor for breast cancer

Casodex (bicalutamide) anti-androgen for prostate cancer

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 citrate) anti-oestrogen for breast cancer

Zoladex (goserelin acetate) 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

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 fumarate) atypical anti-psychotic for schizophrenia and other psychotic disorders

Infection

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

Rhinocort (budesonide) topical nasal anti-inflammatory for control of rhinitis	*Xylocaine* (lidocaine) local anaesthetic for use in surgery and dentistry	
Symbicort (budesonide/formoterol) inhaled combination of anti-inflammatory and fast onset long-acting bronchodilator in a single inhaler	*Zomig* (zolmitriptan) for the treatment of acute migraine with or without aura	

[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 World Health Organization (www.WHO.int), the greatest burden of disease is in the non-communicable disease sector with diseases such as malignant neoplasms, ischaemic heart disease, cerebrovascular disease, chronic obstructive pulmonary disease, schizophrenia, bipolar disorder and asthma being significant contributors. 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 broad 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 11 to 36) provides detailed information about our research, development, manufacturing and marketing activities worldwide and our performance in 2004.

AstraZeneca in brief

> We spend around $15 million each working day on research and development (total R&D spend in 2004: $3.8 billion)

> We employ 11,900 people in research and development at 11 R&D centres in seven countries: Sweden, the UK, the US, Canada, France, India and Japan

> We focus on continued innovation and maintaining a flow of new medicines that meet patients needs

> We have 17 projects in phase 1, 17 projects in phase 2 and 25 projects in phase 3 development, as described on page 30

> 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 30 manufacturing sites in 20 countries

> Around 15,000 people worldwide work in supply and manufacturing, including around 12,400 people in formulation and packaging, and 1,600 in active pharmaceutical ingredient supply

> We have over 64,000 employees worldwide:

37,000 in Europe

18,000 in the Americas

9,000 in Asia, Africa and Australasia

> Our products are available 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 and heart failure, dyslipidaemia, thrombosis and type 2 diabetes.

Therapy area overview

> CV world market value: $116 billion the single largest therapy area in the global healthcare market.

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

> The statin market has a world market value of $26 billion.

2004 in brief

> *Crestor* now approved in 67 markets and launched in 56.

> *Crestor* world sales $908 million with over four million patients treated and more than 15 million prescriptions written. Clinical trials experience and post-marketing surveillance continue to support our belief that *Crestor* has a safety profile in line with other marketed statins.

> *Seloken*/*Toprol-XL* sales again exceeded $1 billion.

> First launches for *Exanta* in orthopaedic surgery in 10 countries and approvals in 17.

> The FDA did not approve *Exanta* for marketing in the US. More data required before approval for long term use in the EU can be considered.

> Approval for *Atacand* for the heart failure indication in the EU and approvable letter in the US.

Products

Crestor (rosuvastatin calcium) is a member of the class of products known as statins. Further regulatory approvals of *Crestor* in 2004 mean it has now been approved in 67 countries (most recently, Japan) and launched in 56, including the US, Canada and the majority of the EU countries.

High cholesterol is now recognised as a major health issue. Of those people currently being treated for high cholesterol, only about half reach their cholesterol goal on existing treatments, while the other half have cholesterol levels that remain unhealthy. More effective treatments continue to be required in this area.

In multiple clinical studies, *Crestor* has been shown to be more effective in lowering low density lipoprotein or bad cholesterol (LDL-C) than other prescribed statins, enabling more patients to reach their LDL-C goals. Additionally, *Crestor* produces an increase in high density lipoprotein or good cholesterol (HDL-C), an effect that is maintained across the 5-40mg dose range.

During 2004, Public Citizen, a US consumer interest organisation, continued to raise allegations concerning the safety of *Crestor* and filed a Citizen s Petition to ask the FDA to withdraw *Crestor* from the US market. In November 2004, public comments by Dr David Graham, an FDA employee, also alleged safety concerns about the drug. An extensive database has been built up of pre- and post-approval clinical trials experience involving more than 40,000 patients and post-marketing surveillance of more than 15 million prescriptions written and four million patients treated with *Crestor* since its launch in 2003. Based on all these data, we continue to believe that *Crestor* has a safety profile in line with other marketed statins. In September 2004, we launched a publicly available website, rosuvastatininformation.com, where clinical trial and post-marketing data are published in the interests of transparency.

The concerns that the safety allegations created in the minds of patients and physicians had an impact upon the sales performance of *Crestor*, particularly in the US. Sales in the rest of the world were also affected by these allegations but to a lesser extent and performance in these markets has been largely in line with expectations. A key priority for 2005 is to restore growth in the US market share for

Crestor. In the US, we are seeing some switches from *Crestor* to the fixed dose combination of simvastatin and ezetimibe. However, the majority of switches (circa 70%) to that drug from statins have come from atorvastatin or simvastatin (as at 24 December 2004) with only circa 10% of those switches coming from *Crestor* (source: Verispan). In the rest of the world, it is still too early to assess the impact.

Our extensive, long term global clinical research initiative known as the GALAXY programme, including studies that investigate cardiovascular risk reduction and patient outcomes with *Crestor*, is now well underway. Over 40,000 patients are involved. Studies are ongoing in important medical areas, including regression of atherosclerosis and in evaluating the reduction in mortality in heart failure and end-stage renal disease. Further clinical studies in high-risk populations have been reported during 2004, showing consistent beneficial lipid effects. In addition, initial results from the first study in the large ongoing pharmacoepidemiology programme, involving over 50,000 patients, are expected to be available in the first half of 2005.

In December 2004, the Pharmaceutical Affairs Council of the Japanese Health Ministry granted conditional approval of *Crestor* at a 2.5-20mg dose range. The condition to be satisfied requires a Post Marketing Surveillance programme to be carried out in a hospital environment prior to a full-scale launch. Whilst the scope and duration of this programme is yet to be agreed, it is unlikely that significant sales of *Crestor* will be made in Japan in 2005.

Following the introduction of a new medicine, the evolving experience of the drug by use in regular clinical practice and further clinical studies being completed, the initial label is updated accordingly. During the year, label changes in the EU regarding dosing of *Crestor* were introduced in order to reinforce proper use of the product. These changes included an emphasis on the starting dose and how to handle patients at risk of class-related side effects. During the year, an application for introduction of a 5mg dose

form in the EU was submitted. The European Regulatory Authorities have set up an arbitration process to agree what may be the most appropriate wording on the label for the 5mg dose. AstraZeneca is closely involved in these discussions. 97% of worldwide sales

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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 38, together with the reasons for its use.

Key product performance

	2004			2003			2002	2004 compared to 2003		2003 compared to 2002	
	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	1,387	78	29	1,280	340	39	901	6	8	38	42
Crestor	908	753	26	129	122	7		n/m	n/m	n/m	n/m
Atacand	879	75	54	750	121	60	569	10	17	21	32
Plendil	455	(104)	19	540	25	26	489	(20)	(16)	5	10
Zestril	440	(71)	33	478	(446)	47	877	(15)	(8)	(50)	(45)
Tenormin	368		26	342	(53)	25	370		8	(15)	(8)
Other	340	(78)	27	391	(17)	45	363	(20)	(13)	(4)	8
Total	**4,777**	**653**	**214**	**3,910**	**92**	**249**	**3,569**	**17**	**22**	**3**	**10**

by volume were at doses of 20mg or less.

Exanta (ximelagatran) is a novel oral direct thrombin inhibitor targeted to prevent and treat the formation of blood clots (thrombosis). A large clinical development programme, involving around 30,000 patients, provided data to support the regulatory filings for *Exanta*, including data regarding fixed oral dosing, rapid onset of action, low potential for drug/food and drug/drug interactions and no need for routine blood coagulation monitoring. *Exanta* was approved for its short term indication by the EU Mutual Recognition Procedure in May fibrillation file to be progressed further. As part of its review process, the FDA held a public Advisory Committee hearing in Washington in September 2004. Following that hearing and its own review of the data, the FDA decided in October 2004 that AstraZeneca had not established a positive benefit/risk profile for *Exanta*. This was due to safety concerns regarding liver toxicity and cardiac events and also the FDA s doubts as to whether the clinical trial design and data were adequate to demonstrate the efficacy of the drug. The FDA did and Renal Drugs Advisory Committee will review the proposed chronic heart failure indication for *Atacand* at its meeting on 24 February 2005. The clinical programme investigating the effect of *Atacand* on retinopathy in diabetic patients (DIRECT) continued during 2004.

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

2004 for the prevention of venous thromboembolism (VTE) in patients undergoing elective hip or knee replacement surgery in 17 countries and subsequently launched in 10. The regulatory review in Europe (with France as the Reference Member State) for use of *Exanta* in the chronic indications (prevention of stroke in patients with atrial fibrillation and treatment of VTE) is ongoing and regulatory submissions have also been made in other parts of the world.

In January 2005, the French Regulatory Authority (AFSSAPS) requested more information before the drug can be considered for approval of long term use for Europe. AFSSAPS has requested further clinical information confirming the efficacy and demonstrating the safety of *Exanta* in atrial fibrillation to allow a definitive benefit/risk assessment to be made while, for VTE treatment, the authority does not believe the data presented in the single THRIVE Treatment study provide adequate support for this use of *Exanta* and is proposing to reject this indication. AstraZeneca will now have discussions with AFSSAPS to examine what additional data need to be generated for the atrial not approve *Exanta* for any of the indications sought (the prevention of stroke in patients with atrial fibrillation, prevention of VTE in patients undergoing knee-replacement surgery, or the long term secondary prevention of VTE following standard treatment of a clot). Discussions are ongoing with the FDA to determine if there is now a realistic prospect of bringing *Exanta* to the US market. (See Financial Review for financial impacts.)

Atacand (candesartan cilexetil) is an angiotensin II antagonist for the first line treatment of hypertension. The *Atacand* family of products has been well accepted in the market and competes in the fastest growing sector of the global hypertension market (angiotensin II antagonists plain and combinations with diuretic). During 2004, regulatory filings for the heart failure indication were submitted in the EU and the US, based on the CHARM programme, a comprehensive clinical study programme in heart failure, showing significant reduction in cardiovascular mortality and hospitalisation for heart failure in patients treated with *Atacand*. The heart failure indication was approved in the EU in November 2004 and an approvable letter was received from the FDA in the US in December 2004. The FDA Cardiovascular with diuretic) class. Patent litigation is progressing in the US against three companies that are challenging AstraZeneca s patents and seeking FDA approval to sell generic metoprolol succinate. Further information about this litigation is set out on page 115.

Plendil (felodipine) is a calcium antagonist for the treatment of hypertension and angina. Information regarding patent challenges for *Plendil* is set out on page 114.

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

Pipeline

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

Galida is in phase 3 development and is a PPAR agonist with effects on both the alpha and gamma receptors, thereby offering potential benefits in treating insulin resistance and lipid abnormalities associated with type 2 diabetes and

metabolic syndrome. Stimulation of both the alpha and gamma receptors could also potentially be associated with adverse effects and the clinical studies are being carefully monitored, since the balance of dose dependent benefits and risks will form the basis for final recommendations for the product.

During 2004, the FDA and other regulatory authorities reviewed all development products in this class of drugs and the FDA has required that carcinogenicity studies be completed before initiation of clinical studies lasting more than six months. *Galida* has completed these carcinogenicity studies. The FDA has further required that two year clinical studies be completed for the New Drug Application and these are now underway for *Galida*. The estimated date for regulatory filings is now in 2007.

Our further research in thrombosis includes **AZD6140**, an oral anti-platelet therapy which is in phase 2. **AZD0837** (thrombosis) and **AZD9684** (a carboxy peptidase-U inhibitor for thrombosis) are in phase 2. Novel research in atrial fibrillation includes **AZD7009**, a new anti-arrhythmic in phase 2 that works predominantly on the atria to restore and maintain normal heart rhythm (sinus rhythm) in patients with atrial fibrillation. **AZD7806**, **AZD4619** and **AZD6610** (in the dyslipidaemia area) are in phase 1. **AZD8294**, **AZD8677**, **AZD8450** and **AZD6370** for the treatment of metabolic disorders (diabetes mellitus and dyslipidaemia), are all in pre-clinical development.

We have discontinued the development of **AZD0303** for thrombosis as a result of its failure to meet the target product profile.

Performance 2004

Reported performance

CV sales grew by 22%, rising by $867 million from $3,910 million in 2003 to $4,777 million in 2004. This growth was driven by the first full year s sales of *Crestor*.

Underlying performance

Excluding exchange effects of $214 million, CV sales grew by 17%.

Sales of *Crestor* worldwide for the full year reached $908 million, compared with $129 million in 2003. Sales in Europe were $231 million. Prescription market share has increased in all the major markets and is now 10.3% in the Netherlands, and 3.8% in the

UK. *Crestor* was launched in the spring of 2004 in France and Italy. Based on the latest weekly data, value share of the statin market for *Crestor* is 4.4% in France and 8.0% in Italy. Sales in Canada for the full year were $98 million, and the latest market share of monthly total prescriptions for *Crestor* was 12.1%.

In the US, market share progress has been more volatile, as a result of episodic media coverage of challenges to the safety profile of *Crestor* as discussed above. Sales for the year were $543 million. In the week ending 14 January 2005, *Crestor* share of new prescriptions was 6.0%. Market share in the dynamic segment (new and switch patients) was 8.2%.

Prescriptions for *Toprol-XL* in the US increased by 18% for the full year, twice the rate of growth in the beta-blocker market, and sales reached $977 million. Market share of total prescriptions in December 2004 was 28.1%, up 1.9 points versus last year. Full year sales growth rate was 7%, which is still below estimated underlying growth as a result of net stock movements year on year. Sales of *Seloken* outside the US were up 3% for the year at $410 million.

More than 70% of sales of *Atacand* come from markets outside the US. In these markets sales continued to show good growth (up 18% for the year) with sales increasing to $627 million, driven primarily by volume gains in Europe. Sales in the US at $252 million were down 4% for the full year, in line with prescription trends.

The rate of decline in *Zestril* sales reduced in 2004, with revenues falling by 15%. Falls were seen in all regions, with US sales down 29% at $69 million. Outside the US sales were $371 million, an underlying fall of 12%.

Plendil sales also fell in 2004, again in all regions. In particular, sales declined in the US in the second half of the year to end down 30% at $166 million.

Tenormin worldwide sales were flat in 2004 compared to 2003. Growth in the US was offset by declines in Europe; sales elsewhere were broadly unchanged.

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 erosion of *Zestril* sales following patent expiry.

Underlying performance

Excluding exchange effects of $249 million, CV underlying sales growth was $92 million or 3%.

Global sales of *Seloken/Toprol-XL* exceeded $1 billion for the first time, on continued strong growth in the US (up 47%), where market share of total beta blocker prescriptions of *Seloken/Toprol-XL* reached 26.2% in December 2003. Despite destocking in the last quarter, wholesaler stocks 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. US sales growth exceeded growth in total prescriptions, indicating some increase in wholesaler stocks.

Crestor sales were $129 million, including $62 million in the US. The early launch markets for *Crestor* included the Netherlands, Canada and the UK. 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% and the dynamic share of new statin treatments (new and switch therapy only) was 13.7%.

Lisinopril, the active ingredient in *Zestril*, lost patent protection in most major markets during 2002 with significant sales erosion taking place during 2003. In the US, generic lisinopril held an 80% share of sales by the end of 2003.

Plendil sales rose by 5% to $540 million. Growth in the US was offset by lower 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 PPI market value: $21 billion.
- In the western world, 40% of adults regularly experience heartburn and 10-20% have gastro-oesophageal reflux disease (GERD). The prevalence rate of GERD in Asia is lower but increasing.
- Helicobacter pylori (H.pylori) is the major cause of peptic ulcer disease and is a risk factor for gastric cancer. The prevalence rate of H.pylori infection in the western world is 40% but declining.
- Irritable bowel syndrome (IBS) is a common gastrointestinal disease which is inadequately treated. The prevalence rate in the population is 20%.
- Inflammatory bowel disease (IBD) is an area of significant unmet medical need.

2004 in brief

- Global sales of *Nexium* were $3,883 million.
- *Nexium* confirmed as the most successful US pharmaceuticals launch with in excess of $3.5 billion sales in 30 months.
- *Nexium* parenteral is approved in 47 countries and approval of *Nexium* for healing and prevention of ulcers associated with NSAID therapy has been granted in the first 11 EU countries.
- Global sales of *Losec* $1,947 million with continued strong sales growth in Japan.

Products

Nexium (esomeprazole magnesium) is the first proton pump inhibitor (PPI) to offer clinical improvements over other PPIs (such as *Losec/Prilosec,*lansoprazole and pantoprazole) and other treatments. *Nexium* has been evaluated in clinical studies involving 73,000 patients in over 60 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 peptic 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 therapy.

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

Nexium was first launched in Sweden in August 2000 and it is now available in approximately 100 markets, including the US, Canada and all European countries. It has been well received by patients and physicians alike and close to 250 million patient treatments had been administered by the end of 2004.

First regulatory approval and launch of parenteral *Nexium* were achieved in 2003. The parenteral form of *Nexium* was approved through the Mutual Recognition Procedure (MRP) in Europe in December 2003 for when oral administration is not applicable for the

treatment of GERD. Subsequent approvals have been obtained during 2004 and parenteral *Nexium* is now approved in 47 countries. Regulatory filings of *Nexium* for healing and prevention of ulcers, associated with NSAID (non-steroidal anti-inflammatory drug) therapy were made in January 2004. The application was approved through the MRP in Europe in September 2004 and subsequent, national approvals have been obtained in 11 EU countries to date. Approval for the reduction in the occurrence of gastric ulcers associated with continuous NSAID therapy in patients at risk of developing gastric ulcers was granted in the US in November 2004.

In March 2004, Dr Reddy s Laboratories Ltd. opened a Drug Master File with the FDA relating to the active ingredient of *Nexium*, esomeprazole magnesium. However, AstraZeneca is not aware of the filing of an Abbreviated New Drug Application relating to esomeprazole magnesium.

Losec*/*Prilosec (omeprazole), the first PPI, became established in the short and long term treatment of acid-related diseases in the 1980s and 1990s. Patients have benefited from over 780 million treatments with *Losec/Prilosec* since launch. Continued strong sales growth of *Losec/Omepral* was seen in Japan in 2004.

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. Further information about the status of omeprazole patents and patent litigation, including details of generic omeprazole launches, is set out on pages 112 and 113.

In July 2003, the European Commission served a Statement of Objections on AstraZeneca, referring to alleged infringements of European competition law relating to certain omeprazole intellectual property and regulatory rights, details of which are set out on page 113.

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. *Entocort* maintained its growth during 2004, based on its increasing acceptance as first line therapy for mild to moderate, active Crohn s disease. In 2004 *Entocort* was approved for paediatric use in nine countries, representing the first such use for a Crohn s disease therapy worldwide.

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, peptic ulcer disease, IBD and other gastrointestinal diseases, such as IBS and functional dyspepsia.

AZD0865 is a compound in a new class, potassium-competitive acid blockers

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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 38, together with the reasons for its use.

Key product performance

	2004			2003			2002	2004 compared to 2003		2003 compared to 2002	
	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	3,883	479	102	3,302	1,225	99	1,978	15	18	62	67
Losec/Prilosec	1,947	(764)	146	2,565	(2,259)	201	4,623	(30)	(24)	(49)	(45)
Other	88	7	5	76	8	5	63	9	16	13	21
Total	**5,918**	**(278)**	**253**	**5,943**	**(1,026)**	**305**	**6,664**	**(4)**		**(16)**	**(11)**

(P-CABs), 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 currently in phase 2.

AZD3355 and **AZD9343**, now in 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), namely inhibition of transient relaxations of the lower oesophageal sphincter.

AZD7371 is being evaluated in clinical studies for the treatment of functional GI diseases and is in phase 2.

AZD8081, for the treatment of functional GI diseases, and **AZD5745**, for the treatment of acid-related diseases, are both in pre-clinical development.

Performance 2004

Reported performance

GI performance in 2004 was broadly the same as 2003, with sales falling by only $25 million.

Underlying performance

On an underlying basis, GI sales fell by 4% ($278 million) as declines in *Losec/Prilosec* exceeded growth in *Nexium*.

In the US, dispensed tablet volume for *Nexium* increased by 20% for the year. As the impact of price was broadly neutral, reported sales growth of 10% (up to $2,716 million) reflects stock movements. *Nexium* share of total prescriptions in the US PPI market was 27.1% in December 2004. The increase of 1.8 points in market share versus 2003 outpaced all other PPI products. Sales of *Nexium* outside the US were $1,167 million for the full year, up 29% on a strong performance in all major markets. Sales in Europe reached $873 million (up 26%) as volume growth was offset in part by pricing pressures. Strong

volume growth was also the driver behind the 41% increase in the rest of the world.

US sales for *Prilosec* for the full year at $366 million were down 58% in line with the decline in prescriptions.

Outside the US, sales of *Losec* were $1,581 million, down 16% for the year. Full year sales increased 24% in Japan to $185 million. Sales in Europe declined by 25%, principally through volume, to $855 million.

Performance 2003

Reported performance

Reported sales in the GI therapy area fell by 11% to $5,943 million as increases in *Nexium* sales were offset by declines in *Losec/Prilosec* sales.

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%.

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.

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.

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Neuroscience

We aim to deliver a range of life-changing medicines in the three key areas of psychiatry, analgesia and neurology and to maintain our world leading position in anaesthesia.

Therapy area overview

> Neuroscience world market value: over $98 billion, growing at 11% per annum.

Psychiatry (market value: $42 billion)

> More than six million people suffer from schizophrenia and 17 million suffer from bipolar disorder in the major markets.

Neurology (market value: $25 billion)

> Migraine is one of the leading causes of disability in the world. Stroke is the second leading cause of death and the leading cause of adult disability in industrialised countries. Alzheimer s disease, the most common cause of dementia, affects more than 4.5 million people in the US.

Analgesia (market value: $28 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.

2004 in brief

> *Seroquel* sales grew by an underlying 33% to $2 billion.
> *Seroquel* successfully launched in Europe and the US for the treatment of acute manic episodes in bipolar disorder with strong market share growth.
> *Seroquel* achieved market leadership in the US (number one atypical by monthly new prescriptions).
> Ground-breaking data on *Seroquel* in bipolar depression presented in May (BOLDER study).

> *Cerovive* phase 3 (SAINT) trials continue as planned.
> Anaesthesia portfolio sales exceeded $1 billion.

Products

Seroquel (quetiapine fumarate) is an atypical anti-psychotic drug for the treatment of schizophrenia and acute manic episodes in bipolar disorder. It is a first line, first choice treatment for a broad range of symptoms. It delivers excellent efficacy and unique patient tolerability, including placebo-like effects on extrapyramidal symptoms and prolactin across the dose range, thus offering high patient acceptance.

This unique profile has led to the increased use of *Seroquel*, substantially exceeding world market growth. In September 2004, *Seroquel* became the market leading atypical in the US in terms of monthly new prescriptions. In Europe, *Seroquel* is growing two to three times faster than the atypical market, with key countries, such as Italy and Germany showing excellent market share gains.

The launch of *Seroquel* for the treatment of bipolar mania in over 40 countries has been highly successful, with strong market share growth. Physician feedback regarding key patient benefits, including rapid onset (four days), unique patient tolerability and no emergent depression has been extremely encouraging.

Approval was received in July 2004 from the FDA for new labelling to include 12-week data in the treatment of acute mania associated with bipolar disorder. This makes *Seroquel* the first product in its class to include monotherapy efficacy and safety data beyond three weeks in its label for acute bipolar mania.

Seroquel is not currently approved for the treatment of bipolar depression or agitation associated with dementia.

The results of the BOLDER study were presented at a meeting in May 2004 of the American Psychiatric Association, the world s largest psychiatry congress. BOLDER was a study of *Seroquel* monotherapy for the treatment of bipolar depression. The study results indicated that *Seroquel* was effective in treating depressive episodes associated with bipolar I and II disorders and a range of depressive and anxiety symptoms associated with bipolar disorder.

The STAR trial data were announced in July 2004 at the International Conference on

Alzheimer s Disease and Related Disorders, a leading Alzheimer s disease conference. The results of this study indicated that *Seroquel* was effective in the treatment of agitation associated with dementia in elderly patients residing in long term care facilities.

In November 2004, AstraZeneca submitted a regulatory application to the French health authorities for a licence to market *Seroquel* in France for the treatment of schizophrenia and acute manic episodes associated with bipolar disorder. AstraZeneca received approval in Canada to market *Seroquel* as a monotherapy for the acute management of manic episodes associated with bipolar disorder.

In January 2004, Dr Reddy s Laboratories Ltd. opened a Drug Master File with the FDA relating to quetiapine, the active ingredient in *Seroquel*. However, AstraZeneca is not aware of the filing of an Abbreviated New Drug Application relating to quetiapine.

Zomig (zolmitriptan) is indicated for the treatment of migraine with or without aura. It 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 and *Zomig* is available in a unique range of formulations to provide rapid migraine relief. *Zomig* is the prescription market leader in Europe.

Zomig Nasal Spray is a formulation that delivers fast pain relief. The nasal spray has been successfully launched in Europe and the US. Launch in Japan is expected in 2005.

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. The 5mg tablet is now approved and launched in several EU countries.

Diprivan (propofol), the world s best selling intravenous 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.

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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 38, together with the reasons for its use.

Key product performance

	2004			2003			2002	2003 compared to 2002		2004 compared to 2003	
	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	2,027	496	44	1,487	304	38	1,145	33	36	27	
Diprivan	500	24	18	458	(7)	22	443	5	9	(2)	
Zomig	356	(12)	19	349	(3)	24	328	(3)	2	(1)	
Local anaesthetics	542	41	35	466		34	432	8	16		
Other	71	(7)	5	73	(5)	8	70	(10)	(3)	(7)	
Total	**3,496**	**542**	**121**	**2,833**	**289**	**126**	**2,418**	**19**	**23**	**12**	

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.

We divested the marketing authorisations for the manufacture and sale of Mysoline to Acorus Therapeutics Ltd. in July 2004. This allowed the continued supply of Mysoline to patients in countries where it was previously sold by AstraZeneca.

Pipeline

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

Psychiatry

A sustained release formulation of *Seroquel* is being developed as part of a strategic approach to expand the treatment options available for patients.

AZD8129 (previously AR-A2) is a novel $5HT_{1B}$ antagonist in phase 2 for the treatment of depression and anxiety. The portfolio has been expanded by the nomination of **AZD2327**, as a candidate drug in pre-clinical development with a novel mechanism of action for treating anxiety.

We have discontinued the development of **AZD5455** and the granules formulation of *Seroquel* as a result of their failure to meet the target product profiles.

The collaboration with Shanghai Jiaotong University, established in 2001, continues to progress well and has identified several genetic variants that may predispose certain populations to schizophrenia.

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**, an NMDA antagonist in phase 1 for the treatment of neuropathic pain.

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. **AZD9272** and **AZD6538**, targeting neuropathic pain, are the first two candidate drugs from the collaboration to be nominated.

Neurology

Cerovive, licensed from Renovis, Inc., is a neuroprotectant with free radical trapping properties under development for the treatment of acute ischaemic stroke, a disease with substantial unmet medical need for new effective therapies. Pre-clinical data show that *Cerovive* preserves neurologic function and brain tissue even when given at substantial delay following the onset of ischaemia.

The development of neuroprotectants for stroke is known to be a highly challenging area of drug development. It is difficult to achieve controlled clinical trial conditions in a setting where patients have just suffered a stroke and require immediate emergency care. It is also technically difficult. Our two pivotal SAINT (Stroke Acute Ischaemic NXY Treatment) trials were designed to mitigate the technical risks by aligning time to treatment and dosing in accordance with pre-clinical efficacy results. The SAINT trials compare the efficacy and safety of a placebo with a 72-hour intravenous infusion of *Cerovive* given within six hours of the onset of symptoms. Recruitment for the SAINT I trial being conducted in Europe, Asia, Australia, New Zealand and South Africa was completed in November 2004.

In October 2004, an independent data monitoring board recommended that the SAINT trials should continue as planned based on a review of the first 1,000 treated patients with three months follow up of stroke outcomes. Read out of the SAINT I trial is expected in the second quarter of 2005.

The CHANT (Cerebral Haemorrhage And NXY Treatment) trial assessing safety and tolerability in intracerebral haemorrhagic stroke was initiated in 2004.

AZD7371 is in phase 2 for overactive bladder, a highly prevalent condition and an unsatisfied market. We have discontinued the development of **ZD0947** as a result of its failure to meet the target product profile.

AZD1080 is a new candidate drug for the treatment of Alzheimer s disease, a core strategic focus of our research**AZD3102** is being developed in collaboration with Dyax Corp. and is one of the first ventures for AstraZeneca in human monoclonal antibodies. We have discontinued the development of **AZD0328** and **AZD2858** as a result of their failure to meet the target product profile.

AZD5904 is a new candidate drug for the treatment of multiple sclerosis. We have discontinued the development of **AZD4750** as a result of its failure to meet the target product profile.

Performance 2004

Reported performance

Neuroscience sales in 2004 grew by $663 million from $2,833 million in 2003 to $3,496 million, an increase of 23%.

Underlying performance

After excluding exchange effects of $121 million, underlying growth was 19%.

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Seroquel sales reached a new milestone in 2004, exceeding $2 billion in annual sales for the first time. Sales growth is well ahead of the atypical anti-psychotic class in most major markets, fuelled by successful launches of the bipolar mania indication.

Seroquel sales in the US for the full year were up 33% at $1,504 million, in line with prescription growth of 30%. In December 2004, new prescription share reached 27.5%, a class leading increase of 4.6 points over December 2003.

Seroquel sales outside the US increased 36% for the year to $523 million. For the year sales were up 45% in Europe ($331 million in 2004 compared to $209 million in 2003), up 44% in Canada ($74 million in 2004 compared to $48 million in 2003), and grew 13% in Asia Pacific (rising to $107 million in 2004 from $87 million in 2003).

Zomig performance in the full year reflects the 10% decline in the US (down from $163 million in 2003 to $147 million in the current year), partially offset by slight growth (up 2% to $209 million) in the rest of the world.

Diprivan sales worldwide increased by 5%; growth of 15% in the US (sales of $264 million, up from $230 million in 2003) more than compensated for declines in Europe. Local anaesthetics enjoyed growth in all markets, particularly in the US (up to $131 million from $106 million) and Europe (increasing 9% to $217 million from $181 million).

Performance 2003

Reported performance

Reported growth for Neuroscience was 17%, with sales up $415 million to $2,833 million in 2003.

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 and a combined growth of 12% worldwide.

In the US, *Seroquel* sales reached $1,134 million for the year, an increase of 22%. Total prescriptions for *Seroquel* in the US were up 34%. The share of total prescriptions for *Seroquel* in the US anti-psychotic market reached a new high at 21.2% in December 2003.

Sales of *Seroquel* in markets outside the US increased 45% for the year. Sales in Europe were up 40%, and sales in Japan rose 67%. *Zomig* sales for the 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.

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

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Oncology

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

Therapy area overview

- World market value for cancer therapies: $22 billion and growing strongly.
- In 2004, over 10 million people were diagnosed with cancer; by 2020 this is forecast to reach 15 million.
- Six million people die from cancer every year - representing 12% of deaths worldwide.

2004 in brief

- Rapid uptake in sales of *Iressa* continued until disappointing ISEL data in December led to comprehensive reassessment of *Iressa* including withdrawal of MAA in Europe.
- *Faslodex* now available in the EU.
- *Casodex* approved for use in EPC in over 60 countries.
- ATAC data showed *Arimidex* is significantly more effective than tamoxifen in prolonging disease-free survival of post-menopausal women with early breast cancer.

Products

Casodex (bicalutamide) is the world s leading anti-androgen therapy for the treatment of prostate cancer. The growth of *Casodex* has continued mainly through a renewed interest in the potential benefits of combination use of *Casodex* 50mg with *Zoladex* and other luteinising-hormone releasing hormone (LHRH) agonists. *Casodex* 150mg is approved for use in early prostate cancer (EPC) in over 60 countries and applications for the EPC indications are under review in several other markets. During 2004, the German regulatory authority did not agree a revised indication for *Casodex* 150mg, which is now no longer available in that country though 50mg remains on the market. Elsewhere, sales of *Casodex* 150mg continue to grow.

Zoladex (goserelin acetate) available in one month and three month depots, is the world s second largest LHRH agonist by value. It is used for the treatment of prostate cancer, breast cancer and gynaecological disorders. It is approved for the treatment of prostate cancer in 105 countries. In EPC, *Zoladex* is the only LHRH agonist shown to improve overall survival when used in addition to either radical prostatectomy or radiotherapy. In breast cancer, *Zoladex* is 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. It is also widely approved for use in advanced breast cancer in pre-menopausal women. *Zoladex* offers proven survival benefits for breast cancer patients with a favourable tolerability profile.

Iressa (gefitinib) is a highly researched, first in class, new type of anti-cancer agent (epidermal growth factor receptor-tyrosine kinase inhibitor (EGFR-TKI)) that acts to block signals for cancer cell growth and survival. It is indicated for the treatment of non-small cell lung cancer (NSCLC) in patients who have failed chemotherapy. Patients with NSCLC generally have a short survival time and their quality of life is seriously impaired. Previously published clinical trials with *Iressa*, used alone in patients treated for advanced NSCLC who have failed chemotherapy, reported that up to 50% of patients may experience benefit (including tumour shrinkage in 12-18% of patients). Over 40% of these patients were reported to experience early symptomatic improvement in the symptoms of lung cancer, such as cough, breathlessness

and chest pain. It has consistently demonstrated good tolerability and is not associated with the typical side effects of chemotherapy.

However, preliminary results from the recently reported ISEL clinical study (which compared *Iressa*, when used alone, to placebo in patients with advanced NSCLC, who had failed chemotherapy,) showed that, whilst there was a statistically significant improvement in tumour shrinkage (objective response rate) and time to treatment failure, the difference in favour of increased survival with *Iressa* treatment failed to reach statistical significance compared to placebo in the overall population.

Prospective subgroup analyses from the ISEL study did show statistically significant differences in survival in favour of *Iressa* in patients of East Asian origin and non-smokers. In the East Asian subgroup, there was a near doubling of median survival, which supports the positive benefit/risk ratio observed in previous studies in these patients.

In 2004, two publications appeared, describing how patients who had dramatically responded to *Iressa* had a genetic alteration (mutation) in the EGF Receptor (EGFR) within the tumour cells, the biological target for the drug. These mutations appear to be a predictor of tumour response to *Iressa*. The publication of these data sparked great scientific and clinical interest in the drug, and may explain why the response rates observed in the ISEL study in patients from East Asian origin, and non-smokers were relatively high. We will be working to better understand the ISEL outcome in the context of further analysis of survival data, secondary endpoints, EGFR status and other biomarkers.

Iressa is currently approved in 35 countries, including the US and Japan. AstraZeneca is now actively consulting with regulatory authorities to determine the impact of the ISEL data. It is possible that some regulatory authorities may require AstraZeneca to withdraw its marketing authorisation for *Iressa*. In January 2005, after consultation with the European Medicines Evaluations Agency we withdrew the European Marketing Authorisation Application (MAA) for *Iressa* because the ISEL survival results did not meet the

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Key product performance

	2004			2003			2002	2004 compared to 2003	
	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 %
Casodex	1,012	92	66	854	140	70	644	11	19
Zoladex	917	(13)	61	869	6	69	794	(1)	6
Arimidex	811	249	43	519	152	36	331	48	56
Iressa	389	147	14	228	152	9	67	65	71
Nolvadex	134	(54)	10	178	(314)	12	480	(31)	(25)
Faslodex	99	21	1	77	42		35	28	29
Other	14	(5)	1	18	(1)	1	18	(28)	(22)
Total	**3,376**	**437**	**196**	**2,743**	**177**	**197**	**2,369**	**16**	**23**

approval requirements in Europe. The submission of a new MAA will be considered after evaluation of the full ISEL data and new emerging studies.

In the US, we have voluntarily suspended promotion of *Iressa*. AstraZeneca has urged physicians to consider other treatment options in the recurrent NSCLC population, in light of positive survival data with other agents, including another oral EGFR inhibitor. AstraZeneca intends to continue to make *Iressa* available for those patients whose physicians feel they

more effective in prolonging disease-free survival and has important tolerability benefits compared with tamoxifen. Further data from the ATAC study presented in December 2004 also showed that women switching from tamoxifen to *Arimidex* suffered fewer recurrences of their early breast cancer than those who stayed on tamoxifen throughout the standard five-year course of treatment. *Arimidex* is also approved for the treatment of advanced breast cancer in post-menopausal women based on demonstrated advantages over

Signalling processes, which are critical to cancer cell division and survival, are the targets of a number of AstraZeneca s novel compounds designed with a different biological effect in mind, including anti-angiogenesis, anti-proliferation and anti-invasion.

ZD6474 is a novel, orally active, anti-cancer agent that selectively inhibits two key cancer pathways: tumour blood vessel development (through VEGFR inhibition) and tumour cell growth and survival (through EGFR inhibition).

are benefiting from the drug.

Based on the total data available for *Iressa*, we continue to believe that it has a place in the management of NSCLC and potentially other tumour types, providing substantial benefits for some patients in clinical practice and a favourable tolerability profile. New studies will report in the first half of 2005, which will provide further information on the efficacy and safety of *Iressa* and will further influence our thinking on the future of *Iressa*. In the US, we anticipate a rapid reduction in new prescriptions. While commercial prospects have certainly been reduced in Western markets, the positive results in patients of East Asian origin offer the prospects of a continuing successful business in these important markets. (See Financial Review for financial impacts.)

Arimidex (anastrozole) is the world s leading aromatase inhibitor. *Arimidex* continues to grow strongly as it replaces tamoxifen as the preferred adjuvant treatment for post-menopausal women with early breast cancer. The large-scale ATAC study, first reported in December 2001 and then most recently updated in December 2004, showed that *Arimidex* is significantly 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. *Faslodex* offers patients with hormone-sensitive, advanced breast cancer more hormonal options before having to resort to expensive and poorly tolerated cytotoxic chemotherapy. Due to its novel mode of action, *Faslodex* offers an effective, well tolerated additional treatment for patients, with the compliance and convenience benefits of a once monthly injection. Following the EU approval in March 2004, *Faslodex* is now available in Europe, as well as the US, Brazil and Argentina for the second line treatment of hormone receptor positive, advanced breast cancer in post-menopausal women.

Nolvadex (tamoxifen citrate) remains a widely prescribed breast cancer treatment.

Pipeline

Further trials are underway to evaluate the potential benefits of *Iressa* in other EGFR driven tumours such as head, neck and breast cancers. The clinical trial programme in lung cancer is under review in light of the recent developments described in detail above.

ZD6474 is scheduled to complete phase 2 clinical trials during 2005.

AZD2171 is an anti-angiogenic agent in phase 1 that targets the growth of blood vessels of tumours. **AZD9935** is another anti-angiogenic in pre-clinical development.

ZD6126 is a vascular targeting agent. Phase 2 clinical trials were stopped due to cardiac events. Pre-clinical work is now in progress to re-examine its potential. **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. **ZD4054**, which is being evaluated in clinical trials for the treatment of hormone-resistant prostate cancer, has recently been granted fast track designation by the FDA.

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

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tumour cells. **AZD1152**, an aurora kinase inhibitor designed to target cell division in proliferating tumours, is now in pre-clinical development. **AZD6244** (ARRY142886), in phase 1 development, is a selective MEK inhibitor targeting proliferating tumour cells.

AZD4769, an anti-proliferative agent, is in pre-clinical development for solid tumours including NSCLC.

AZD3841 and **AZD8931**, both anti-proliferative agents, are in pre-clinical development for solid tumours.

The collaboration with Abgenix Inc., which aims to discover fully human monoclonal antibodies for the treatment of cancer, has entered its second year. This arrangement is complementary to our major activity in small molecules and is allowing us to tackle a broader range of targets. It is anticipated the collaboration will contribute candidate drugs to the development pipeline by 2006.

Performance 2004

Reported performance

Oncology sales increased by 23% rising $633 million from $2,743 million in 2003 to $3,376 million in 2004.

Underlying performance

After eliminating the effects of exchange of $196 million, the underlying sales growth rate was 16%.

Casodex sales outside the US were up 11% for the year totalling $780 million. Sales in Japan continue to grow strongly to $240 million, up 24% for the year. Reflecting the maturity of the market in advanced prostate cancer, underlying performance in the US was estimated underlying growth. New prescription market share for aromatase inhibitors plus tamoxifen reached 29.0% in December 2004 up 7.5 points over last year. We now estimate that more than 50% of newly diagnosed patients are receiving *Arimidex*. Outside the US, sales of *Arimidex* were up 46% for the year at $511 million. Full year sales were up 48% in Europe ($358 million), and increased 41% in Japan ($100 million).

Iressa sales reached $389 million for the full year (up 65%), including $176 million in the US (up 73%) and $136 million in Japan (an increase of 24%). However, fourth quarter sales in the US for *Iressa* were $17 million (down 65%) in view of the regulatory uncertainties and the increased probability of returns of unused product, we have not recognised the revenue from sales made in the latter half of the quarter. Until the situation stabilises, revenue from *Iressa* sales in the US will be recognised on confirmed patient usage rather than wholesaler shipment.

Zoladex sales remained substantially unchanged. Declines in the US ($152 million) and Europe ($386 million), down 13% and 9% respectively, were mitigated by a strong performance in Japan (up 16% to $231 million).

The rate of fall in *Nolvadex* sales slowed to 31%; sales in the US were negligible although in Europe and Japan revenue declines were less pronounced (falling by 11% to $119 milion).

Faslodex sales increased by 28% to reach $99 million. Launches in Europe contributed to the majority of this increase.

disease. In the US the underlying demand was broadly unchanged with *Casodex* share of total prescriptions in this market being 83% in December 2003 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.

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. Sales of *Nolvadex* declined by 66% following patent expiry in the US in February 2003.

essentially unchanged with sales for the year up 9% to $232 million.

Arimidex had another year of excellent sales growth, with sales up 48% to $811 million as a result of increased use in the adjuvant treatment of early breast cancer. The growing importance of aromatase inhibitors such as *Arimidex* to this patient population was affirmed in the recently updated treatment guidelines published by ASCO. As the only aromatase inhibitor indicated for primary adjuvant treatment (approved now in 80 countries) *Arimidex* is well positioned to benefit from continued adoption of these treatment guidelines in clinical practice. Sales in the US for *Arimidex* for the full year were up 52% at $300 million, in line with

Performance 2003

Reported performance

Oncology s reported sales growth was 16% as revenues grew by $374 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 was driven by the expanding use of *Casodex* in early stage

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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: $37 billion.

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

2004 in brief

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

> The regulatory submission in Europe for *Symbicort* as a single inhaler treatment of asthma was withdrawn to allow more data to be submitted. Approvals have been gained in two markets outside Europe.

> Regulatory application for *Symbicort* pMDI formulation submitted in Europe for asthma and COPD in July.

> *Symbicort* US filing scheduled for the second or third quarter of 2005.

Products

Symbicort (budesonide/formoterol) is an innovative and effective asthma treatment that offers superior efficacy with 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 90 countries and launched in more than 70. Phase 3 trials in asthma are complete in the US.

On 15 January 2005 results from the STAY trial (one of the largest asthma studies ever conducted) were published in the American Journal of Respiratory and Critical Care Medicine. Data revealed for the first time that *Symbicort* Single inhaler Therapy (SiT), a new asthma treatment concept which develops *Symbicort* adjustable maintenance dosing, offers superior control in the main measures of asthma management compared to traditional *Symbicort* fixed dose, including a significant 45% reduction in the frequency of severe exacerbations.

In Europe, in November 2004, we withdrew our regulatory application for *Symbicort* SiT to allow more data to be submitted. We expect to submit a *Symbicort* SiT regulatory filing in Europe in the second half of 2005 containing additional data from further ongoing studies, including in total 13,000 patients with mild to moderate asthma.

A file for *Symbicort* pressurised metered dose inhaler (pMDI) in asthma and COPD was submitted to EU regulatory authorities in July 2004.

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.

Pulmicort Respules (budesonide inhalation suspension) 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. A regulatory application for *Pulmicort Respules* was filed in Japan in October 2004.

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.

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* pMDI 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

US development of the *Symbicort* pMDI is progressing and the phase 3 clinical programme in asthma is complete. Following a pre-NDA meeting with the FDA in the fourth quarter of 2004, a New Drug Application for this formulation is now targeted for the second or third quarter of 2005, although the FDA has identified some issues associated with the inhaler that require the generation of additional chemistry and manufacturing data or possible modification of the device in order to achieve approval.

Seven new compounds have entered pre-clinical development, targeted at COPD (**AZD7928** and **AZD2914**), asthma and rhinitis (**AZD2392** and **AZD1744**), osteoarthritis (**AZD6357**) and rheumatoid arthritis (**AZD6703** and **AZD5672**). In addition, **AZD0902** is in pre-clinical development for rheumatoid arthritis. The respiratory pre-clinical portfolio comprises **AZD2098** and **AZD1981** for asthma as well as **AZD6067** for COPD.

Compounds currently in clinical development include **AZD3778** for asthma and rhinitis and **AZD3342** for COPD. **AZD8955** is in clinical development for osteoarthritis and **AZD8309** for rheumatoid

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Key product performance

	2004			2003			2002	2004 compared to 2003		2003 compared to 2002	
	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	1,050	40	42	968	101	55	812	4	8	12	1
Symbicort	797	176	72	549	180	70	299	32	45	61	8
Rhinocort	361	(11)	8	364	56	9	299	(3)	(1)	19	2
Accolate	116	7	2	107	(40)	3	144	6	8	(28)	(2
Oxis	101	(28)	9	120	(14)	14	120	(24)	(16)	(12)	
Other	158	(8)	13	153	(8)	17	144	(5)	3	(6)	
Total	**2,583**	**176**	**146**	**2,261**	**275**	**168**	**1,818**	**8**	**14**	**15**	**2**

arthritis as well as COPD. **AZD9056**, a P2X7 ion-channel blocker, is in phase 2 clinical development for rheumatoid arthritis and osteoarthritis as well as in phase 1 for COPD. All five compounds currently in clinical development for various indications are based on novel mechanisms of actions.

We have discontinued the development of **AZD0902** for the indication of COPD as a result of its failure to meet the target product profile.

In December 2004, AstraZeneca and Cambridge Antibody Technology entered into in a five-year discovery alliance to generate monoclonal antibody therapeutics principally in inflammatory disorders, including respiratory diseases.
For AstraZeneca, this collaboration provides access to leading technology for the generation of fully human monoclonal antibodies for application across all relevant disease areas, working alongside a leading company in the field.

Performance 2004

Reported performance

R&I sales grew by 14% from $2,261 million to $2,583 million, an increase of $322 million, principally as a result of higher sales of

Symbicort.

Underlying performance

R&I underlying growth was $176 million, with sales up 8%.

Symbicort sales were up 32% to $797 million in the year on share gains in the fast growing combination product segments of the asthma and COPD markets. The majority of *Symbicort* sales were in Europe (up 29% to $701 million). Sales elsewhere rose by 65% to $96 million.

More than 40% of global *Pulmicort* sales

came from the sales of *Pulmicort Respules* in the US. A 17% increase in US *Pulmicort Respules* sales resulted in a 4% increase in worldwide sales (to $1,050 million) for *Pulmicort*. Sales of *Pulmicort* in the US rose 13% to $576 million, more than compensating for the 9% decline in Europe (sales of $364 million).

Sales for *Rhinocort* were down 3% for the year to $361 million as a result of a broadly flat performance for the US market for inhaled nasal steroids in general, including *Rhinocort Aqua*.

The increase in *Accolate* sales was driven by price increases in the US (sales up 18% to $84 million).

Performance 2003

Reported performance

Reported growth for R&I was 24%. Sales increased from $1,818 million to $2,261 million.

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 gained share in the rapidly growing market for fixed combination asthma treatments.

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%.

Rhinocort sales in the US were up 27% accounting for almost all of the global growth of 19%. Growth in *Rhinocort Aqua* (58%) continued to more than offset the sales lost from the discontinuation of the *Rhinocort Nasal Inhaler* formulation.

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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 38, together with the reasons for its use.

Infection

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 Discovery technologies to bring new products to market.

Key product performance

	2004			2003			2002	2004 compared to 2003		2003 compared to 2002	
	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	423	53	24	346	46	15	285	15	22	16	21
Other	116	(20)	6	130	(36)	11	155	(16)	(11)	(24)	(17)
Total	**539**	**33**	**30**	**476**	**10**	**26**	**440**	**7**	**13**	**2**	**8**

Therapy area overview

> Infection world market value: $53 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.

2004 in brief

> Steady underlying growth for *Merrem* in the US (8%), Europe (14%) and globally (15%).

> Supplementary New Drug Application filed in the US for treating skin and skin structure infections.

Products

Merrem*/*Meronem (meropenem) is an intravenous carbapenem antibiotic for the treatment of serious, hospital-acquired infections. A Supplementary New Drug Application was filed in the US in July 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.

Work continues at our new R&D facility opened in Bangalore, India which is dedicated to finding a new treatment for tuberculosis. Tuberculosis remains a worldwide threat and is newly diagnosed in approximately two million people every year in India and over eight million people worldwide.

Performance 2004

Reported performance

Infection sales growth was 13% as revenues rose by $63 million to $539 million.

Underlying performance

Excluding exchange effects of $30 million, underlying sales in Infection increased by $33 million, 7%.

The performance of the therapy area was driven by *Merrem* sales, particularly in Europe with growth of 14% to $221 million.

Performance 2003

Reported performance

Sales grew by 8% on a reported basis, rising 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.

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Geographic Review

US

While the US remained the world s largest market for pharmaceuticals, 2004 illustrated both the rewards and risks inherent in such a complex and dynamic operating environment. Our pharmaceutical sales rose by 10% in 2004 from $8,449 million to $9,308 million, reflecting our continuing commitment to driving growth in this important market. The US represents 45% 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. *Nexium*, *Seroquel, Toprol-XL* and *Crestor*, with combined sales of $5.7 billion, continue to underpin our sales performance in this highly competitive market. Sales from Salick Health Care and Astra Tech rose by 9% in 2004 to $323 million.

Nexium is now approaching market leadership in total prescriptions and achieved market leadership in capsules dispensed in December 2004. During 2004, discounting and rebating increased in the prescription proton pump inhibitor market, driven mainly by the launch of *Prilosec* OTC (over-the-counter), generic omeprazole and competitive pressures. However, *Nexium* was not significantly impacted due to its superior clinical profile. *Prilosec* OTC had a significant impact on the omeprazole molecule but branded PPI s (including *Nexium*) were only modestly impacted.

Toprol-XL became the most prescribed drug among cardiologists and *Seroquel* continued to gain share in the atypical anti-psychotic market, overtaking risperidone as the leading atypical agent measured in new prescriptions during the third quarter of 2004. In its seventh year on the market, *Seroquel* had its best year yet in terms of absolute growth in market share and sales volume. Other key growth products, including *Arimidex* and *Pulmicort Respules*, outperformed the market in both sales and prescription growth.

Sales of *Crestor* were $543 million. *Crestor* is the most effective statin at lowering LDL-C, with the advantage of a significant increase in HDL-C. We continue to believe that its safety profile is in line with that of other marketed statins, a view based on extensive clinical trial and post-marketing data. However, during 2004, *Crestor* continued to face what we consider to be unfounded allegations concerning its safety

(as described on page 12) which slowed the uptake of the product in the US. In September 2004, AstraZeneca launched the publicly available website rosuvastatininformation.com, which contains clinical trial and post-marketing data on *Crestor*.

In the US, Inventory Management Agreements (IMA) were implemented with 15 wholesalers with the intent to help manage stock in the trade channel. This reduced stock volatility and, by the end of the year, stocks were close to target levels.

As explained in more detail on page 13, in October 2004, the FDA did not approve *Exanta* due primarily to safety concerns. Discussions are ongoing with the FDA to determine if there is now a realistic prospect of bringing *Exanta* to the US market.

Despite increased cost pressures and the challenging market environment, the number of sales representatives in the industry remained relatively constant during the year. During 2004, AstraZeneca continued to work on both the effectiveness and efficiency of our sales organisation which resulted in improving the number and quality of interactions with key target audiences across all of our key brands. Throughout the year, we used the flexibility and size of our contract sales team to match our resources to the changing needs of our portfolio. Other initiatives included providing broadband to all selling staff and upgrading their hand-held technology to remain competitive with the best practices in the industry. For the third consecutive year, AstraZeneca was recognised with the industry s Representative of the Year award by Pharmaceutical Representative magazine, after an intense competition across the pharmaceutical field.

In October 2004, we completed the implementation of mySAP, new financial software, providing the organisation with a solid technical foundation for driving efficiency and effectiveness throughout the business. This system replaced 42 legacy systems to enhance and streamline core business processes, improve integration of information and create a single platform, allowing AstraZeneca to achieve a uniform process across all sites for supply planning, quality assurance, purchasing and more.

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. Immediate effects of the law in 2004 were changes to Medicare reimbursement for physician-administered products under Medicare Part B, and the launch of prescription drug discount cards as an interim measure until the full drug benefit takes place in 2006. We are actively participating in the current discount card programmes extending access to our products to Medicare recipients who are utilising the cards. The terms of the final regulations to be implemented to roll out the full benefit in 2006 and market forces will ultimately determine the full effect of this legislation 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 state and federal elected officials, the media and special interest groups during 2005. We will continue to provide free and discounted medicines to qualifying patients through our patient assistance programmes.

Canada

In 2004, we improved our market ranking in Canada to second with sales in excess of C$1 billion (US$876 million). Overall growth in excess of 13% outperformed the market, which grew at 10%. This growth was due to the strong performance of the growth brands, including *Nexium* (+36%), *Seroquel* (+44%), *Crestor* (+296%), *Symbicort* (+48%) and *Atacand* (+26%). *Crestor* and *Nexium*, in particular, reached milestones with sales in excess of C$100 million each and *Crestor* is now the second largest product in the statin market. Despite a court ruling that allowed early market entry of generic omeprazole, AstraZeneca Canada commands 52% of the PPI market because of the non-interchangeability of *Losec*, combined with the success of *Nexium*. We may see the interchangeability of *Losec* in 2005. Approval of *Arimidex* for early breast cancer treatment further supports our leadership position in oncology with a 19% market share.

In support of our efforts to enhance profitability of mature brands, we entered into a partnership with P&G Pharmaceuticals Canada Inc. in late 2004, to manage the promotion and marketing of all *Zomig* formulations.

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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 38, together with the reasons for its use.

Key product performance

	2004			2003			2002	2004 compared to 2003		2003 compared to 2002	
	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	9,631	883	1	8,747	(608)	4	9,351	10	10	(6)	(6)
Europe	7,649	204	736	6,709	75	939	5,695	3	14	2	18
Japan	1,430	130	111	1,189	129	83	977	11	20	14	22
ROW	2,716	362	150	2,204	294	92	1,818	17	23	16	21
Total	**21,426**	**1,579**	**998**	**18,849**	**(110)**	**1,118**	**17,841**	**9**	**14**		**6**

Europe

With a market share of 5%, we were ranked as the fifth largest prescription drug company in Europe. Our sales growth (+3%) was driven by *Crestor (*now launched in most countries and progressing well), *Nexium* (+26%), *Symbicort* (+29%), *Arimidex* (+48%) and *Seroquel* (+45%), all of which gained significant market shares and more than offset the expected impact of patent expiries.

Widespread government actions continued to slow the overall rate of market growth in Europe. These included price-related initiatives (price cuts, reference pricing and maximum reimbursed prices), regulations to encourage generic substitution and industry-specific taxes.

Sales in France of $1,597 million gave us a market ranking of fourth (taking into account the Sanofi-Aventis merger). Good performances from *Nexium* (+31%), *Symbicort* (+28%), *Arimidex* (+102%) and *Crestor* ensured that we maintained sales at 2003 levels, despite the impact from *Losec* patent expiry.

In Germany, sales growth of 2% was driven by *Nexium*, *Symbicort* and *Seroquel*. Effective January 2004, the government increased the mandatory rebate on patent-protected products from 6% to 16%, which led to a flat market growth. *Crestor* is still subject to ongoing regulatory review and with discussions on the reference pricing of statins continuing, we will not make any decision regarding a future launch until the outcome is known.

In the UK, pharmaceutical sales grew by 9% driven by *Nexium* (+29%), *Symbicort* (+26%), *Seroquel* (+70%) and *Crestor*.

In Italy, the highly successful launch of *Crestor*, capturing a market share of 9% (monthly market share figure for November

2004 including licensee sales), contributed to underlying sales growth of 5%.

In Spain, *Symbicort*, *Arimidex*, *Casodex* and *Seroquel* helped drive sales up by 5%.

At 7%, our sales growth in Central and Eastern Europe exceeded overall market growth. Commercial investments in Russia and the Czech Republic expanded our businesses there.

Late in 2004, we received approval through the European Mutual Recognition Procedure for new uses of both *Atacand* (chronic heart failure) and *Nexium* (healing of gastric ulcers and, for patients at risk, the prevention of gastric and duodenal ulcers, associated with NSAID drug therapy).

Japan

We were the second fastest growing major pharmaceutical company in 2004, ending the year ranked 13. Sales reached $1,430 million, up from $1,189 million, driven by the strongly performing oncology portfolio of *Arimidex*, *Casodex*, *Zoladex* and *Iressa*, together with good growth from *Losec*. Overall, underlying sales grew by 11% despite the impact of the biennial government price cut which limited market growth to 2%.

In December 2004, the Pharmaceuticals Affairs Council of the Japanese Health Ministry granted conditional approval of *Crestor* with a dose range of 2.5-20mg, as described on page 12.

Asia Pacific (excluding Japan)

Overall sales grew by an impressive underlying rate of 18% to $1,155 million and the region represents an area of high growth potential. In Australia, the largest market in the region, sales of $450 million gave us a ranking of fourth among prescription drug companies. In China, we are the largest

multi-national prescription drug company (third ranking overall), and with growth of 30%, we are one of the fastest growing pharmaceutical companies (source: the Hong Kong Association of the Pharmaceutical Industry). In South Korea and Taiwan, we gained further momentum following targeted investment in these markets. In South East Asia, we enjoyed average underlying growth of 22%.

Products driving growth in the region were *Nexium* (+45%), *Iressa* (+209%), *Atacand* (+41%), *Symbicort* (+77%) and *Seroquel* (+43%). *Crestor* has made a good start, gaining significant market share in a number of countries.

Latin America

We are the fastest growing major pharmaceutical company in the region, with underlying growth of 27%. In Mexico, the largest market in the region, sales reached $206 million, with growth of 19%. In Brazil we achieved underlying growth of 34% and we gained further momentum in Venezuela with underlying growth of 66%. In each of Argentina, Colombia, Chile, Uruguay and Peru our growth significantly out-stripped overall market growth.

Nexium showed a very strong performance across the region with sales growing by 40%. *Crestor* has now been launched in all markets in Latin America, has already achieved a market share of 17% in Mexico and is making rapid gains in Brazil, Venezuela, Argentina and Colombia.

Middle East

During 2004 we approved an investment of $40 million for the construction of a tablet manufacturing plant in Egypt. This investment is part of our expansion strategy and commitment to emerging markets. The plant will make products in our cardiovascular, oncology and neuroscience portfolios.

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Development Pipeline at 27 January 2005

Compound	Mechanism	Areas under investigation	Phase				Estimated filing date	
			PC	1	2	3	MAA	NDA
Cardiovascular								
NCEs								
Exanta	thrombin inhibitor	prevention of VTE					Launched	Filed*
Exanta SC formulation	thrombin inhibitor (sc)	prevention of VTE					Launched	>2007
Galida	PPAR agonist	diabetes /metabolic syndrome					2007	2007
AZD6140	ADP receptor antagonist	arterial thrombosis					>2007	>2007
AZD7009	anti-arrhythmic IV	AF conversion					>2007	>2007
AZD7009	anti-arrhythmic oral	AF maintenance					>2007	>2007
AZD9684	CPU inhibitor	thrombosis					>2007	>2007
AZD0837	thrombin inhibitor	thrombosis					>2007	>2007
AZD7806	IBAT inhibitor	dyslipidaemia					>2007	>2007
AZD4619		dyslipidaemia					>2007	>2007
AZD6610		dyslipidaemia/diabetes					>2007	>2007
AZD8294		dyslipidaemia					>2007	>2007
AZD8677		dyslipidaemia/diabetes					>2007	>2007
AZD8450		dyslipidaemia					>2007	>2007
AZD6370		diabetes					>2007	>2007
Line Extensions								

Atacand	angiotensin II antagonist	CHF outcomes (CHARM study)	Approved	Filed
		diabetic retinopathy	>2007	>2007
Crestor	statin	atheroma	2H 2006	2H 2006
		outcomes CHF	>2007	>2007
		outcomes renal	2007	2007
Seloken/Toprol-XL	beta blocker	HCTZ combination		3Q 2005
Exanta	thrombin inhibitor	prevention of stroke in AF	Filed	Filed*
		treatment of VTE	Filed	>2007
		arterial/post MI	>2007	>2007

*Discussions are ongoing with the FDA to determine if there is now a realistic prospect of bringing *Exanta* to the US market. The NDA file remains open.

Gastrointestinal

NCEs

AZD0865	P-CAB	acid-related GI disease	2007	2007
AZD7371		functional GI disease	>2007	>2007
AZD3355	inhibitor of TLESR	GERD	>2007	>2007
AZD9343	inhibitor of TLESR	GERD	>2007	>2007
AZD5745		acid-related GI disease	>2007	>2007
AZD8081		functional GI disease	>2007	>2007

Line Extensions

Nexium	proton pump inhibitor	NSAID GI side effects symptom resolution	Promotable*	Filed
		parenteral formulation	Launched	Filed
		NSAID GI side effects ulcer prevention	Launched	Launched
		NSAID GI side effects ulcer healing	Launched	Filed
		extra-oesophageal reflux disease	>2007	>2007

*Authorities stated these symptoms were already captured within the GERD label. Text stating No clinical interaction with naproxen or rofecoxib was approved.

Infection

Line Extensions

Merrem	carbapenem antibiotic	skin and soft tissue infections		Filed

Neuroscience

NCEs

Cerovive	free radical trapping agent	stroke	2H 2006	2H 2006
AZD7371		overactive bladder	>2007	>2007
AZD8129 (AR-A2)	$5HT_{1B}$antagonist	anxiety/depression	>2007	>2007
AZD4282	NMDA antagonist	neuropathic pain	>2007	>2007
AZD3102		Alzheimer s disease	>2007	>2007
AZD1080		Alzheimer s disease	>2007	>2007
AZD9272		neuropathic pain	>2007	>2007
AZD2327		anxiety	>2007	>2007
AZD5904		multiple sclerosis	>2007	>2007
AZD6538		neuropathic pain	>2007	>2007

Line Extensions

Seroquel	$D_2/5HT_2$ antagonist	sustained release	1H 2006	1H 2006
		bipolar maintenance	2007	2007
		bipolar depression	2007	1H 2006

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Compound	Mechanism	Areas under investigation	Phase				Estimated filing date	
			PC	1	2	3	MAA	NDA
Oncology								
NCEs								
Iressa	EGFR-TKI	NSCLC					Withdrawn	Launched
ZD6474	angiogenesis inhibitor (VEGFR-TKI)	solid tumours					>2007	>2007
ZD4054	endothelin A receptor antagonist	solid tumours					>2007	>2007
AZD2171	angiogenesis inhibitor (VEGFR-TKI)	solid tumours					>2007	>2007
AZD3409	farnesyl-transferase inhibitor	solid tumours					>2007	>2007
AZD0530	SRC kinase inhibitor	solid tumours and haematological malignancies					>2007	>2007
AZD5438	selective cyclin dependent kinase inhibitor	solid tumours					>2007	>2007
AZD6244	MEK inhibitor	solid tumours					>2007	>2007
ZD6126	vascular targeting agent	solid tumours					>2007	>2007
AZD4440	vascular targeting agent	solid tumours					>2007	>2007
AZD9935	angiogenesis inhibitor (VEGFR-TKI)	solid tumours					>2007	>2007
AZD0424	SRC kinase inhibitor	solid tumours					>2007	>2007
AZD1152	aurora kinase inhibitor	solid tumours and haematological malignancies					>2007	>2007
AZD4769		solid tumours					>2007	>2007
AZD3841		solid tumours					>2007	>2007
AZD8931		solid tumours					>2007	>2007

Line Extensions

Faslodex	oestrogen receptor antagonist	1st line advanced breast cancer	>2007	>2007
Iressa	EGFR-TKI	head and neck cancer*	2H 2006	2H 2006
		breast cancer*	>2007	>2007
		colorectal cancer*	>2007	>2007

* Under review

Respiratory and Inflammation

NCEs

AZD9056	ion channel blocker	rheumatoid arthritis	>2007	>2007
AZD9056	ion channel blocker	osteoarthritis	>2007	>2007
AZD8309	chemokine receptor antagonist	rheumatoid arthritis	>2007	>2007
AZD8955	collagenase inhibitor	osteoarthritis	>2007	>2007
AZD8309	chemokine receptor antagonist	COPD	>2007	>2007
AZD3778	chemokine receptor antagonist	asthma/rhinitis	>2007	>2007
AZD9056	ion channel blocker	COPD	>2007	>2007
AZD3342	protease inhibitor	COPD	>2007	>2007
AZD6067	protease inhibitor	COPD	>2007	>2007
AZD2098		asthma	>2007	>2007
AZD1981		asthma	>2007	>2007
AZD0902	ion channel blocker	rheumatoid arthritis	>2007	>2007
AZD6703		rheumatoid arthritis	>2007	>2007
AZD6357		osteoarthritis	>2007	>2007
AZD7928		COPD	>2007	>2007
AZD2914		COPD	>2007	>2007
AZD2392		asthma/rhinitis	>2007	>2007

AZD1744	asthma/rhinitis		>2007	>2007
AZD5672	rheumatoid arthritis		>2007	>2007

Line Extensions

Symbicort Turbuhaler	inhaled steroid/fast onset, long-acting beta$_2$ agonist	single therapy for asthma		2H 2005	
Symbicort pMDI	inhaled steroid/fast onset, long-acting beta$_2$ agonist	asthma		Filed	2Q/3Q 2005*
		COPD		Filed	2007

* The FDA has identified some issues associated with the inhaler that require the generation of additional chemistry and manufacturing data or possible modification of the device in order to achieve approval.

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

Compounds in development are displayed by phase.

Abbreviations:

5HT – 5-hydroxytryptamine (serotonin)
5HT$_{1B}$ (– 1B subtype of 5HT receptor)
5HT$_2$ (– 2 subtype of 5HT receptor)
ADP – adenoside diphosphate
AF – atrial fibrillation
CHF – congestive heart failure
COPD – chronic obstructive pulmonary disease
CPU – carboxy peptidase-U
D$_2$ (– 2 subtype of dopamine receptor)
EGFR-TKI – epidermal growth factor receptor-tyrosine kinase inhibitor
GERD – gastro-oesophageal reflux disease
GI – gastrointestinal
H – half year
HCTZ – hydrochlorothiazide
IBAT – ilial bile acid transport
IV – intravenous
MAA – marketing authorisation application (Europe)
MEK – mitogen activated (extra-cellular signal-regulated kinase) kinase
MI – myocardial infarction
NCE – new chemical entity
NDA – new drug application (US)
NMDA – N-methyl-D-aspartate
NSAID – non-steroidal anti-inflammatory drug
NSCLC – non-small cell lung cancer
P-CAB – potassium-competitive acid blocker
PC – pre-clinical: candidate drug accepted for development but not yet administered to man
pMDI – pressurised metered dose inhaler
PPAR – peroxisome proliferator-activated receptor
Q – quarter
sc – subcutaneous
TLESR – transient lower oesophageal sphincter relaxations
VEGFR-TKI – vascular endothelial cell growth factor receptor-tyrosine kinase inhibitor
VTE – venous thromboembolism
>2007 – not earlier than 2008

Discontinued projects:
AZD4750 – multiple sclerosis
AZD5455 – anxiety
AZD0328 – Alzheimer's disease
Seroquel – granules
AZD2858 – Alzheimer's disease
ZD0947– overactive bladder
AZD0902 – COPD
AZD0303 – thrombosis

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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.

The consequences of the strong drive to increase productivity are becoming evident in the size of the early development portfolio. During 2004, 18 CDs were selected (15 in 2003 and 11 in 2002). At the end of 2004, there were 31 projects in the pre-clinical phase and 17, 17 and 25 projects in clinical phases 1, 2 and 3 respectively.

AstraZeneca employs around 11,900 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 2004, our R&D investment totalled $3.8 billion.

R&D remains an integrated, project-driven organisation. Our approach is therapy arealed 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.

Global knowledge expertise is recognised as a key competitive advantage for AstraZeneca. An R&D information and knowledge management initiative has introduced a knowledge sharing system, initially directed towards supporting our global R&D staff and their internal partners.

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

Discovery

In Discovery our highly skilled scientists work together across boundaries to exchange ideas, to promote best practice and to maximise the opportunities that are offered by our size and global reach. We focus on finding novel medicines for targeted unmet medical needs. This is supported by other specialised Discovery groups in Safety Assessment, Process R&D and Global Science & Information who also support the projects in their progress through Development and lifecycle management.

Our core priority is to support increased productivity in R&D. This includes improving the quality of biological targets and chemical leads, so that we can expect reduced later stage clinical product attrition. Discovery-Medicine (the partnership between clinical medicine and basic science) is embedded in the organisation. There are many examples where this initiative has helped us gain a better understanding of human diseases and the suitability of future drugs to prevent and treat those diseases. We also continue to introduce, earlier in the process, more stringent and, where possible, high throughput testing of safety and drug metabolism/pharmacokinetics, so that CDs chosen for development are more likely to succeed.

Our Global Science & Information group supports all research areas with skills in compound management, structural chemistry, bio-imaging, transgenics, protein science and information science and informatics.

We continue to invest in R&D facilities. New or upgraded laboratory facilities were opened in 2004 in Sweden, the UK and the US. Ongoing training and development of our highly skilled employees continue.

Development

People in our Development organisation specialise in clinical research, regulatory affairs and pharmaceutical development. They work globally in therapy area-led product teams that bring together all the relevant functional skills and experience needed for the robust, rapid progress of new medicines and the management of development risks.

Our focus in 2004 was to progress regulatory filings for *Exanta*, to support the continued launches of *Crestor* and *Iressa*, and to make regulatory submissions for new uses that broaden the claims or

geographic coverage of *Nexium*, *Symbicort* and *Atacand*. In 2004, the phase 3 programmes for *Cerovive* and *Galida* have continued to progress as planned. Progression of the early development portfolio has resulted in six projects achieving positive proof of principle in clinical studies during 2004.

To enhance productivity during 2004, we continued to focus on simplifying the processes for delivery of clinical trial data while maintaining the flexibility of a global organisation. A new clinical organisational structure was announced in October 2004 to support implementation of these new working practices. We have also continued to progress the operation of e-based clinical and regulatory systems that significantly increase the speed of access to data worldwide and reduce regulatory file preparation and submission timelines. In January 2005, following a year where there have been a number of disappointments, a new Executive Director was appointed with responsibility for Development as part of an accelerated significant programme of change to review our pipeline and optimise the contribution of our Development and Regulatory functions.

Collaborations

To complement our in-house R&D capabilities, over 250 new collaborations have been entered into in 2004 with leading academic centres and biotechnology companies, bringing the total number of active R&D collaborations and agreements to more than 1,700.

We entered into a strategic alliance with Cambridge Antibody Technology (CAT) with the aim of discovering and developing human antibody therapeutics in inflammatory disorders. The five year collaboration includes a minimum of 25 programmes to be initiated in the discovery phase and following the completion of the phase, CAT and AstraZeneca may each elect to continue funding programmes into development.

Other examples of external collaborations include those with Abgenix Inc., Sumitomo Pharmaceuticals Co. Ltd., NeoGenesis Pharmaceuticals, Inc., Cytokinetics, Inc., Biosignal Inc., Array Biopharma Inc., Astex Technology Ltd, BG Medicine (Beyond Genomics Inc.), Dyax Corp., Shanghai Jiaotong University, Procardis, Griffith University, the University of Dundee and Institut Curie.

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Commercialisation and Portfolio Management

AstraZeneca continues to have one of the most competitive portfolios of marketed products in the pharmaceutical industry. Maintaining the quality of this portfolio and of our development pipeline of new products requires careful prioritisation both to manage the progression of promising compounds from development to market place and to maximise the value of high potential marketed products. We are committed to organic growth, but in common with other leading pharmaceutical companies, our licensing activities seek to bring in new products and/or technologies and to support growth products in a cost-effective manner.

Product Strategy & Licensing (PS&L), while working closely with R&D and our major marketing companies, leads the commercial aspects of drug development and co-ordinates global market strategy. This includes selecting the right products and projects for investment, developing effective marketing platforms in time for new product launches and directing the creation and delivery of product marketing strategies that successfully align global and national plans.

To ensure the success of our medicines, we aim to address unmet medical needs, find novel solutions, minimise technical risk and maximise commercial opportunity. We have clearly defined lifecycle management programmes for all our products, which maximise not just the commercial potential of the brands, but also the value they bring to patients lives. In addition, our customer base has broadened over the past year and our marketing programmes have widened accordingly to take account of every aspect of building global brands. This includes working with, among others, patient advocacy groups, caregivers, opinion leaders and pharmacists.

Target product profiles (TPPs) for each new product are clearly defined at a very early stage in Discovery in order to set parameters for R&D activity and to help shape the marketing strategy. The profile is based on our insight into the needs in the market place and the drivers behind recommending, prescribing, paying for and taking the medication. Among the factors considered in developing a TPP are product features and benefits, medical and health outcomes information, market positioning, demonstration of value and the competitive environment. At each major stage in

development, the product is tested against this target profile and is only prioritised for further investment if it meets or exceeds the target.

Where appropriate, we exploit internet strategy and marketing technologies to facilitate and enhance our commercial activities. Growing numbers of doctors and patients actively seek information from us via the internet and, where allowed, we are able to share knowledge, best practice and expertise via this channel.

Direct and timely communication via the internet facilitates some of the important goals for the organisation such as supporting our sales efforts; augmenting our brands; maintaining and building longer term relationships; and ensuring appropriate use of our products. Internet services continue to grow in diversity and value to our customer groups, requiring us to monitor and evaluate new techniques and technology to achieve our business objectives and ensure ongoing competitiveness. AstraZeneca is recognised as one of the industry leaders for online marketing and communication to customers.

We have undertaken a number of consumer initiatives to increase disease awareness and fully recognise the importance of patients and patient groups in making healthcare choices across the globe. Drug and disease physician and patient education modules developed across our therapy areas have been deployed internally and externally to great effect and we continue to seek to leverage these resources across a wider group of stakeholders, particularly where first-in-class products are reaching our markets and demand for such education is high.

Internet-enabled processes have brought efficiency and effectiveness gains across R&D and commercial activities, facilitating the rapid sharing and distribution of information within and outside the organisation. Additionally, a number of internet-enabled sourcing projects are enhancing our purchasing practices and delivering clear, measurable value.

As part of our commitment to exploring all the ways in which we can bring benefit to patients, we are expanding our thinking beyond medicines to include a focus on ways in which we can help them get access

to the information and services they need. This includes IT collaborations that will aim to deliver innovative channels for providing patients with information about their treatment and/or their disease. Through closer partnership with patients, we aim to build our understanding of their needs and how we can best respond.

Our products are marketed primarily to physicians (both general and specialist) as well as to other healthcare professionals. Marketing efforts are also directed towards explaining the value and the therapeutic benefits of our products to governments and healthcare buying groups, for example, managed care organisations in the US, trust hospitals and budget-holding medical groups in the UK and other organisations which pay for healthcare costs in various countries. In the US, we invest a significant amount of money in direct-to-consumer (DTC) advertising campaigns for certain of our products (notably *Nexium* and *Crestor*). These DTC efforts are part of a comprehensive and, we believe, valuable campaign to educate consumers about certain conditions and potential treatment options. Research among physicians supports our view that DTC advertising provides this educational value to consumers.

AstraZeneca s principal competitors are other international, research-based pharmaceutical and biotechnology companies which also sell branded, patent-protected, prescription pharmaceuticals.

Following patent expiry, our products also compete with generic pharmaceuticals. Competition with generic pharmaceuticals is principally on price since generic pharmaceutical companies typically incur only limited R&D costs compared to those of research-based companies such as AstraZeneca.

Our ability to maintain and enhance our competitive position in our chosen therapy areas depends mainly on our development of new, innovative, cost-effective products from our R&D and in-licensing activities, the manufacture and supply of products to high quality standards and the effective marketing of products to our global customer groups.

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Supply and Manufacturing

With 30 manufacturing sites in 20 countries and around 15,000 employees worldwide, our Operations organisation provides secure, high quality, cost-effective supply of AstraZeneca s product range globally. We measure our performance using four key metrics: customer service, supply capability, cost efficiency and licence to operate.

Customer service

The fast and effective introduction of new products is key to success. Our supply chains are designed to maximise flexibility. For example, the global roll-out of *Crestor* continued, European *Exanta* launches were supported, and all major markets completed the launch of *Zoladex Safesystem* which is designed to protect against needlestick injuries when handling the injectable *Zoladex* therapy. With a few temporary exceptions, major products and line extensions were successfully supported with supplies available to meet market demand.

Supply capability

Our strategy remains to operate a small number of sites for the manufacture of active ingredients and combine it with effective use of outsourcing. AstraZeneca has active ingredient sites in the UK, Puerto Rico, Sweden and France and a bulk drug purification plant in Germany. Around 1,600 people are employed in active pharmaceutical ingredient supply.

Principal formulation sites for tablets and capsules are in six countries - the UK, Sweden, Puerto Rico, France, Germany and the US. There are also major formulation sites for the global supply of parenteral and inhalation in 2004. New plant authorised included formulation capacity for *Symbicort* in France, for *Pulmicort* in the US and for *Nexium* and *Seloken/Toprol-XL* in Sweden.

AstraZeneca s global purchasing policies and processes together with our business interruption risk management (BIRM) process are aimed at ensuring the supply of raw materials and other key supplies, all of which are purchased from a range of suppliers. The BIRM process systematically examines a range of risk scenarios to global supply, such as disasters that remove supply capability or the unavailability of key raw materials and ensures that these risks are mitigated by the implementation of contingency plans, including the appropriate use of dual or multiple suppliers and maintenance of appropriate stock levels. Although the price of raw materials may fluctuate from time to time, our global purchasing policies seek to avoid such fluctuations becoming material in our business.

Cost efficiency

2004 saw the continued implementation of our new supply system which has demonstrated progressive benefits, with higher customer service levels, reduced manufacturing lead times and consequently reduced requirements for the build up of stock. The programme has now been substantially implemented throughout the supply network. In 2004, improvements in stock levels on mature products were partly offset by stock increases on launched products with exchange movements also increasing the view to focusing stock reductions to improve working capital utilisation.

The introduction of new purchasing category management proceeded throughout 2004 in key areas of spend to maximise value from external expenditure, and implementation will continue in 2005.

Licence to operate

We are committed to delivering a secure basis for assured product quality that ensures both the safety and efficacy of our medicines. As part of this, the outcomes of routine internal inspections as well as those by regulatory authorities are rigorously reviewed and, if required, actions are taken to further enhance compliance. Device presentations of inhalation products present manufacturing challenges and where appropriate, like other manufacturers, we keep these under review with relevant regulators. The results of all external inspections carried out during 2004 were satisfactory and we did not experience any delays to approvals due to regulatory compliance issues at our sites or those of our contractors.

Safety, health and environment (SHE) operating standards are increasingly stringent with regulators placing particular emphasis on environmental issues and the safety of chemicals. AstraZeneca s manufacturing sites operate under various regulatory and licensing regimes and we are focused on meeting all regulatory requirements and current good practice standards. There are currently no environmental issues that constrain AstraZeneca from fully utilising any sites. The Company continues to track, participate actively in, and pursue internal initiatives

products in Sweden, France and the UK. Packaging is undertaken at a large number of locations, both at AstraZeneca sites and at contractors facilities, located close to our marketing companies to ensure rapid and responsive product supply. Around 12,400 people are employed in formulation and packaging.

Process improvements, additional capacity investments and the effective use of external contractors ensure the secure and effective supply of our products. As part of our overall risk management, we carefully consider the timing of investment to ensure that secure supply chains are in place for our products.

Capital expenditure on supply and manufacturing facilities totalled $352 million

financially reported figures.

Cost efficiencies are also driven by continuous review of our manufacturing assets to make sure that they are being used most effectively, whilst preserving the flexibility we need to respond to fluctuations in demand. Our facility in Karlskoga (Sweden) was sold during 2004 and we will continue to make further adjustments to our manufacturing base to ensure optimum utilisation of production facilities.

The new supply system has also increased the focus on managing costs throughout the product lifecycle. Product supply chains are being modelled with a view to targeting cost of goods reductions through improving yields, undertaking process changes and adjusting buying patterns to reduce material costs. Stock levels and stock turns are also being modelled for major products with a

relating to, international research and policy developments associated with emerging environmental, health and safety policy matters such as pharmaceuticals in the environment , chemical control regulations and global climate change. It is possible that we could incur capital or operational costs in connection with future voluntary activities or regulatory developments relating to these issues including, for example, process or equipment changes associated with wastewater quality, raw material substitutions, green chemistry initiatives or energy efficiency. We are addressing these matters proactively and they are not expected to have a material impact on the Company s competitive or financial position.

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We are making steady progress against our targets for the reduction of waste and energy usage and the overall level of accidents with injury is falling. However, sadly an employee died in an accident at one of our manufacturing locations during the year. When any accidents occur, we use a range of investigation procedures to help us understand the causes and avoid repetition. Our aim for continuous improvement includes learning from incidences of non-compliance and sharing best practice to further promote high standards.

Further information and statistics about our SHE performance can be found in the separate Corporate Responsibility Summary Report 2004 or on our website: astrazeneca.com.

Main Facilities

AstraZeneca owns and operates numerous production, marketing and R&D facilities worldwide. Our corporate headquarters are in London, UK and our R&D headquarters are in Södertälje, Sweden.

Our principal R&D facilities are in the UK (Alderley Park and Charnwood); Sweden (Lund, MöIndal and Södertälje); the US (Boston, Massachusetts and Wilmington, Delaware); Canada (Montreal, Quebec); and India (Bangalore). Other R&D activity is carried out at Macclesfield and Avlon in the UK, Reims in France and Osaka in Japan.

Out of a total of 30 manufacturing sites in 20 countries, our principal manufacturing facilities are in the UK (Avlon and Macclesfield); Sweden (Snäckviken and Gartuna, Södertälje); the US (Newark, Delaware and Westborough, Massachusetts); Australia (North Ryde, New South Wales); France (Dunkirk, Monts and Reims); Germany (Plankstadt and Wedel); Italy (Caponago); Japan (Maihara) and Puerto Rico (Canovanas, Guayama and Carolina).

Bulk drug production is concentrated in the UK, Sweden, France and Puerto Rico.

Substantially all of our properties are held freehold, free of material encumbrances and we believe such properties are adequate for their purposes.

Other Businesses

Astra Tech

Astra Tech is engaged in the R&D, manufacture and marketing of medical devices and implants for use in healthcare, primarily in urology and odontology, as well as in surgery and diagnostic radiology. Astra Tech has a leading position in several countries in Europe and is expanding its operations in key markets, particularly in the US.

All products showed good sales growth, in particular the Dental Implant System, which is gaining market share in several key markets. Further investments have been made in R&D, clinical research and new production facilities to strengthen the product portfolio and, in the US, in sales and marketing.

Salick Health Care

Salick Health Care (SHC) is a leading provider of outpatient oncology management and consulting services. Ownership of SHC provides AstraZeneca with a unique window on the provider sector of the US oncology market and access to many opinion leaders in the field of oncology.

SHC manages full-service outpatient comprehensive cancer centres in affiliation with major teaching and community hospitals in California, Florida and New York and is affiliated with a large network of over 160 physicians, working in specialised areas such as haematology and medical, radiation and surgical oncology.

In 2004, SHC continued to perform well in its cancer centre management business with positive profit and cash contributions. We implemented a long term management agreement with

NYU Hospitals Center with the opening of a new 85,000 square foot cancer centre in Manhattan in July 2004. Focused on growth, SHC is actively pursuing consulting and management relationships in new markets in the US as well as exploring opportunities to bring its unique model of cancer care to the UK.

SHC also continued the development of its innovative clinical research network to improve patient care and cancer treatment. The SHC Research Network is conducting a growing number of centrally co-ordinated phase 2 and 3 clinical trials.

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Corporate Responsibility (CR)

The trust and confidence of all our stakeholders, together with our reputation, are among our most valuable assets. Along with our commitment to competitiveness and performance, we will continue to be led by our core values to achieve sustainable success.

Management

Good corporate responsibility depends on the right level of commitment from all employees, led by the AstraZeneca Board and Senior Executive Team, who approve the strategic direction, and our senior management, who are accountable for the development and implementation of appropriate programmes in their areas of responsibility. Based on the global CR policy, local implementation programmes are required to take account of regional, site or functional priorities and objectives. Individually, everyone at AstraZeneca has a responsibility to integrate CR considerations into their day-to-day decision-making, actions and behaviours.

The common platform that supports this effort worldwide includes our Group CR Policy, Group CR Standards and Global CR Priority Action Plan, which together provide the framework for understanding and managing the challenges and opportunities associated with our responsibility.

We are making progress, but there is more work to do to ensure that CR is consistently embedded throughout the organisation and actively interpreted and managed at a local level. An important step forward has been the creation of national CR committees in the US, the UK and Sweden where more than 60% of our employees are

We have also begun to integrate CR into our leadership development programmes and during the year we launched an intranet site dedicated to providing managers with the tools and guidance they need to put CR into practice at a local level.

Evaluating performance

We have for some time had processes in place for monitoring our economic, environmental, safety and health performance. More recently, we have been focusing on developing key performance indicators (KPIs) in other areas of social responsibility. During 2004, we established new KPIs for animal use and welfare, and for marketing and sales practices, which will be introduced in 2005 to promote a consistent approach to monitoring performance globally. We continue to explore the ways in which we can meaningfully benchmark our performance in the area of social responsibility.

Corporate governance

An essential part of our corporate responsibility is to continue to operate to high standards of corporate governance. Auditing compliance is a fundamental part of this. Our Group Internal Audit function (GIA) works to review, among other things, compliance with laws, regulations and Group policies. During 2004, 42 of our GIA audits focused on marketing and sales practice. Such audits are an effective tool in helping to drive consistent standards of practice worldwide.

Alongside the work of GIA, we continue to build on the experience of our long-standing SHE audit programme to include aspects of CR

Product donations and patient assistance programmes

Our product donations and patient assistance programmes make products available free of charge or at reduced prices. In 2004, our commitment in this area totalled $870 million valued at average wholesale price.

Community support

We aim to make a positive contribution to our local communities through charitable donations and sponsorships that help to make a difference. In particular, we make contributions that are consistent with our business of improving health and quality of life and which promote the value of science among young people. In 2004, our spend on community support totalled $20.7 million, including charitable donations of over $5 million excluding the $2.1 million tsunami disaster relief support.

More information about our commitment to CR, our priority action areas and our 2004 performance in these areas is available in the separate Corporate Responsibility Summary Report 2004 and on our website: astrazeneca.com/responsibility.

located. National CR action plans, including local priorities and objectives are now in place in these three cornerstones of our global presence.

Another significant move was our decision in 2004 to formally integrate CR into the personal targets and performance reviews of all employees, including AstraZeneca s Senior Executive Team and senior management. This will further support the integration of CR considerations into business strategy development and everyday business thinking.

not previously covered elsewhere. Our rolling programme of site audits included 24 in 2004, all of which covered CR.

Priority action planning

Stakeholder expectations are constantly evolving and we review annually our Global Priority Action Plan to ensure that it continues to address the issues relating to our business that affect or concern society. We use internal risk assessment, external benchmarking and stakeholder dialogue to inform our thinking on what needs to be included in the Plan. In 2004, we added Clinical Trials and Pharmaceuticals in the Environment to the Plan.

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Industry Regulation

Our products are subject to numerous regulations concerning their safety and efficacy. In many cases, governments also fix their price and/or restrict access to reimbursement. The degree and scope of regulation varies according to the product and countries concerned. Regulations governing prescription pharmaceuticals are stringent and manufacture and marketing are normally conditional upon regulatory approval. Registration processes are complex and time-consuming and involve significant expenditure. Regulation is concerned not only with a product s chemical composition, but also with matters such as manufacturing, handling, packaging, labelling, distribution, promotion and marketing.

AstraZeneca routinely participates in various industry associations and other bodies which, among other things, seek to ensure that those implementing legislation and regulations affecting pharmaceutical companies are fully informed as to their impact.

Product regulation

Before a pharmaceutical product is approved for marketing, it must undergo exhaustive and lengthy clinical trials. The process of developing a new pharmaceutical product, from discovery to launch in the market, can take up to 12 years, but this period varies considerably in different cases and countries. The time taken from submission of an application for marketing approval to launch of the product is typically one to two years.

After a product has been approved and launched, it is a condition of the product licence that all aspects relating to its safety, efficacy and quality must be kept under review. Depending on the country, fines and other penalties may be imposed for failure to adhere to the conditions of product licences. In extreme cases, the product licence may be revoked resulting in withdrawal of the product from sale. Promotional and marketing activities are also tightly controlled by regulations and self-regulating codes of ethical marketing practices.

During the marketing of a product, strict procedures must be in place to monitor, evaluate and report any potential adverse reactions. Where adverse reactions occur or it is judged that they may occur, changes may be required to prescribing advice and

to the product licences. In extreme cases, the product licence may be revoked resulting in withdrawal of the product from sale.

Manufacturing plants and processes are subject to periodic external inspection by regulators as part of their monitoring procedures to ensure that manufacturers are complying with prescribed standards of operation.

Price regulation

Prescription medicines are subject to government controls on price and reimbursement which operate in most countries in which we sell our products. This can result in large price differentials between markets, which may be further aggravated by currency fluctuations.

US

Currently, there is no direct government control of prices for non-government drug sales in the US. Federal legislation mandates minimum discounts to US government agencies purchasing drugs for the active military, military veterans and other selected populations. Providing these substantial discounts to the US government is also a condition for the manufacturers drugs to be reimbursed by state Medicaid programmes and an additional rebate is required if manufacturer price increases after 1990 exceed the increase in inflation.

In addition, certain states have taken action to require additional manufacturer rebates on Medicaid drug utilisation for the indigent population. State Medicaid programmes will continue to be a challenge to the market in the US. Innovative partnering opportunities have been established with select key states for several years, and new opportunities continue to be pursued, as appropriate. However, this becomes more difficult with each passing year.

The Medicare Prescription Drug, Improvement, and Modernisation Act of 2003 was signed into law in December 2003. The legislation makes drug discount cards available in 2004 and 2005. These will be replaced by a prescription drug benefit for Medicare beneficiaries in 2006. The Act also legalises importation of drugs from Canada if the US Secretary of Health and Human Services certifies that implementation will pose no additional safety risk and it will result in a significant reduction in cost to the American consumers. As with previous laws

with similar provisions, the US Secretary of Health and Human Services has not yet provided the required certification.

Europe

Most governments in Europe control the price and reimbursement of medicines after taking into account the medical, financial and social impact of a product. This budget-based approach reflects increasing constraints in overall healthcare spending. Governments increasingly require more assurance of value in their expenditures on medicines.

In several European countries, the pricing and reimbursement systems are being reviewed, with the aim of controlling and limiting drug budgets. This is an ongoing process that puts a downward pressure on pricing and reimbursement of medicines in Europe. One example of this is the increasing focus on, and support of generic versions of branded drugs, as seen in a number of countries such as France and Spain.

In Germany, so-called jumbo groups were introduced in support of a general aim to reduce spending on drugs, by calculating new and lower reimbursement price levels. These groups are formed around drug classes such as statins and PPIs. In the statin group, which includes branded as well as generic products, this has led to significant decreases in reimbursement levels for branded drugs, as the reference price levels that determine reimbursement have dropped.

Japan

There is formal central government control of prices in Japan. New product prices are determined primarily by comparison with existing product classes. All existing products are subject to a price review based on the market price at least every two years. In addition, products with generic competition are forced to further reduce prices by 4-6%. Regulations also include an overseas price referencing system, under which prices can be adjusted according to the average price of four major countries (the US, the UK, Germany and France). Generally, if the US pricing environment remains unchanged, these regulations are likely to have a positive impact on pharmaceutical prices in Japan.

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Intellectual Property

Product regulation: Astra Tech

Product registration and certified quality management systems form the basis of the regulatory environment relating to medical devices. In Europe, compliance with regulatory requirements involves the implementation and maintenance of a quality management system and, for certain products, a design dossier review. Medical devices in the US are regulated through a product registration requirement. Astra Tech continues to maintain a European and US compliant quality management system.

Product regulation: Salick Health Care (SHC)

The healthcare facilities to which SHC provides administrative and management services on behalf of certain hospitals are subject to extensive US federal, state and local legislation and regulations, such as those relating to the reimbursement and control of healthcare costs. The largest single component of SHC revenue continues to be fees that are affected by the reimbursement rates for healthcare services, which are set or regulated by federal or state authorities.

During 2004, AstraZeneca invested $3.8 billion in R&D activities. Obtaining adequate protection for the intellectual property associated with these activities continues to be a key business imperative. The range of protection includes patents, trade marks, design registrations, copyrights and internet domain name registrations.

Our policy is to apply for patent and/or other appropriate intellectual property protection for all of the inventions and innovations of significant commercial value, which arise from our drug discovery, development, manufacturing, marketing and other business activities. It is also our policy to apply for intellectual property protection for all inventions and innovations being created as a result of the investments in R&D throughout the AstraZeneca organisation.

This policy is designed to provide each of our new products with an effective portfolio of valid, enforceable patent and other intellectual property rights in all significant markets to protect against unauthorised competition during commercialisation. This shield of intellectual property rights extends to those areas of target identification, genomics and other research technologies in which we invest significant resources. The adequacy of the patent, design, trade mark and domain name portfolio for individual products is kept under review during product development, clinical evaluation and marketing so that, wherever possible, additional protection may be sought for new applications and other developments. The therapy area focus of our R&D operating model allows appropriate intellectual property strategies to be formulated and regularly updated from an early stage in product development.

We vigorously defend our intellectual property rights, including taking appropriate infringement action in various courts throughout the world.

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Financial Review

Introduction

The purpose of the Financial Review, which should be read in conjunction with the Operational Review on pages 11 to 36, is to provide a balanced and comprehensive analysis, including the key business factors and trends, of the financial performance of the business during 2004, the financial position as at the end of the year and the main business factors and trends which could affect the future financial performance of the business.

The key sections of the Financial Review are:

> Business background and major events affecting 2004.
> Key performance indicators.
> Results of operations summary analysis of year to 31 December 2004.
> Financial position, including cash flow and liquidity.
> Capitalisation and shareholder return.
> Financial risk management policies.
> Future prospects.
> Critical accounting policies and estimates.
> Off-balance sheet transactions, contingent liabilities and commitments.
> New accounting standards.
> International accounting.
> Sarbanes-Oxley Act section 404.

Additionally, in accordance with US requirements:

> Results of operations summary analysis of year to 31 December 2003.
> US GAAP information 2002-2004.

Business background and major events affecting 2004

The business background is covered in the Operational Review and Global Market Overview and describes in detail the developments in both our products and geographical regions. The following comments highlight how these and other factors affect our financial performance.

Our operations are focused on prescription pharmaceuticals and more than 97% of our sales are made in that sector. Sales of pharmaceutical products tend to be relatively insensitive to general economic circumstances in the short term. They are more directly influenced by medical needs and are generally financed by health insurance schemes or national healthcare budgets.

Our operating results in both the short and long term can be affected by a number of factors other than normal competition:

> The risk of generic competition following loss of patent exclusivity or patent expiry with the potential adverse effects on sales volumes and prices.
> The timings of new product launches which can be influenced by national regulators and the risk that such new products do not succeed as anticipated.
> The rate of sales growth and costs following new product launches.
> The adverse impact on pharmaceutical prices as a result of the regulatory environment. Although there is no direct governmental control on prices in the US, pressures from individual state programmes and health insurance bodies are leading to downward forces on realised prices. In other parts of the world, there are a variety of price and volume control mechanisms and retrospective rebates based on sales levels which are imposed by governments.
> Currency fluctuations, which can significantly affect our results. Our functional and reporting currency is US dollars as this is our single largest currency, but we have substantial exposures to other currencies, in particular, significant euro and

Japanese yen denominated income and sterling and Swedish krona denominated costs.

Over the longer term, the success of our research and development is crucial. In common with other pharmaceutical companies we devote substantial resources to R&D, the benefit of which emerges over the long term and carries considerable uncertainty as to whether it will generate future products.

The business events which were the most significant for our financial results in 2004 are as follows:

- Strong sales performances from our key growth products to $11,161 million (52% of sales), particularly in the second half of the year.
- Slowing rate of decline of patent expired products, again in the second half of the year.
- Growth of *Crestor* sales to $908 million, despite what we believe are unfounded allegations about safety.
- Following a period of high investment in selling and marketing in support of *Nexium* and *Crestor* in the first half of 2004, we have reduced our cost growth rate significantly in the second half of the year.
- The decision by the FDA not to approve *Exanta*, whilst not materially affecting sales in 2004, has led us to make provisions against product stocks, goodwill and other assets of $151 million.
- Similarly, the preliminary results of the ISEL study on *Iressa* reported in December 2004 have led to provisions against product stocks and manufacturing assets of $85 million.
- In the year, we disposed of our investment in the joint venture Advanta BV, realising an exceptional gain of $219 million.

Key performance indicators (KPIs)

The primary KPIs used by management to understand and manage the financial performance of the business include:

- The analysis of sales growth with products allocated to three groups; growth , patent expiry and base which allow us to understand how the business is regenerating itself in the short term.
- Trends in prescription volumes which give insights into the underlying

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Financial Review continued

Sales by therapy area (2004 and 2003)

	2004			2003	2004 compared to 2003	
	$m	Growth underlying $m	Growth due to exchange effects $m	$m	Growth underlying %	Growth reported %
Cardiovascular	4,777	653	214	3,910	17	22
Gastrointestinal	5,918	(278)	253	5,943	(4)	
Infection	539	33	30	476	7	13
Neuroscience	3,496	542	121	2,833	19	23
Oncology	3,376	437	196	2,743	16	23
Respiratory and Inflammation	2,583	176	146	2,261	8	14
Other pharma	177	10	15	152	7	17
Others	560	6	23	531	1	5
Total	**21,426**	**1,579**	**998**	**18,849**	**9**	**14**

Sales by growth, patent expiry and base products (2004 and 2003)

	2004			2003	2004 compared to 2003	
	$m	Growth underlying $m	Growth due to exchange effects $m	$m	Growth underlying %	Growth reported %
Growth*	11,161	2,476	441	8,244	30	35
Patent expiry**	2,521	(889)	189	3,221	(28)	(22)
Base	7,744	(8)	368	7,384		5

Total	**21,426**	**1,579**	**998**	**18,849**	**9**	**14**

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

** *Losec*, *Zestril* and *Nolvadex*

business growth, as opposed to invoiced sales which depend on the timing of wholesaler demand.

> Cost growth rates, through which we manage the cost base to ensure that it is growing appropriately in relation to sales.

> Operating profit margin progression over time, which demonstrates the overall quality of the business.

Financial growth rates in sales, costs and operating profit, both in US dollar and percentage terms, are not referred to specifically in the Financial Statements but, as indicated above, we use them extensively as part of our KPIs and, accordingly, include them in our discussions in both the Operating and Financial Reviews. In particular, we calculate underlying growth using constant exchange rates (CER), which is defined as a non-GAAP measure because, unlike actual growth, it cannot be derived directly from the information in the Financial Statements. This measure removes the effects of currency movements to focus on the changes in product sales and expenses driven by volume, prices and cost levels

relative to the prior period. However, we recognise that CER growth should not be used in isolation and, accordingly, we also discuss the comparable GAAP actual growth measures which reflect all the factors that affect our business in the reported performance sections of this document. Underlying CER growth is calculated by retranslating the current year performance at the previous year s exchange rates and adjusting for other exchange effects, including hedging.

Results of operations summary analysis of year to 31 December 2004

The tables on this page show our sales analysed both by therapy area and by growth/patent expiry/base products and operating profit for 2004 compared to 2003.

Reported performance

Our sales increased by 14% compared to 2003, representing a rise of $2,577 million from $18,849 million to $21,426 million. Operating profit increased by 16% from $4,111 million to $4,770 million.

Underlying performance

Sales

After excluding the effects of exchange, underlying sales for the full year increased by 9%. Global sales of key growth products* reached $11,161 million for the full year (up 30%) and now comprise 52% of total sales (compared to 44% in 2003). Patent expiry products** declined by 28%, recording sales in aggregate of $2,521 million in 2004, 12% of our total sales (compared to 17% in 2003). Sales of base products remained constant, although the relative percentage of total sales fell from 39% in 2003 to 36% in 2004.

In the Gastrointestinal therapy area, *Nexium* sales reached $3,883 million for the full year, up 15%. Sales in the US reached $2,716 million on strong growth in dispensed tablet volume (up 20%). Pricing was broadly neutral in its impact for the full year; the reported 10% sales growth rate in the US for the full year was lower than underlying growth as a result of wholesaler stock reductions. Sales outside the US increased 29% to $1,167 million.

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Operating profit (2004 and 2003)

	2004			2003	2004 compared to 2003	
	$m	Growth underlying $m	Growth due to exchange effects $m	$m	Growth underlying %	Growth reported %
Sales	21,426	1,579	998	18,849	9	14
Cost of sales	(5,150)	(421)	(260)	(4,469)	(9)	(15)
Other operating costs	(11,821)	(651)	(709)	(10,469)	(6)	(13)
Other operating income	315	91	24	200	5	58
Operating profit	**4,770**	**598**	**53**	**4,111**	**15**	**16**

Sales of Cardiovascular products increased by 17% for the full year, chiefly on sales of *Crestor* which totalled $908 million (including $543 million in US sales). In the US, market share has been volatile, as a result of episodic media coverage of challenges to the *Crestor* safety profile, despite mounting evidence amassed from clinical trials experience and thorough analysis of post-marketing surveillance reports supporting our view that the safety profile of *Crestor* is in line with that of other marketed statins. In late November 2004, US Senate hearings related to Merck s Vioxx fuelled news reports on *Crestor* and four other products, which has interrupted market share progress. In the week ending 14 January 2005, *Crestor* share of new prescriptions was 6.0%. Market share in the dynamic segment (new and switch patients) was 8.2%. We are determined to restore market share momentum, as we have done previously. In addition, discussions with the FDA are ongoing to determine whether there is a realistic prospect of bringing *Exanta* to the US market following the FDA s decision in October 2004 not to approve the product.

Oncology sales enjoyed strong growth, with a notable performance from *Arimidex* (up 48%). The disappointing results from a preliminary analysis of the ISEL study into *Iressa* patients survival had little impact outside the US on sales in 2004. In 2005 in the US, we anticipate a rapid reduction in new prescriptions and sales will be recognised on confirmed patient usage. While commercial prospects have certainly been reduced in Western markets, the positive results in patients of East Asian origin offer the prospect of a continuing successful business in these important markets.

Neuroscience also saw significant growth driven by *Seroquel* sales which increased by 33% to exceed $2 billion for the first time.

Symbicort sales growth of 32% to $797 million was the principal contributor to growth of 8% in Respiratory and Inflammation sales.

In the US, the Inventory Management Agreements (IMAs) entered into during 2004 have successfully reduced wholesaler stock volatility and by the end of the year wholesaler stocks were close to target levels. Over the year wholesaler stocks are estimated to have declined by around $150 million. Adjusting both 2004 and 2003 for net wholesaler stock movements, it is estimated that total sales growth for 2004 would increase from 9% to 11%.

We discuss the performances of the therapy areas and the individual products in those areas in more detail in the appropriate sections of the Operational Review.

Geographical analysis

Underlying sales growth in the US was 10%. However, growth for the full year was estimated to be 15% when adjusted for net wholesaler stock movements in 2003 and 2004. Increased sales of *Crestor*, *Seroquel*, *Nexium* and *Arimidex* more than offset a further $500 million decline in sales of *Prilosec* for the year.

Sales in Europe were up 3% for the full year, with increased volume partially offset by declining realised prices. The launch roll out for *Crestor* and good growth for *Nexium*