

# THERAPY AREA REVIEW

## PIPELINE BY THERAPY AREA

CARDIOVASCULAR	GASTROINTESTINAL	INFECTION	NEUROSCIENCE	ONCOLOGY	RESPIRATORY & INFLAMMATION
▲ NO CHANGE	❖ ADDITION	+	▶ NEW FILING		
				<i>Recentin</i> ▲	
		AZD8931 ▲		AZD6244 (ARRY-142886) <sup>1</sup> ▲	
		AZD7762 ▲	AZD0837 ▲		
		AZD8330 (ARRY-424704) <sup>1</sup> ▲	AZD1305 +	AZD2281 ▲	<i>Atacand</i> +
			AZD6370 +	AZD0530 ▲	<i>Atacand Plus</i> ▶
AZD6482 ❖		CAT-8015 ▲	AZD1656 ❖	AZD4877 +	<i>Crestor</i> ▲
AZD4017 ❖		MEDI-538 <sup>1</sup> ▲	AZD3355 ▲	AZD1152 +	<i>Onglyza</i> <sup>TM1</sup> ▶
AZD2066 ▲		AZD8055 ❖	CytoFab <sup>TM1</sup> ▲	AZD9056 ▲	<i>Brilinta</i> (AZD6140) ▲
AZD1386 ▲	AZD5904 ▲	AZD6918 ❖	EBV vaccine <sup>1</sup> ▲	AZD5672 ▲	<i>Crestor/Trilipix</i> <sup>TM1</sup> ▲
MEDI-534 ▲	AZD3241 ▲	AZD4769 ▲	AZD7295 ❖	AZD1981 ▲	<i>Dapagliflozin</i> <sup>1</sup> ▲
MEDI-560 ▲	AZD2066 ▲	Pneumococcal vaccine <sup>1</sup> ▲	AZD3480 <sup>1</sup> ▲	MEDI-528 ▲	<i>Motavizumab</i> ▶
MEDI-566 ▲	AZD6280 ▲	CAM-3001 ▲	AZD6765 ▲	CAT-354 +	<i>PN-400</i> <sup>1</sup> ▲
AZD9639 (MEDI-564) <sup>1</sup> ▲	TC-5619 <sup>1</sup> ▲	AZD8848 ❖	AZD1940 +	AZD9668 +	<i>Zactima</i> ▲
GMV vaccine ▲	AZD2516 ❖	AZD8566 ❖	AZD1386 +	AZD1236 +	<i>Recentin</i> ▲
MEDI-557 ▲	AZD1446 ❖	AZD8075 ❖	AZD2624 +	AZD3199 +	<i>Recentin</i> <sup>2</sup> ▲
MEDI-559 ❖	AZD7268 ❖	AZD5985 ❖	AZD2327 +	MEDI-563 +	ZD4054 ▲
			AZD7325 +	MEDI-545 +	
	PHASE I		PHASE II	PHASE III/REGISTRATION	LIFE-CYCLE MANAGEMENT
					<i>Seroquel</i> +
					<i>Seroquel XR</i> +
					<i>Seroquel XR</i> ▶
					<i>Seroquel XR</i> +
					<i>Seroquel XR</i> ▶
					<i>Seroquel XR</i> ▶
					<i>Iressa</i> ▶
					<i>Zactima</i> <sup>2</sup> ▲
					<i>Faslodex</i> ▲
					<i>Faslodex</i> ▲
					<i>Symbicort pMDI</i> ▶
					<i>Symbicort pMDI</i> ▲
					Unit Dose
					Budesonide <sup>1</sup> ❖

<sup>1</sup> Partnered product.  
<sup>2</sup> Orphan indication.  
<sup>3</sup> Moved from NCE to Life-cycle management portfolio.

This section contains further information about the therapy areas on which our efforts are focused: Cardiovascular, Gastrointestinal, Infection, Neuroscience, Oncology, and Respiratory and Inflammation. We describe the business environment, trends and other factors that have influenced our decision to focus on diseases in these six areas, our strategic objectives for each and our progress towards achieving these objectives. We include information about our marketed medicines and how they are designed to make a meaningful difference for patients, together with an overview of performance during the year. We also report in detail on the potential new products and product life-cycle developments in our pipeline that reflect our commitment to maintaining a flow of innovation that adds value for our shareholders and society.

Detailed information about relevant continuing litigation can be found in Note 25 to the Financial Statements from page 144.

## SALES BY THERAPY AREA (\$ MILLION)

### CARDIOVASCULAR

	08	07	06	GROWTH
	6,963	6,686	6,118	0%
				+5%
				+15%

### NEUROSCIENCE

	08	07	06	GROWTH
	5,837	5,340	4,704	+6%
				+10%
				+16%

### GASTROINTESTINAL

	08	07	06	GROWTH
	6,344	6,443	6,631	-4%
				-6%
				+4%

### ONCOLOGY

	08	07	06	GROWTH
	4,954	4,819	4,262	-2%
				+8%
				+12%

### INFECTION AND OTHER<sup>1</sup>

	08	07	06	GROWTH
	2,451	1,714	875	+41%
				+89%
				+4%

### RESPIRATORY & INFLAMMATION

	08	07	06	GROWTH
	4,128	3,711	3,151	+7%
				+12%
				+10%

<sup>1</sup> Includes *Synagis* and *FluMist* which were acquired in June 2007.

**2008 IN BRIEF**

- > *Crestor* sales up 26% to \$3.6 billion and *Crestor* is now approved in every EU country.
- > *Crestor* study demonstrates significant reduction in major cardiovascular events (44% compared to placebo in men and women with elevated hsCRP but low/normal cholesterol levels).
- > *Atacand* sales up 10% to \$1.5 billion.
- > Worldwide collaboration with Bristol-Myers Squibb to develop and commercialise dapagliflozin expanded to include Japan.
- > US submission for fixed dose combination of *Crestor* and Abbott's Trilipix™, for the treatment of mixed dyslipidaemia, anticipated for third quarter 2009.
- > *Toprol-XL* US sales down 70% for the full year.

**OUR MARKETED PRODUCTS**

**Crestor**<sup>1</sup> (rosuvastatin calcium) is a statin for the treatment of dyslipidaemia and hypercholesterolemia, and to slow the progression of atherosclerosis.

**Atacand**<sup>2</sup> (candesartan cilexetil) is an angiotensin II antagonist for the first-line treatment of hypertension and symptomatic heart failure.

**Seloken/Toprol-XL** (metoprolol succinate) is a once daily tablet for 24-hour control of hypertension and for use in heart failure and angina.

**Tenormin** (atenolol) is a cardioselective beta-blocker for hypertension, angina pectoris and other cardiovascular disorders.

**Zestril**<sup>3</sup> (lisinopril dihydrate), an ACE inhibitor, is used for the treatment of a wide range of cardiovascular diseases, including hypertension.

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

<sup>1</sup> Licensed from Shionogi & Co. Ltd.

<sup>2</sup> Licensed from Takeda Chemicals Industries Ltd.

<sup>3</sup> Licensed from Merck & Co., Inc.

**OUR STRATEGIC OBJECTIVE**

Backed by over 40 years' experience, AstraZeneca is a world leader in cardiovascular (CV) medicines. We aim to build on our strong position, focusing on the growth areas of atherosclerosis (hardening of the arteries), thrombosis (blood clotting), diabetes and atrial fibrillation.

**HYPERTENSION, ATHEROSCLEROSIS AND DYSLIPIDAEMIA**

High blood pressure (hypertension) and abnormal levels of blood cholesterol (dyslipidaemia) are well known to damage the arterial wall and thereby lead to atherosclerosis. CV events driven by atherosclerotic disease remain the leading cause of death in the western world. Lipid-modifying therapy, primarily statins, is a cornerstone of treating atherosclerotic risk. Within the lipid-modifying market, generics are taking a significant share of the market and it is anticipated that generic atorvastatin will be available late 2011. Recent studies of some competitor products created uncertainty about clinical efficacy leading to reduced sales of these products, whilst AstraZeneca's study (see below) provided positive data on the effect of rosuvastatin.

**OUR FOCUS****Our key marketed products**

Since its launch in 2003, our statin, *Crestor*, has continued to gain market share, based on its differentiated profile in managing cholesterol levels and its unique recent label indication for treating atherosclerotic disease. Following new approvals during 2008 in Germany, Spain, Poland, Norway and Malta, *Crestor* is now approved in every EU country.

Less than half of the people thought to have high levels of low-density lipoprotein cholesterol (LDL-C) 'bad cholesterol' get diagnosed and treated and of those people, only about half reach their physician's recommended cholesterol target using existing treatments. *Crestor* is the most effective statin in lowering LDL-C and the majority of patients reach their LDL-C goals using the usual 10mg starting dose. *Crestor* also produces an increase in high-density lipoprotein cholesterol (HDL-C) 'good cholesterol', across a range of doses. At its usual 10mg starting dose, *Crestor* has been shown, versus placebo, to reduce LDL-C by up to 52% and raise HDL-C by up to 14% with eight out of 10 patients reaching their lipid goals.

In the US, *Crestor* is also approved for use as an adjunct to diet for slowing the progression of atherosclerosis in patients with elevated cholesterol. *Crestor* is the only statin with an

atherosclerosis indication in the US which is not limited by disease severity or restricted to patients with coronary heart disease.

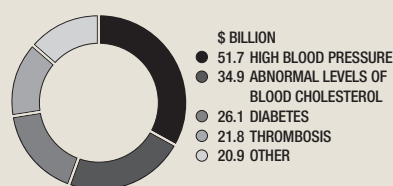
*Atacand*, first launched in 1997, is approved for the treatment of hypertension in over 100 countries and for symptomatic heart failure in over 70 countries. Angiotensin II antagonists are the fastest growing sector of the global hypertension market. Available as a once a day tablet, launches of the 32mg dosage strength outside the US continued during the year, and this dosage is now available in most Established Markets. In July 2008, we sought approval in Europe for two dose strengths of *Atacand Plus* (candesartan cilexetil/hydrochlorothiazide) which is a fixed combination of *Atacand* and the diuretic hydrochlorothiazide (HCTZ), indicated for the treatment of hypertension in patients who need more than monotherapy.

**Clinical trial developments**

GALAXY, our long-term global clinical research programme for *Crestor* investigating links between optimal lipid control, atherosclerosis and CV morbidity and mortality, has completed a number of studies involving over 69,000 patients in over 55 countries.

Data from the latest study, JUPITER, published in November 2008, demonstrated that *Crestor* 20mg significantly reduced major CV events (defined in this study as the combined risk of myocardial infarction, stroke, arterial revascularisation, hospitalisation for unstable angina, or death from CV causes) by 44% compared to placebo among men and women with elevated high-sensitivity C-reactive protein (hsCRP) (and other risk factors) but low to normal cholesterol levels. Results also showed that for patients taking *Crestor*, the combined risk of heart attack, stroke or CV death was reduced by nearly half, risk of heart attack was cut by more than half, risk of stroke was cut by nearly half and total mortality was significantly reduced by 20%. *Crestor* 20mg was well tolerated in nearly 9,000 patients during the course of the study. There was no difference between treatment groups for major adverse events, including cancer or myopathy. There was a small increase in physician reported diabetes consistent with data from other large placebo controlled statin trials.

GISSI-HF, an investigator sponsored study published in September 2008, evaluated *Crestor* 10mg and placebo in a heart failure population and confirmed the results of our CORONA study in showing no difference between the treatments in the primary endpoints of death or CV hospitalisation in patients with heart failure, over and above optimised heart failure treatment. Both studies

**THERAPY AREA WORLD MARKET (MAT/Q3/08)**

**CV is the single largest therapy area in the global healthcare market. World market value of \$155 billion.** CV disease remains the greatest risk to life for most adults, accounting for 17 million deaths worldwide each year. In the US, 21 million people suffer from diabetes and two in five people with diabetes still have poor cholesterol control, one in three have poor blood pressure and one in five have poor glucose control.

OUR FINANCIAL PERFORMANCE

	2008			2007			2006	2008 compared to 2007		2007 compared to 2006	
	Sales \$m	CER growth \$m	Growth due to exchange effect \$m	Sales \$m	CER growth \$m	Growth due to exchange effect \$m	Sales \$m	CER growth %	Reported growth %	CER growth %	Reported growth %
<i>Seloken/Toprol-XL</i>	807	(667)	36	1,438	(393)	36	1,795	(46)	(44)	(22)	(20)
<i>Crestor</i>	3,597	714	87	2,796	673	95	2,028	26	29	33	38
<i>Atacand</i>	1,471	123	61	1,287	99	78	1,110	10	14	9	16
<i>Plendil</i>	268	(18)	15	271	(20)	16	275	(7)	(1)	(7)	(1)
<i>Tenormin</i>	313	(17)	22	308	(24)	12	320	(6)	2	(8)	(4)
<i>Zestril</i>	236	(72)	13	295	(30)	18	307	(24)	(20)	(10)	(4)
Other	271	(34)	14	291	(14)	22	283	(12)	(7)	(5)	2
<b>Total</b>	<b>6,963</b>	<b>29</b>	<b>248</b>	<b>6,686</b>	<b>291</b>	<b>277</b>	<b>6,118</b>	<b>-</b>	<b>4</b>	<b>5</b>	<b>9</b>

were also consistent with the safety profile of *Crestor* in this vulnerable population. In both studies, outcome events appeared to be driven primarily by heart muscle failure rather than ischemic events where statins would be expected to have an effect.

Ongoing studies of *Crestor* include SATURN, which is designed to measure the impact of *Crestor* 40mg and atorvastatin (*Lipitor*<sup>™</sup>) 80mg on the progression of atherosclerosis in high-risk patients and is expected to report in 2011. AURORA, an outcomes study in patients with end stage renal disease is expected to present data by mid 2009.

The clinical programme (DIRECT) investigating the effect of *Atacand* (up to 32mg dosage) on retinopathy in hypertensive and normotensive diabetic patients completed in 2008 but failed to meet the primary endpoint. The results were published in September 2008.

**In the pipeline**

We continue the search for the next major therapy to reduce atherosclerotic risk. In collaboration with Abbott, we are developing a fixed dose combination of *Crestor* and Abbott's *Trilipix*<sup>™</sup> and are anticipating a US submission in the third quarter of 2009.

The combination of *Crestor* (a statin) and *Trilipix*<sup>™</sup> (a fibrate) is a potential new approach to helping patients with mixed dyslipidaemia achieve their treatment goals using a single capsule targeting all three major blood lipids: LDL-C, HDL-C, and triglycerides. Study results presented in 2008 showed that the combination of *Crestor* and *Trilipix*<sup>™</sup> provides greater benefit across multiple lipid parameters than monotherapy, with significantly improved HDL-C and triglycerides compared to statin therapy alone, and significantly improved LDL-C compared to *Trilipix*<sup>™</sup> alone.

We have stopped work on cholesterol absorption inhibitors because of failure to meet target product profiles.

**DIABETES**

The number of people affected by Type 2 diabetes continues to grow, driven by obesity in western markets. Type 2 diabetes is a chronic progressive disease and patients often require multiple medications to control their condition. There are a number of established oral generic and branded classes, such as sulfonylureas and thiazolidinediones (TZDs), however, newer classes, such as oral dipeptidyl peptidase-IV (DPP-IV) are entering the market successfully by offering effective blood sugar control and improved tolerability. Several new classes of drugs are in development in this area. The safety of anti-diabetic drugs continues to be an important focus of regulatory agencies and additional patient safety requirements for new medicines can be anticipated.

**OUR FOCUS**

In 2007, AstraZeneca and Bristol-Myers Squibb (BMS) announced the collaboration on a worldwide basis excluding Japan to develop and commercialise two compounds discovered by BMS (saxagliptin and dapagliflozin) being studied for the treatment of Type 2 diabetes. The development and commercial strategy for the two compounds is agreed jointly with BMS. In December 2008, AstraZeneca and BMS announced the extension of their collaboration to include dapagliflozin in Japan.

During 2008, AstraZeneca and BMS submitted a New Drug Application to the FDA and received the validation of a Marketing Authorisation Application to the European Medicines Agency for saxagliptin (*Onglyza*<sup>™</sup>). *Onglyza*<sup>™</sup> was specifically designed to be a selective inhibitor with extended binding to the DPP-IV enzyme, with dual routes of clearance. Phase III data published during 2007 and 2008 showed improved glycaemic control when assessed as a monotherapy, as well as when assessed in combination with metformin, sulfonylureas and TZDs.

Dapagliflozin is a potential oral anti-diabetic belonging to the novel class of sodium-glucose cotransporter 2 (SGLT2) inhibitors. It is selective and designed to be used both as monotherapy and in combination with other therapies for Type 2 diabetes. Phase IIb data demonstrated that, when compared with a placebo, 12 weeks treatment with dapagliflozin improved blood glucose parameters, resulted in weight loss and was well tolerated in patients with Type 2 diabetes. An extensive Phase III programme is ongoing.

Our activities in the GKA (glucokinase activator) area continued during 2008, and clinical studies in Phase II are ongoing. The GKA mechanism of action induces insulin release from the pancreas and reduces glucose output from the liver, with marked blood glucose reducing effects in situations of hyperglycaemia.

We also progressed our AZD4017 (11-βHDS inhibitor) project into early clinical testing which aims to increase insulin sensitivity and thereby induce better glycaemic control with potential beneficial effects also on body weight and blood lipids.

We have stopped work on cannabinoid receptor 1 inhibitors because the tolerability profile of these inhibitors was considered unacceptable.

In July 2008, AstraZeneca and Columbia University Medical Center announced a strategic research collaboration to develop novel therapeutics for Type 2 diabetes and obesity. The research will focus on discovering mechanisms and identifying new biological targets for successful and commercially viable treatments for these diseases.

## ARRHYTHMIA AND THROMBOSIS

Atrial fibrillation (AF) is the most common cardiac arrhythmia. Rhythm-control therapy to control the symptoms of AF is dominated by generic amiodarone, which is effective at maintaining patients in normal heart rhythm, but very poorly tolerated. There remains an unmet need for a safe and tolerated therapy with effective symptom relief. Two competitor products are in late development for use in AF and recent data from an outcome study of one of them versus placebo in AF patients showed clinical benefit in addition to symptom relief – the first time for an anti-arrhythmic agent.

Patients surviving an acute coronary event are at increased risk from further thrombosis and treatment guidelines advocate anti-platelet therapy. New guidelines issued in 2007 by the European Society of Cardiology for the treatment of acute coronary syndrome (ACS), have highlighted the negative consequences of drug induced bleeding in conjunction with the treatment of ACS, reinforcing the need for new anti-thrombosis drugs with acceptable bleeding risk.

During the year, two new anti-coagulants (dabigatran and rivaroxaban) were approved in Europe for use in prevention of deep vein thrombosis in conjunction with orthopaedic surgery. No Phase III data are yet available for the ability of new anti-coagulants to prevent strokes in AF, the major chronic indication for anti-coagulants, without the risks and repeated monitoring of warfarin or other vitamin K antagonists.

### OUR FOCUS

#### In the pipeline

*Brilinta* (ticagrelor AZD6140), the first reversible, oral, adenosine diphosphate (ADP) receptor antagonist, is being developed to reduce the risk of blood clots and thrombotic events in patients diagnosed with ACS. Ticagrelor is currently being studied in the Phase III PLATO clinical trial, involving over 18,000 ACS patients in 43 countries, to determine if it is superior to clopidogrel for reducing the risk of thrombotic events in ACS patients.

The effectiveness of AZD0837 (an oral, direct thrombin inhibitor) in preventing strokes and other embolic events in AF patients will be studied in more than 35 countries, using a once-daily extended release formulation that provides sustained anti-coagulation effect throughout the dosing interval. We anticipate starting these Phase III studies in 2009.

Our lead compound in the treatment of AF is AZD1305, a combined ion channel blocker, which has progressed into Phase IIa testing in both the IV and oral form.

## FURTHER INFORMATION

In December 2007, we filed patent infringement actions against seven generic drug manufacturers in the US following receipt of notices of their intent to market generic copies of *Crestor* before the 2016 expiry of our licensed patent covering the active ingredient in *Crestor*. In July 2008, we filed a patent infringement action against Teva Pharmaceuticals in the US following receipt of its notice of its intent to market generic copies of *Crestor* before the 2016 expiry of our licensed patent covering the active ingredient in *Crestor*. These eight cases are proceeding as a consolidated action in US District Court, District of Delaware.

Also in the US, Teva Pharmaceuticals (Teva's Israeli parent company) filed a patent infringement lawsuit concerning *Crestor* on 6 October 2008. Teva alleges that *Crestor* tablets infringe a recently re-issued Teva US patent that claims stabilised pharmaceutical compounds.

AstraZeneca has full confidence in its *Crestor* product and the intellectual property protecting it, and will vigorously defend and enforce it.

Further information is set out in Note 25 to the Financial Statements on page 148.

## FINANCIAL PERFORMANCE 2008/2007

### PERFORMANCE 2008

#### Reported performance

CV sales were up 4% as reported to \$6,963 million (2007: \$6,686 million). Strong growth from *Crestor*, fuelled by the promotion of the atherosclerosis indication and increased sales of *Atacand* offset the continuing significant declines in *Seloken/Toprol-XL*.

#### Performance – CER growth rates

CV sales were unchanged from 2007 at CER. *Crestor* sales increased by 26% to \$3,597 million. US sales for *Crestor* for the full year increased by 18% to \$1,678 million. *Crestor* total prescription share in the US statin market increased to 9.9% in December 2008 from 8.6% in December 2007, and was the only branded statin to gain market share. *Crestor* sales in the Rest of World were up 34% for the full year to \$1,919 million, over half of global sales for the product. Sales were up 16% in Western Europe to \$836 million and 93% in Japan driving sales growth in the Established Markets and the Rest of World up 33% in total. Sales in Emerging Markets increased by 41%.

*Toprol-XL* and authorised generic sales of the drug in the US were down 70% for the full year to \$295 million. For the full year, *Seloken* sales in the Rest of World were up 1% to \$512 million.

US sales for *Atacand* for the full year increased 1% to \$262 million. Sales in other markets were up 12% to \$1,209 million, on a 10% increase in Established Markets and an 18% increase in Emerging Markets.

### PERFORMANCE 2007

#### Reported performance

CV sales rose by 9% from \$6,118 million in 2006 to \$6,686 million in 2007. Continued strong growth from *Crestor* more than offset the significant declines in *Seloken/Toprol-XL*.

#### Performance – CER growth rates

CV sales grew by 5% at CER. *Crestor* sales increased by 33% to \$2,796 million. In the US, *Crestor* sales for the full year were \$1,424 million, a 24% increase over 2006. Total prescriptions in the US statin market increased 8% for the year; *Crestor* prescriptions were up 22%. Sales outside the US for the full year increased 45% to \$1,372 million, nearly half the total worldwide sales for the product. Sales were up 26% in Western Europe with good growth in France and Italy. Sales in Canada increased 43%.

Global sales of *Seloken/Toprol-XL* fell by 22% to \$1,438 million. US sales of the *Toprol-XL* product range, which includes sales of the authorised generic were down 30% for the full year, as the full range of dosage strengths were subject to generic competition from August 2007. Sales of *Seloken* in other markets were up 5% for the full year as a result of growth in Emerging Markets.

*Atacand* sales in the US were unchanged for the full year whilst sales in other markets increased 12%.

Continued small declines were seen in *Zestril* (down 10% to \$295 million) and *Plendil* (down 7% to \$271 million), with general global falls compensated by increases in discrete markets.

# GASTROINTESTINAL

## 2008 IN BRIEF

- > Sales of *Nexium* \$5.2 billion, down 2%.
- > *Nexium* submissions in the EU for the short-term maintenance of haemostasis and prevention of re-bleeding in patients with peptic ulcer bleeding following therapeutic endoscopy and in the US for use in patients with peptic ulcer bleeding following therapeutic endoscopy.
- > In late 2008, a Complete Response Letter received from the FDA in connection with our *Nexium* submission for peptic ulcer bleeding.
- > *Losec/Prilosec* sales \$1.05 billion declining in the EU and US due to continuous generic pressure following the recent patent expiry in Italy. Overall sales down 14%; Japan sales still growing, up 5%.
- > Settlement of patent litigation in the US brought by AstraZeneca against Ranbaxy, with enforceability of disputed *Nexium* patents conceded and an agreement for licensed sales of generic *Nexium* from May 2014.
- > Other patent litigation continuing in the US against generic manufacturers following abbreviated new drug applications relating to *Nexium*.

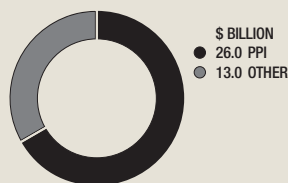
## OUR MARKETED PRODUCTS

***Nexium*** (esomeprazole) is the first proton pump inhibitor (PPI) for the treatment of acid-related diseases to offer clinical improvements over other PPIs and other treatments.

***Losec/Prilosec*** (omeprazole) is used for the short-term and long-term treatment of acid-related diseases.

***Entocort*** (budesonide) is a locally acting corticosteroid for the treatment of inflammatory bowel disease (IBD).

## THERAPY AREA WORLD MARKET (MAT/Q3/08)



The GI world market is valued at \$39 billion, with the proton pump inhibitor market accounting for \$26 billion. In the West (ie Europe and North America combined), according to different estimates, between 10% and 20% of adults suffer from GERD. The prevalence of GERD in Asia is lower but increasing. In spite of effective treatments with PPIs, around 40% of patients do not achieve full relief from symptoms.

## OUR STRATEGIC OBJECTIVE

We aim to maintain our strong position in gastrointestinal (GI) treatments by continuing to focus on PPIs. New *Nexium* line extensions include prevention of re-bleeding in patients with peptic ulcer bleeding, and prevention of low dose aspirin associated peptic ulcer. Our research and development is focused on finding new, innovative ways for treating acid reflux related disease.

## GASTRO-OESOPHAGEAL REFLUX DISEASE (GERD)

### OUR FOCUS

#### Our key marketed products

*Nexium* is an effective, long-term therapy for patients with GERD. 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. Since it was first launched in 2000, *Nexium* has been used in the treatment of acid-related diseases in over one billion patient treatments.

*Nexium* is available in approximately 100 countries for the treatment of acid-related diseases. In the US and EU, *Nexium* is also approved for the treatment of children aged 12 to 17 years with GERD and in 2008 was approved for use in these countries in children aged one to 11 years old. *Nexium* is also approved in the US, the EU, Canada and Australia for the treatment of patients with the rare gastric disorder, Zollinger-Ellison syndrome. In Europe, *Nexium* is approved for the healing and prevention of ulcers associated with non-steroidal anti-inflammatory drug (NSAID) therapy including Cox2 inhibitors. In the US, *Nexium* is approved for reducing the risk of gastric ulcers associated with continuous NSAID therapy in patients at risk of developing gastric ulcers.

*Nexium IV*, which is used when oral administration is not suitable for the treatment of GERD and upper GI side effects induced by NSAIDs, is approved in 86 countries including the US and all EU countries.

During 2008, we announced the submission of a supplemental new drug application (sNDA) to the FDA for *Nexium IV* (esomeprazole sodium) injection, seeking approval for use in patients with peptic ulcer bleeding following therapeutic endoscopy. This was followed by an EU submission for *Nexium IV* and tablets, seeking approval for the short-term maintenance of haemostasis and prevention of re-bleeding in patients with peptic ulcer bleeding following therapeutic endoscopy.

In late November 2008, we received the FDA Complete Response Letter regarding our *Nexium IV* sNDA for peptic ulcer bleed. The application has not received FDA approval in its present form. We are reviewing their comments and will respond in due course. The EU submission is still being reviewed by the European regulatory authorities.

Since its launch in 1988, we estimate that patients have benefited from over 900 million treatments with *Losec/Prilosec*. We continue to maintain patent property covering *Losec/Prilosec*. Further information about the status of omeprazole patents and patent litigation, including details of generic omeprazole launches, is set out in Note 25 to the Financial Statements on page 150.

*Entocort* has better tolerability than other corticosteroids in inflammatory bowel disease and greater efficacy than aminosalicilic acid medicines. It is prescribed as first-line therapy for both acute treatment and maintenance of clinical remission of mild to moderate, active Crohn's disease and is approved in more than 40 countries.

### Clinical trial developments

Data from the *Nexium IV* Peptic Ulcer Bleed study (a multinational, randomised trial of 767 patients with peptic ulcer bleeding) is the basis for submissions in the US and EU referred to above. The study shows that use of *Nexium IV* for three days, followed by oral *Nexium* therapy for 27 days, was statistically more effective in reducing gastric ulcers compared to placebo after both three and 30 days.

### In the pipeline

Our activities focus on reflux inhibitors and hypersensitivity therapy. Our lead compound, AZD3355, is undergoing clinical trials. Follow-up compounds are in Phase I testing.

Non-GERD related GI projects were successfully transferred to the spin-out company Albireo, in which AstraZeneca holds a large minority stake.

## FURTHER INFORMATION

In the US, we are continuing to pursue patent litigation against various generic manufacturers who have filed abbreviated new drug applications (ANDAs) and are seeking to market esomeprazole magnesium products before the expiration of certain of our patents relating to *Nexium*.

## OUR FINANCIAL PERFORMANCE

	2008			2007			2006	2008 compared to 2007		2007 compared to 2006	
	Sales \$m	CER growth \$m	Growth due to exchange effect \$m	Sales \$m	CER growth \$m	Growth due to exchange effect \$m	Sales \$m	CER growth %	Reported growth %	CER growth %	Reported growth %
<i>Nexium</i>	5,200	(121)	105	5,216	(104)	138	5,182	(2)	–	(2)	1
<i>Losec/Prilosec</i>	1,055	(156)	68	1,143	(277)	49	1,371	(14)	(8)	(20)	(17)
Other	89	2	3	84	2	4	78	2	6	3	8
<b>Total</b>	<b>6,344</b>	<b>(275)</b>	<b>176</b>	<b>6,443</b>	<b>(379)</b>	<b>191</b>	<b>6,631</b>	<b>(4)</b>	<b>(2)</b>	<b>(6)</b>	<b>(3)</b>

On 15 April 2008, AstraZeneca announced it had settled its *Nexium* patent infringement litigation against Ranbaxy Pharmaceutical Industries and affiliates (Ranbaxy). As a consequence of the settlement, the patent litigation filed by AstraZeneca following Ranbaxy's submission to the FDA of an ANDA for a generic version of *Nexium* has been dismissed. Under the settlement Ranbaxy concedes that all six patents asserted by AstraZeneca in the patent litigation are valid and enforceable. Ranbaxy also accepts that four of the patents would be infringed by the unlicensed sale of Ranbaxy's proposed generic product. The settlement agreement allows Ranbaxy to commence sales of a generic version of *Nexium* under a licence from AstraZeneca from 27 May 2014, the expiry date of US Patent Numbers 5,877,192 and 6,875,872. We are co-operating fully with the Federal Trade Commission inquiry regarding this settlement.

AstraZeneca's *Nexium* patent infringement litigation against Teva/IVAX and Dr Reddy's Laboratories remains ongoing. No trial date has been set in either case.

During 2008, we received additional notices that patent challenges had been filed by generic drug manufacturers in respect of 20mg and 40mg delayed-release esomeprazole magnesium capsules. Details of these filings and of new and continuing litigation are set out in Note 25 to the Financial Statements on page 153.

The European Patent Office ruled in 2007 that the European process patent for *Nexium* and the European patent for the multiple unit pellet (MUPS) formulations of PPI, which expire in 2015, are valid in amended form following post-grant oppositions. These decisions are now subject to appeal proceedings.

Further, the European Patent Office granted a new European patent on 19 November 2008 for the MUPS formulations of esomeprazole and omeprazole, which expires in 2015.

We continue to have full confidence in our intellectual property protecting *Nexium* and will vigorously defend and enforce it.

The decision of the European Court of First Instance on our appeal against the European Commission's Decision in 2005 to impose fines on us totalling €60 million (\$75 million) for alleged infringements of European competition law relating to certain omeprazole intellectual property and regulatory rights is still pending. Further information about this case is set out in Note 25 to the Financial Statements on page 151.

In 2008 we filed complaints for patent infringement against two generic manufacturers (Barr Laboratories and Mylan Pharmaceuticals) in response to notices of ANDA submissions in respect of generic forms of *Entocort EC*.

## FINANCIAL PERFORMANCE 2008/2007

## PERFORMANCE 2008

## Reported performance

Sales for 2008 were down 2% on a reported basis to \$6,344 million from \$6,443 million in 2007.

## Performance – CER growth rates

GI sales fell by 4% at CER. Global *Nexium* sales were down 2%, excluding the effects of exchange, to \$5,200 million from \$5,216 million the previous year. The decline was driven by the decrease in the US of 8% to \$3,101 million, however this was largely mitigated by sales in other markets increasing by 9% to \$2,099 million. In the US, dispensed retail tablet volumes increased by 2% and *Nexium* was the only major PPI brand to do so in 2008. In the Rest of World, growth in Canada (9%), Japan (5%) and Emerging Markets (20%) more than offset the 5% decline in Western European sales.

For the full year, sales of *Losec* fell 14% to \$1,055 million. *Prilosec* sales in the US were down 25% as a result of generic competition for the 40mg dosage form in the second half of the year. In the Rest of World, sales declined by 11%, despite increases in China (19%) and Japan (5%).

## PERFORMANCE 2007

## Reported performance

GI sales fell by 3% to \$6,443 million in 2007 from \$6,631 million in the previous year.

## Performance – CER growth rates

GI sales fell by 6% at CER. Worldwide, *Nexium* sales fell by 2% to \$5,216 million. In the US, *Nexium* sales for the full year were \$3,383 million, down 4%. Estimated volume growth was 2% for the year. *Nexium* market share in the branded segment of the PPI market increased by 1.5 percentage points in 2007; however, generic omeprazole share of the prescription PPI market increased to 27.4% by December 2007, an increase of nearly 7 percentage points since December 2006. Realised prices declined by around 8% for the year. *Nexium* sales in other markets were up 2% for the full year to \$1,833 million, as growth in Emerging Markets more than offset the declines in Western Europe.

For the full year, *Losec* sales declined by 20% to \$1,143 million. *Prilosec* sales in the US were down 3% to \$226 million. *Losec* sales in other markets were down 24%, although sales increased in Japan and China; sales in these two markets accounted for almost 30% of the brand's performance.

2008 IN BRIEF

- > **Merrem sales of \$897 million, up 13%.**

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- > **Strong reported growth for Merrem of 16% globally; 39% in the US.**

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- > **Synagis sales of \$1.23 billion; in the US \$923 million.**

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- > **Biologics Licence Application submitted for motavizumab, an improved anti-respiratory syncytial virus monoclonal antibody. A Complete Response Letter subsequently received from the FDA.**

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- > **Market authorisation application submitted to European Medicines Agency for Live Attenuated Influenza Vaccine.**

OUR MARKETED PRODUCTS

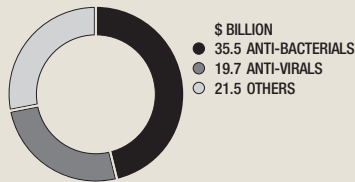
**Synagis** (palivizumab) is a humanised monoclonal antibody used for the prevention of serious lower respiratory tract disease caused by RSV in paediatric patients at high risk of acquiring RSV disease.

**Merrem/Meronem**<sup>1</sup> (meropenem) is a carbapenem anti-bacterial used for the treatment of serious infections in hospitalised patients.

**FluMist** (Influenza Virus Vaccine Live, Intranasal) is a live, attenuated, trivalent influenza virus vaccine licensed in the US for active immunisation of people two to 49 years of age against influenza disease caused by influenza virus subtypes A and type B contained in the vaccine.

<sup>1</sup> Licensed from Dainippon Sumitomo Pharma Co., Ltd.

OTHER THERAPY AREA WORLD MARKET (MAT/Q3/08)



The world infection market is valued at \$77 billion, with anti-bacterials accounting for approximately 46% and anti-virals for 25%.

World demand for antibiotics remains high, due to escalating resistance and the increased risk of serious infections in both immuno-suppressed patients and ageing populations. Approximately half of all infants are infected with RSV during the first year of life. Seasonal influenza results in three to five million cases of severe illness and up to half a million deaths globally each year.

OUR STRATEGIC OBJECTIVE

We aim to build a leading franchise in the treatment of infectious diseases through continued commercialisation of the in-line brands such as *Synagis*, *Merrem* and *FluMist*, effective use of our structural and genomic-based discovery technologies and antibody platforms, and through continued research of novel approaches in areas of unmet medical need.

RESISTANT BACTERIAL INFECTIONS

World demand for antibiotics remains high, due to escalating resistance and the increased risk of serious infections in both immuno-suppressed patients and ageing populations. Many bacterial infections currently have few satisfactory treatment options prompting demand for new and better therapies.

OUR FOCUS

Our key marketed products

*Merrem/Meronem* (meropenem) is a carbapenem antibiotic, which is active against most bacteria that cause serious infections in hospitalised patients. *Merrem* is the leading carbapenem and has a growing share of the intravenous antibiotic market because of its activity against bacteria resistant to many other agents. To meet the high and growing need for new and better therapies for resistant bacterial infections we have built an anti-bacterials discovery capability that places AstraZeneca among the industry leaders with the capability to create novel mechanism anti-bacterials.

RESPIRATORY SYNCYTIAL VIRUS (RSV)

Approximately half of all infants are infected with RSV during the first year of life and nearly all children in the US have been infected by the time they reach their second birthday. Unlike other viral infections, there is no complete and durable immunity created by RSV, so repeated infection is likely and common. Premature babies (earlier than 36 weeks gestational age, especially those less than 32 weeks) or babies with chronic lung disease or congenital heart disease are at an even greater risk of contracting severe RSV disease than full-term babies.

OUR FOCUS

Our key marketed products

*Synagis* is used for the prevention of serious lower respiratory tract disease caused by RSV in children at high risk of the disease. It was the first monoclonal antibody (MAb) approved in the US for an infectious disease and since its launch in 1998 it has become the standard of care for RSV prevention. *Synagis* remains the only immunoprophylaxis in the marketplace

indicated for the prevention of RSV in paediatric patients at high risk of RSV. *Synagis* is administered by intra-muscular injection.

In the pipeline

During 2008, we filed a biological licence application with the FDA for an improved anti-RSV MAb, motavizumab. We recently completed a Phase III study with motavizumab as a prophylaxis in infants with haemodynamically significant congenital heart disease. We are also conducting a Phase IIb study with motavizumab as a treatment for children hospitalised with severe RSV disease. In November 2008 we received a Complete Response Letter from the FDA asking for additional information on motavizumab which we are confident we can respond to and does not lead us to believe it is necessary to conduct further clinical trials.

In addition, three intranasal vaccines are being developed for the prevention of lower respiratory tract illness caused by RSV and parainfluenza virus-3 (PIV3): MEDI-559 (RSV), MEDI-560 (PIV3) and MEDI-534 (RSV-PIV3). We are conducting several Phase I and Phase I/II studies for these vaccines alone and in collaboration with the US National Institute of Allergy and Infectious Diseases under a Co-operative Research and Development Agreement.

INFLUENZA VIRUS

Influenza is the most common vaccine-preventable disease in the developed world. According to World Health Organization estimates, seasonal influenza results in three to five million cases of severe illness and up to half a million deaths globally each year, primarily among the elderly. Rates of infection are highest among children, with school-aged children significantly contributing to the spread of the disease. Influenza also has socio-economic consequences related to both direct and indirect healthcare costs, including hospitalisations, work absence and loss of work productivity when either a caregiver or child is sick with influenza.

OUR FOCUS

Our key marketed products

*FluMist* is the first live, attenuated nasally delivered vaccine approved in the US for the prevention of disease caused by influenza A and B viruses in eligible children and adults, ages two to 49 years. In 2008, the US Centres for Disease Control and Prevention's Advisory Committee on Immunization Practices voted to expand recommendations for routine seasonal influenza vaccination to include all school-age children up to the age of 18 years as soon as feasible but no later than the 2009/2010 influenza season. During the year,

## OUR FINANCIAL PERFORMANCE

	2008			2007			2006	2008 compared to 2007		2007 compared to 2006	
	Sales \$m	CER growth \$m	Growth due to exchange effect \$m	Sales \$m	CER growth \$m	Growth due to exchange effect \$m	Sales \$m	CER growth %	Reported growth %	CER growth %	Reported growth %
<i>Merrem</i>	897	97	27	773	121	48	604	13	16	20	28
<i>Synagis</i> <sup>1</sup>	1,230	612	–	618	618	–	–	n/m	n/m	n/m	n/m
<i>FluMist</i> <sup>1</sup>	104	51	–	53	53	–	–	n/m	n/m	n/m	n/m
Other	220	(54)	4	270	(12)	11	271	(20)	(19)	(4)	–
<b>Total</b>	<b>2,451</b>	<b>706</b>	<b>31</b>	<b>1,714</b>	<b>780</b>	<b>59</b>	<b>875</b>	<b>41</b>	<b>43</b>	<b>89</b>	<b>96</b>

<sup>1</sup> Acquired in June 2007.

we began rolling out the international marketing plan for our nasal spray influenza vaccine. The first milestone was the filing of a market authorisation application to the European Medicines Agency in late 2008.

### HEPATITIS C VIRUS (HCV)

HCV infects an estimated 170 million people worldwide and the current market for HCV therapy exceeds \$2 billion annually. However, therapy for the strains that predominate in the US and Western Europe require 12 months' treatment and produces a durable cure in only 50% of patients. Key opinion leaders expect the current standard of treatment (interferon plus ribavirin) to change to a form of combination therapy involving one or more new mechanism of action direct-acting anti-virals and there are several small and large pharmaceutical companies with varying HCV pipelines focused on such therapies. A future paradigm of combinations of anti-virals as standard care offers the opportunity for several new therapies to be widely used.

#### OUR FOCUS

##### In the pipeline

Projects in development include AZD7295, a novel HCV compound, currently in Phase II.

### SEPSIS

Sepsis is a life-threatening condition resulting from uncontrolled severe infections, which affects an estimated three million people a year worldwide. Few industry pipelines are focused on the development of products specifically for registration for the treatment of sepsis or septic shock.

#### OUR FOCUS

##### In the pipeline

The development programme for CytoFab™, our potential treatment for severe sepsis licensed from Protherics, continues in Phase II development. CytoFab™ has the potential to be one of a limited number of medicines specifically developed for such patients.

### TUBERCULOSIS (TB)

TB remains a worldwide threat and is newly diagnosed in over eight million people worldwide every year. It is one of the greatest causes of death from infectious disease in the developing world.

#### OUR FOCUS

As part of our commitment to making a contribution to improving health in the developing world, we are working to find a new, improved treatment for TB. We have a dedicated research facility in Bangalore, India that is focused on finding a treatment for TB that will act on drug-resistant strains, simplify the treatment regime (current regimes are complex and lengthy, meaning many patients give up before the infection is fully treated) and be compatible with HIV/AIDS therapies (TB and HIV/AIDS form a lethal combination, each speeding the other's progress). Over 80 scientists in Bangalore work closely with our infection research centre in Boston, US as well as with academic leaders in the field, and they have full access to all AstraZeneca's platform technologies, such as high throughput screening and compound libraries. It is a complex area of research, but we hope to have identified a candidate drug for testing in man within the next two to three years.

### FINANCIAL PERFORMANCE 2008/2007

#### PERFORMANCE 2008

##### Reported performance

Total Infection sales increased on a reported basis by 43% to \$2,451 million as a full year of *Synagis* and *FluMist* sales were taken in the Group for the first time, and *Merrem* sales enjoyed another year of good growth.

##### Performance – CER growth rates

Infection sales were up 41% at CER. For the full year, *Synagis* sales were \$1,230 million. Sales in 2007 were \$618 million, but this only reflected sales since the acquisition of MedImmune in June 2007. Worldwide sales of *Synagis* in the fourth quarter were \$506 million, a 5% increase over the same period in 2007 when the product was included in sales.

*FluMist* sales were \$104 million for the full year. In contrast to 2008, all of 2007 *FluMist* sales of \$53 million were realised in the fourth quarter as a result of the timing of regulatory approvals for the new formulation and expanded label.

#### PERFORMANCE 2007

##### Reported performance

Infection sales grew by 96% to \$1,714 million from \$875 million in 2006, driven by the inclusion of seven months of *Synagis* and *FluMist* sales and an increase in *Merrem* sales of 28%.

##### Performance – CER growth rates

Infection sales grew by 89%, after excluding the effect of exchange. CER growth of 20% from *Merrem*, with sales of \$773 million, and the inclusion of *Synagis* and *FluMist* were the principal drivers of this growth. Sales of *Synagis* totalled \$618 million for the period post-acquisition of MedImmune, with \$480 million arising in the fourth quarter. *Synagis* sales are highly seasonal, with the majority of sales recorded in the fourth and first quarters.

Sales of *FluMist* were \$53 million for the full year, all of which were recorded in the fourth quarter. As with *Synagis*, there were no corresponding sales in the prior year period.

Sales of *Merrem* increased by 20% to \$773 million, with strong growth in the US (sales up 32% to \$149 million) and Western Europe (sales up 20% to \$307 million).

# NEUROSCIENCE

## 2008 IN BRIEF

- > **Seroquel sales up 9% to over \$4.45 billion.**
- > **Seroquel XR approved in the US for acute bipolar depression, acute bipolar mania and bipolar maintenance.**
- > **Seroquel XR approved under the European Mutual Recognition Procedure for the treatment of acute bipolar depression and acute bipolar mania in October. Seroquel also approved at the same time for the treatment of acute bipolar depression.**
- > **FDA Complete Response Letter received on Seroquel XR for Major Depressive Disorder in December.**
- > **Regulatory submissions made for Seroquel XR for the treatment of Major Depressive Disorder and for Generalised Anxiety Disorder in both the US and EU.**
- > **Summary Judgment Motion granted to AstraZeneca in the patent infringement actions commenced against two generic drug manufacturers in the US following abbreviated new drug applications relating to Seroquel.**
- > **Separate lawsuits filed in the US against third party manufacturers relating to infringement of the Seroquel XR patents.**
- > **Personal injury actions in the US and Canada involving Seroquel being defended vigorously.**

## OUR MARKETED PRODUCTS

**Seroquel** (quetiapine fumarate) is an atypical anti-psychotic drug approved for the treatment of adult schizophrenia and bipolar disorder (mania, depression and maintenance).

**Zomig** (zolmitriptan) is for the treatment of migraine with or without aura.

**Diprivan** (propofol) is an intravenous general anaesthetic used in the induction and maintenance of anaesthesia, light sedation for diagnostic procedures and for intensive care sedation.

**Naropin** (ropivacaine) is a long-acting local anaesthetic, replacing the previous standard treatment of bupivacaine.

**Xylocaine** (lidocaine) is a widely used short-acting local anaesthetic.

**EMLA** (lidocaine + prilocaine) is a local anaesthetic for topical application.

## OUR STRATEGIC OBJECTIVE

We aim to strengthen our position in neuroscience through further growth of *Seroquel* and *Seroquel XR* and by the successful introduction of a range of new medicines aimed at significant medical need in psychiatry, analgesia (pain control) and cognition (including Alzheimer's disease and cognitive disorders in schizophrenia).

## PSYCHIATRY

Most branded schizophrenia products will face generic competition in the period 2012 to 2015, with all current atypical anti-psychotic patents expiring by 2018. Future demand will be for products with significantly improved efficacy and tolerability.

The depression and anxiety markets are currently dominated by generic selective serotonin re-uptake inhibitors and serotonin norepinephrine re-uptake inhibitors. As growth in the US slows, the Japanese market continues to grow. Generic growth is anticipated over the next five years as patents expire.

## OUR FOCUS

### Our key marketed products

*Seroquel* is a leading atypical anti-psychotic treatment for adult schizophrenia and bipolar disorder. *Seroquel* remains the most commonly prescribed atypical anti-psychotic in the US, where it is the only atypical anti-psychotic approved as monotherapy treatment for both bipolar depression and bipolar mania as well as the leading atypical brand globally by sales value. Its clinical development programme was substantially completed during 2008 resulting in worldwide launches of *Seroquel XR* for schizophrenia. We have also made the associated regulatory submissions and data presentations in bipolar disorder, major depressive disorder (MDD) and generalised anxiety disorder (GAD).

First launched in 1997, *Seroquel* is now approved in 92 countries. *Seroquel XR*, an extended release formulation that offers patients and doctors a once-daily treatment, was launched in the US for the treatment of schizophrenia in 2007 and is now approved in 45 countries for schizophrenia, 12 countries for bipolar mania, seven countries for bipolar depression and four countries, including the US, for bipolar maintenance, in one market for MDD, and in one market for GAD.

In 2008, the FDA approved *Seroquel XR* for the treatment of depressive episodes associated with bipolar disorder, the manic and mixed episodes associated with bipolar 1 disorder and both *Seroquel* and *Seroquel XR* for the maintenance treatment of bipolar 1 disorder as adjunctive therapy to lithium or divalproex. In addition, *Seroquel XR* and *Seroquel* were approved in the EU for the treatment of major depressive episodes in bipolar disorder. *Seroquel XR* was also licensed in the EU for moderate to severe manic episodes in bipolar disorder.

During 2008, regulatory submissions were made in both the US and in the EU for GAD and for MDD. AstraZeneca received a Complete Response Letter from the FDA for its sNDA for *Seroquel XR* for the treatment of MDD in adult patients. AstraZeneca is continuing discussions with the FDA. A separate regulatory submission was made to the FDA for the treatment of schizophrenia in adolescents (13 to 17 year olds) and for the treatment of acute manic episodes in children and adolescents (10 to 17 year olds) with bipolar 1 disorder. The US prescribing information for *Seroquel* and *Seroquel XR* is being updated to include new safety information regarding use in children and adolescents. *Seroquel* and *Seroquel XR* are not approved currently for use in paediatric patients under 18 years of age.

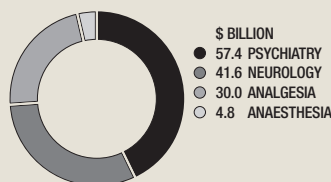
In January 2009, the FDA granted an additional six-month period of market exclusivity to *Seroquel* for its licensed indications, based on studies we conducted in adolescents with schizophrenia and children and adolescents with bipolar mania. The *Seroquel* patent expires in September 2011. The allowed six-month paediatric exclusivity period, which takes effect upon expiration of the patent, will extend the exclusivity of *Seroquel* to March 2012.

### In the pipeline

We have progressed AZD8529 into Phase I and AZD2624 into Phase II for the treatment of schizophrenia, with AZD2327 entering Phase IIa and AZD6765 and AZD7325 entering into Phase IIb clinical development for the treatment of anxiety and/or depression.

We also continued to build our alliance/partnership network in 2008 by entering into a collaboration with the Columbia University Medical Center to examine further the relevance of adult neurogenesis in anti-depressant action and novel approaches to treat depression and anxiety.

## THERAPY AREA WORLD MARKET (MAT/Q3/08)



### The Neuroscience world market totals \$134 billion.

The medical need in Neuroscience is significant. Depression and anxiety disorders remain under-diagnosed and under-treated, with 15% of the population suffering from major depression at least once in their lives. Schizophrenia affects around 1% of the adult population, and 17 million people suffer from bipolar disorder across the major markets. Chronic pain affects over 20% of the population and pain management is the most common reason for seeking medical care. Alzheimer's disease affects approximately 24 million people worldwide (predicted to reach 40 million by 2020). Current therapy does not significantly change the course of this progressive neuro-degenerative disorder.

## OUR FINANCIAL PERFORMANCE

	2008			2007			2006	2008 compared to 2007		2007 compared to 2006	
	Sales \$m	CER growth \$m	Growth due to exchange effect \$m	Sales \$m	CER growth \$m	Growth due to exchange effect \$m	Sales \$m	CER growth %	Reported growth %	CER growth %	Reported growth %
<i>Seroquel</i>	4,452	346	79	4,027	526	85	3,416	9	11	15	18
<i>Diprivan</i>	278	(3)	18	263	(53)	12	304	(1)	6	(17)	(13)
<i>Zomig</i>	448	(3)	17	434	18	18	398	(1)	3	5	9
Local anaesthetics	605	13	35	557	(6)	34	529	2	9	(1)	5
Other	54	(7)	2	59	(1)	3	57	(12)	(8)	(2)	4
<b>Total</b>	<b>5,837</b>	<b>346</b>	<b>151</b>	<b>5,340</b>	<b>484</b>	<b>152</b>	<b>4,704</b>	<b>6</b>	<b>9</b>	<b>10</b>	<b>14</b>

### ANALGESIA AND ANAESTHESIA (PAIN CONTROL)

Significant unmet need remains for efficacy and tolerability in the neuropathic pain market. Several novel compounds are in development but recent disappointments highlight continuing uncertainty regarding market approval.

The osteoarthritis (OA) market is steadily growing, due to ageing populations and novel agents entering the market. However, the established use of generic treatment makes market entry more difficult. Biologics are an emerging treatment option for OA.

#### OUR FOCUS

##### Our key marketed products

*Zomig* Nasal Spray was approved for the acute treatment of cluster headache in 14 member states in the EU in 2008.

*Diprivan* is the world's best-selling intravenous general anaesthetic. A complete change over to *Diprivan* EDTA, a microbial-resistant formulation, is expected in 2009, following the approval of this formulation in the last major territory (UK) in 2008.

*Naropin* approvals continue for extended use in paediatric patients to include neonates and infants aged below one year old.

*EMLA* submissions/approvals of patch presentation have continued, particularly in Eastern European countries. In Japan, *EMLA* is out-licensed to SATO who expect to file their Japanese NDA in July 2009.

### In the pipeline

PN400 is a fixed-dose combination tablet of enteric-coated naproxen and immediate release esomeprazole which uses proprietary technology licensed from POZEN Inc. through a collaboration established in August 2006. It is being developed for the relief of signs and symptoms of OA, rheumatoid arthritis and ankylosing spondylitis in patients at risk for developing non-steroidal anti-inflammatory drug (NSAID)-associated gastric ulcers. Approximately half of the 121 million chronic arthritis patients in the US and the five largest European countries are at risk of developing NSAID-associated ulcers based on their age, prior history of ulceration, or use of low dose aspirin. The Phase III trial programme, which was initiated in the third quarter of 2007, has now completed enrolment. The two Phase III ulcer risk reduction studies, comparing PN400 against enteric-coated naproxen 500mg in subjects with chronic pain and who are at risk for NSAID-associated ulcers, achieved their primary endpoints. Subjects taking PN400 experienced statistically significantly fewer endoscopically confirmed gastric ulcers than those taking naproxen. Two additional Phase III studies are still ongoing. Upon completion of the entire PN400 Phase III clinical programme, AstraZeneca will make a final determination regarding regulatory filing. A regulatory submission for PN400 in the US is currently planned for mid 2009.

We progressed three other early development compounds during the year: AZD2516 into Phase I clinical development and AZD1386 and AZD1940 in Phase II clinical development for the treatment of nociceptive (caused by tissue damage) and/or neuropathic (caused by nerve damage) pain.

### COGNITION

Alzheimer's disease remains one of the largest areas of unmet need and also one of high risk for neuroscience product development, due in part to the challenges of establishing efficacy in clinical trials. Current treatments, which physicians consider inadequate, target the symptoms not the underlying cause of the disease. Achieving disease modification is very difficult evidenced by recent late stage product development failures. Growth in this area is strong (20% to 40% across the world) but all existing agents will face patent expiry by 2013.

There are currently no products approved to treat cognitive dysfunction associated with schizophrenia. The first product to market will face the challenge of disease education and the establishment of treatment guidelines.

#### OUR FOCUS

##### In the pipeline

We have expanded the portfolio of potential medicines in this area to five development programmes, of which three are in clinical evaluation, in Alzheimer's disease, cognitive disorders in schizophrenia (CDS) and other cognition disorders. In addition to developing molecules for cognitive disorders, we continue to progress two development phase molecules for the treatment of other neurodegenerative diseases.

Through our collaboration with, amongst others, the Karolinska Institute in Sweden, our research capabilities in positron emission tomography, which provides early signalling of potential efficacy for our Alzheimer's compounds, continue to progress. We now have two C-11 diagnostic compounds and one F-18 compound in development.

Compounds in clinical evaluation include products deriving from our relationship with Targacept (AZD3480, TC-5619 and AZD1446).

AZD3480, a neuronal nicotinic receptor agent, is currently in Phase IIb clinical testing in Alzheimer's disease and TC-5619 is in Phase II clinical testing for CDS. AZD3480 did not meet the Phase IIb trial primary endpoint for CDS and is not expected to progress to Phase III studies in this indication. AstraZeneca and Targacept previously announced top-line results from a Phase IIb study of AZD3480 in mild to moderate Alzheimer's disease and are currently evaluating AZD3480 in a Phase II exploratory study in attention deficit/hyperactivity disorder (ADHD) in adults. A decision by AstraZeneca with respect to potential further development of AZD3480 in Alzheimer's disease or ADHD is now expected in the first half of 2009, pending completion of the adult ADHD study and other ongoing evaluations.

#### FURTHER INFORMATION

AstraZeneca is defending approximately 9,210 served or answered lawsuits involving approximately 15,461 plaintiff groups who have filed *Seroquel*-related product liability claims in the US and Canada. Although the nature of the alleged injuries is not clear from the face of most of the complaints and discovery of the cases is continuing, plaintiffs generally contend that they developed diabetes and/or other related injuries as a result of taking *Seroquel* and/or other atypical anti-psychotic medications. Further information can be found in Note 25 to the Financial Statements on page 155. Trials of these cases are expected to commence in 2009.

In July 2008 AstraZeneca was granted a Summary Judgment Motion from the US District Court for the District of New Jersey in the ongoing patent infringement action against Teva Pharmaceuticals USA Inc and Sandoz, Inc. Teva and Sandoz have filed appeals.

Separate lawsuits have been filed in the US against third party manufacturers relating to infringement of the *Seroquel XR* patents.

We continue to have full confidence in our intellectual property protecting *Seroquel* and will vigorously defend and enforce it. Details of the litigation against generic drug manufacturers in respect of *Seroquel* are set out in Note 25 to the Financial Statements on page 155.

#### FINANCIAL PERFORMANCE 2008/2007

##### PERFORMANCE 2008

###### Reported performance

Neuroscience sales grew by 9% to \$5,837 million in 2008 from \$5,340 million in 2007. All geographic areas experienced growth and *Seroquel* grew strongly by 11%.

###### Performance – CER growth rates

Sales in the Neuroscience therapy area grew by 6% to \$5,837 million from \$5,340 million last year.

US sales for *Seroquel* for the full year were \$3,015 million, 5% ahead of last year. *Seroquel* remains the market leader in the US anti-psychotic market, with a total prescription share of 31.6% in December 2008.

For the full year, *Seroquel* sales in the Rest of World increased by 17% to \$1,437 million, with value and volume growth well ahead of the market in all regions.

Sales of *Zomig* for the full year were up 6% in the US to \$187 million. Sales in the Rest of World were down 5% to \$261 million.

##### PERFORMANCE 2007

###### Reported performance

Sales in the Neuroscience therapy area rose by 14% in 2007, up to \$5,340 million from \$4,704 million in 2006. *Seroquel* was the principal driver of performance, recording an 18% increase in sales.

###### Performance – CER growth rates

Neuroscience sales grew by 10% at CER. Annual *Seroquel* sales exceeded \$4 billion for the first time in 2007. Full year sales were \$4,027 million, up 15% over last year. In the US, *Seroquel* sales increased by 15% to \$2,863 million. *Seroquel* sales in other markets were up 16% for the full year, as a result of market share gain in most markets.

*Zomig* sales for the full year increased 5% in the US (to \$177 million) and 4% in other markets, totalling \$434 million.

## 2008 IN BRIEF

- > *Arimidex* sales up 4% to \$1.86 billion and is the leading branded hormonal breast cancer therapy in the US, Japan and France.
- > *Casodex* sales \$1.26 billion, down 12%. Expiry of EU marketing exclusivity in 2008.
- > *Zoladex* sales \$1.14 billion, down 3%.
- > Results from three Phase III *Zactima* trials in non-small cell lung cancer (NSCLC) showed that *Zactima*, in combination with standard chemotherapy, brings clinical benefits to patients with previously treated NSCLC.
- > Results from the *Iressa* Phase III INTEREST study underpin a marketing authorisation application in the EU and the pan-Asian IPASS study met its primary objective showing superior progression-free survival for *Iressa* compared with two chemotherapies in clinically selected patients.
- > ZD4054 progressed into Phase III development for hormone-resistant prostate cancer.
- > Registration trials ongoing of *Recentin* in first line colorectal cancer and recurrent glioblastoma multiforme.

## OUR MARKETED PRODUCTS

**Arimidex** (anastrozole) is an aromatase inhibitor for the treatment of breast cancer.

**Casodex** (bicalutamide) is an anti-androgen therapy for the treatment of prostate cancer.

**Zoladex** (goserelin acetate implant), in one- and three-month depots, is an LHRH agonist for the treatment of prostate cancer, breast cancer and certain benign gynaecological disorders.

**Iressa** (gefitinib) is an EGFR-TKI that acts to block signals for cancer cell growth and survival in non-small cell lung cancer.

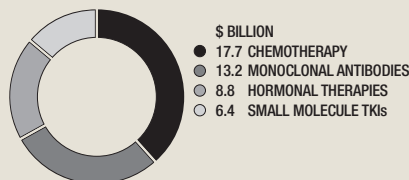
**Faslodex** (fulvestrant) is an injectable oestrogen receptor antagonist for the treatment of breast cancer, with no known agonist effects, that down-regulates the oestrogen receptor.

**Nolvadex** (tamoxifen citrate) remains a widely prescribed breast cancer treatment outside the US.

**Ethiol** (amifostine) is used to help prevent certain side effects of specific types of chemotherapy and radiotherapy that are used to treat head and neck and ovarian cancer.

**Abraxane**<sup>®</sup> (paclitaxel protein-bound particles for injectable suspension) (albumin-bound) for the treatment of breast cancer<sup>1</sup>.

## THERAPY AREA WORLD MARKET (MAT/Q3/08)



The world market value for cancer therapies is \$46 billion and is growing strongly.

An increasing number of large pharmaceutical companies as well as biotech companies have a stated ambition to build their business in oncology. In the last several years there has been a substantial increase of clinical trial activity across all the major tumours and sub-types increasing pressure on innovator companies to deliver best in class or first in class therapies. According to IMS, value growth in oncology will continue at double digit compound annual growth rates. This is well above growth rates for other therapy areas which makes oncology, despite market pressures, an attractive area for investment.

## OUR STRATEGIC OBJECTIVE

We aim to build on our position as a world leader in cancer treatment through continued growth of *Arimidex*, further launches and line extensions of newer products, such as *Faslodex*, and the successful introduction of novel therapeutic approaches currently in development, including both small molecule and biological drugs, targeted at high unmet need.

## CANCER

## OUR FOCUS

## Our key marketed products

During 2008, our breast cancer treatment, *Arimidex* maintained its position as market leader in sales of branded hormonal agents, with approximately four million patient years of clinical experience. This success is largely based on the extensive long-term efficacy and safety results of the ATAC study, which showed *Arimidex* to be significantly superior to tamoxifen at preventing breast cancer recurrence during and beyond the five-year treatment course. (Breast cancer recurrence is defined as loco-regional recurrence, distant recurrence or contra-lateral breast cancer).

*Arimidex* continues to be the leading branded hormonal therapy for new patients in the US, Japan and France, and is also approved in a number of markets in Europe for a switch indication for patients who have already received two to three years of tamoxifen.

*Faslodex*, now approved in more than 60 markets, offers an additional hormonal therapy for patients with hormone-sensitive, advanced breast cancer, delaying the need for cytotoxic chemotherapy. It is a once-monthly injection approved for the second-line treatment of hormone-receptor positive, advanced breast cancer in post-menopausal women.

*Casodex* is used as a 50mg tablet for the treatment of advanced prostate cancer, and as a 150mg tablet for the treatment of locally advanced prostate cancer. European sales declined due to generic erosion following patent and/or marketing exclusivity expiries in July 2008. Sales growth continued in Japan, where *Casodex* is available as an 80mg tablet and is approved for all stages of prostate cancer. In the US, the FDA granted an additional six months' paediatric extension providing marketing exclusivity in the US to April 2009.

<sup>1</sup> In November 2008, we entered into an agreement with Abraxis under which Abraxis re-acquired exclusive rights to market Abraxane<sup>®</sup> in the US.

*Zoladex* is approved in 120 countries. It is approved for the treatment of prostate cancer, breast cancer and gynaecological disorders. In non-metastatic prostate cancer, *Zoladex* is the only luteinising hormone-releasing hormone (LHRH) agonist shown to improve overall survival both when used in addition to radical prostatectomy and when used in addition to radiotherapy. The 10-year follow-up results of a study for the European Organisation for Research and Treatment of Cancer confirmed the long-term survival benefits of *Zoladex* when used as adjuvant to radiotherapy in patients with locally advanced prostate cancer.

In breast cancer, *Zoladex* is widely approved for use in advanced breast cancer in pre-menopausal women. In a number of countries, *Zoladex* is also approved for the adjuvant treatment of early stage pre-menopausal breast cancer as an alternative to and/or in addition to chemotherapy. *Zoladex* offers proven survival benefits for breast cancer patients with a favourable tolerability profile.

Competition in the LHRH agonist market is expected to increase in Europe during 2009, with the anticipated launches of generic goserelin. This follows the announcement of the approval of generic goserelin (one-month depot) in Germany in December.

*Iressa* is approved in 36 countries and is the leading epidermal growth factor receptor-tyrosine kinase inhibitor (EGFR-TKI) in the Asia Pacific region where it continues to be marketed for pre-treated advanced NSCLC. Based on data from the Phase III INTEREST study comparing *Iressa* with docetaxel, a marketing authorisation application for *Iressa* has been submitted to the European Medicines Agency.

Outside the US, we have various distribution and marketing arrangements for branded *Ethiol*. As of June 2008, our two main distribution partners are Pinnacle Biologics for Western Europe, Turkey and Israel, and Schering-Plough International for Rest of World.

## Clinical trial developments

Results from the Phase III pan-Asian IPASS study evaluating the efficacy of *Iressa* as first-line treatment of NSCLC, were also announced. The IPASS study exceeded its primary objective, demonstrating superior

## OUR FINANCIAL PERFORMANCE

	2008			2007			2006	2008 compared to 2007		2007 compared to 2006	
	Sales \$m	CER growth \$m	Growth due to exchange effect \$m	Sales \$m	CER growth \$m	Growth due to exchange effect \$m	Sales \$m	CER growth %	Reported growth %	CER growth %	Reported growth %
<i>Casodex</i>	1,258	(161)	84	1,335	74	55	1,206	(12)	(6)	6	11
<i>Arimidex</i>	1,857	69	58	1,730	151	71	1,508	4	7	10	15
<i>Zoladex</i>	1,138	(31)	65	1,104	39	57	1,008	(3)	3	4	10
<i>Iressa</i>	265	8	19	238	(1)	2	237	3	11	–	–
<i>Faslodex</i>	249	25	10	214	18	10	186	12	16	10	15
<i>Nolvadex</i>	85	(5)	7	83	(8)	2	89	(6)	2	(9)	(7)
<i>Abraxane</i> <sup>®</sup>	64	2	–	62	44	–	18	3	3	244	244
<i>Ethylol</i>	28	(15)	–	43	43	–	–	n/m	n/m	n/m	n/m
Other	10	(1)	1	10	(1)	1	10	(10)	–	(10)	–
<b>Total</b>	<b>4,954</b>	<b>(109)</b>	<b>244</b>	<b>4,819</b>	<b>359</b>	<b>198</b>	<b>4,262</b>	<b>(2)</b>	<b>3</b>	<b>8</b>	<b>13</b>

progression-free survival (PFS) for *Iressa* compared with two chemotherapies (carboplatin/paclitaxel) in clinically selected patients. AstraZeneca is consulting with relevant health authorities regarding the IPASS data. Further Phase II trials are continuing to evaluate the potential benefits of *Iressa* in NSCLC and other EGF receptor-driven tumours.

#### In the pipeline

*Zactima* (vandetanib) is a potential new oral anti-cancer therapy, which has a unique anti-cancer profile through two clinically proven mechanisms. It blocks the development of a tumour's blood supply (anti-angiogenesis) and blocks the growth and survival of the tumour itself (anti-EGFR). *Zactima* also inhibits RET-kinase activity, an important growth driver in certain types of thyroid cancer.

During 2008, we announced results from two Phase III clinical studies of *Zactima* in combination with chemotherapy agents, docetaxel (ZODIAC) and pemetrexed (ZEAL), and one monotherapy clinical study (ZEST) in pre-treated advanced NSCLC. The observed safety profile in these three Phase III studies was consistent with previous studies with *Zactima* in NSCLC.

Results from the ZODIAC and ZEAL studies showed advantages for *Zactima* in combination with standard chemotherapy, compared to chemotherapy alone. The addition of *Zactima* to chemotherapy prolonged PFS, the primary endpoint, which achieved statistical significance in the ZODIAC study, but not in the smaller ZEAL study. Clinical benefits were seen in secondary endpoints. Both studies showed that adding *Zactima* to chemotherapy significantly improved objective response rate, which is a measurement of tumour shrinkage. Additionally, positive trends in prolonging

overall survival (OS) were seen, although these did not reach statistical significance and the data are still immature. Importantly, the studies also showed that adding *Zactima* to chemotherapy controlled the symptoms of lung cancer better than chemotherapy alone, allowing patients to maintain their quality of life for significantly longer.

ZEST, which evaluated the efficacy of *Zactima* monotherapy versus erlotinib, did not meet the primary objective of demonstrating a statistically significant prolongation of PFS for *Zactima*. However, *Zactima* and erlotinib showed equivalent efficacy for PFS and OS in a pre-planned non-inferiority analysis. We plan to file a regulatory submission in the second quarter of 2009 following discussion with regulatory agencies for combination therapy. Full results from studies ZODIAC, ZEAL and ZEST will be presented at an international medical congress in 2009.

Results from the Phase III ZETA study in hereditary and sporadic medullary thyroid cancer are expected in the second quarter of 2009.

The anti-cancer activity of *Zactima* continues to be evaluated in NSCLC and other tumour types, including colorectal, glioma, head and neck, breast and prostate cancers.

*Recentin* (cediranib) is a highly potent and selective-inhibitor of vascular endothelial cell growth factor (VEGF) receptor signalling in solid tumours, which inhibits all three VEGF receptors irrespective of activating ligand, and is suitable for once-daily oral dosing. It is currently in Phase III development in first-line colorectal cancer (CRC) and recurrent glioblastoma (rGBM).

In early 2008, our HORIZON III Phase II/III head-to-head study of *Recentin* with chemotherapy versus Avastin™ with chemotherapy in patients with first-line metastatic CRC progressed directly into Phase III. Patient recruitment was subsequently completed for both HORIZON III and HORIZON II, our Phase III study of *Recentin* with chemotherapy versus chemotherapy alone. The Phase III REGAL trial in rGBM comparing *Recentin* monotherapy versus lomustine +/- *Recentin* began enrolling patients in the fourth quarter of 2008.

Following the announcement that the National Cancer Institute of Canada Clinical Trial Group's (NCIC CTG) *Recentin* BR24 NSCLC trial would not be progressing straight into Phase III, we worked in close collaboration with the NCIC CTG to understand the BR24 data further and to assess the potential of *Recentin* in this disease area. Subsequently the NCIC CTG announced it would now investigate *Recentin* at 20mg plus carboplatin/paclitaxel versus carboplatin/paclitaxel alone in the BR29 study, which is expected to start recruitment in early 2009.

Encouraging Phase II data for *Recentin* from completed and continuing studies to investigate renal, rGBM, ovarian and prostate cancers were also presented in 2008.

ZD4054 is an oral once-daily potent and specific endothelin A-receptor antagonist in Phase III development. Data from Phase II studies suggested that ZD4054 10mg has the potential to increase median overall survival time by approximately seven months in men with metastatic hormone-resistant prostate cancer (HRPC), with the benefit of a generally well-tolerated side effect profile and a convenient once-daily tablet. The Phase III ENTHUSE studies are investigating

efficacy in metastatic HRPC, both as monotherapy and in combination with docetaxel, and in non-metastatic HRPC.

In December 2008, we ceased our collaboration with Infinity Pharmaceuticals for the development and commercialisation of Infinity's drug candidates IPI-504 (MEDI-561) and IPI-493 for the treatment of cancer and related conditions. This decision was taken after reviewing the potential opportunity for these projects and to take account of competing R&D investment priorities.

Our early oncology pipeline includes a range of novel compounds that target signalling pathways believed to be pivotal in cancer cell growth, invasion DNA repair and survival, with nine products in Phase II and 15 others in Phase I development. Phase II data from AZD6244, a potent MEK inhibitor licensed from Array BioPharma, showed biological activity in lung cancer and melanoma and studies will now focus on its use in combination with standard and other novel therapies, rather than its development as monotherapy. Phase II studies with the poly-ADP-ribose-polymerase (PARP) inhibitor AZD2281 have started and will initially focus on BRCA-mutated breast and ovarian cancer as well as other cancers where DNA repair could be defective.

The dual-specific Src/Abl kinase inhibitor, AZD0530, has shown a dramatic effect on biomarkers of cell motility and bone resorption and has started Phase II studies in ovarian cancer with others to follow. Among the compounds from the early portfolio continuing in development are AZD4877, a novel inhibitor of cell cycle; AZD7762, a tumour-selective chemosensitiser; and AZD8931. AZD1152, an aurora kinase inhibitor, has shown activity in acute myelogenous leukaemia and will commence Phase II/III studies in 2009. We are also developing potential new cancer treatments using biological approaches with highly defined molecular targets for patient populations with unmet medical needs.

CAT-8015 is an immunotoxin fusion protein that targets CD22, which is a receptor expressed on the surface of a wide variety of B-cell malignancies. CAT-8015 has orphan drug designation for hairy cell leukaemia in the US and EU. In 2008, the enrolment for studies continued in the CAT-8015 Phase I development programme.

Blinatumomab (MEDI-538) is a recombinant single-chain bi-specific T-cell engager (BiTE™) molecule that is being studied for use in certain

patients suffering from certain lymphomas and leukaemias. Exclusive rights to develop and commercialise blinatumomab in North America have been granted from Micromet.

The US Phase I programme with blinatumomab was suspended during 2008 in order to make appropriate modifications to the dosing regimen based on preliminary results from the EU studies.

#### FURTHER INFORMATION

In April 2008, Sun Pharmaceuticals launched generic amifostine in the US. In response, we extended an agreement with Bedford Laboratories to launch an authorised generic amifostine for oncology in the US. We have ceased all active promotion of branded *Ethyol* in the US. We have an active infringement action against Sun Pharmaceuticals regarding certain *Ethyol* patents.

Abraxane®, discovered, developed and owned by Abraxis, uses a novel technology to deliver paclitaxel for the treatment of breast cancer. During 2008, we co-promoted Abraxane® in the US under an agreement with Abraxis. In November 2008, we entered into an agreement with Abraxis under which Abraxis re-acquired exclusive rights to market Abraxane® in the US. Under the agreement, the board of Abraxis' parent ended the Co-Promotion Agreement. Upon termination, Abraxis will pay AstraZeneca a \$268 million fee on 31 March 2009.

#### FINANCIAL PERFORMANCE 2008/2007

##### PERFORMANCE 2008

###### Reported performance

Sales in Oncology increased by 3% on a reported basis to \$4,954 million up from \$4,819 million in 2007.

###### Performance – CER growth rates

Sales in the Oncology therapy area were down 2% at CER. *Arimidex* sales were up 4% to \$1,857 million. In the US, *Arimidex* sales were up 9% to \$754 million. In other markets, sales increased by 1% to \$1,103 million.

*Casodex* sales decreased by 12% to \$1,258 million, with sales in the US down by 2% and sales in other markets down by 15%.

*Iressa* sales for the year were up 3% as growth in China and other Emerging Markets more than offset the 3% decline in sales in Japan.

*Faslodex* sales were up 12% with a 5% increase in the US and 18% in other markets.

##### PERFORMANCE 2007

###### Reported performance

Oncology sales increased by 13% to reach \$4,819 million in 2007, compared with \$4,262 million in 2006.

###### Performance – CER growth rates

Oncology sales grew by 8% at CER. *Arimidex* sales reached \$1,730 million, up 10%. In the US, sales of *Arimidex* rose by 13% to \$694 million. Total prescriptions for *Arimidex* increased nearly 5.3% compared with 1.3% growth in the market for hormonal treatments for breast cancer. *Arimidex* sales in other markets increased by 8% to \$1,036 million. Sales for the full year were up 6% in Western Europe and increased 9% in Japan.

*Casodex* sales increased by 6% to \$1,335 million. Sales in the US for the full year were up 1% to \$298 million. Sales in other markets, which accounted for more than 75% of product sales, were up 8%, on 6% growth in Western Europe and 13% sales growth in Japan.

*Iressa* sales were unchanged for the full year. Sales in Japan increased 4% for the year; sales in China were up 24%.

*Faslodex* sales increased 10% to \$214 million for the full year, on growth of 3% in the US and 18% sales growth in other markets.

# RESPIRATORY AND INFLAMMATION

## 2008 IN BRIEF

- > *Symbicort* sales over \$2 billion, up 22%.
- > *Symbicort Rapihaler* (pMDI) licensed for long-term maintenance treatment of asthma in the US. Submissions made for use in COPD and paediatric asthma.
- > Outside the US, *Symbicort Turbuhaler SMART* now approved for use in managing asthma in over 90 countries.
- > *Symbicort Turbuhaler* now approved in COPD in over 80 countries.
- > The Joint Advisory Committee of the FDA concluded that the benefits of *Symbicort* outweigh the risks in adult and adolescent asthma patients.
- > Continued growth for *Pulmicort* with sales of \$1.49 billion.
- > Settlement of AstraZeneca's *Pulmicort Respules* patent infringement litigation against Teva including an exclusive licence to Teva to sell generic *Pulmicort Respules* from 15 December 2009 with significant royalties for AstraZeneca.

## OUR MARKETED PRODUCTS

***Symbicort Turbuhaler*** (budesonide/formoterol in a dry powder inhaler) is a combination of an inhaled corticosteroid and a fast onset, long-acting bronchodilator for the treatment of asthma and COPD.

***Symbicort SMART*** is licensed for maintenance therapy as well as for maintenance and reliever therapy in persistent asthma.

***Symbicort Rapihaler*** (pMDI) (budesonide/formoterol in a pressurised metered-dose inhaler) for the maintenance treatment of asthma.

***Pulmicort*** (budesonide) is a corticosteroid anti-inflammatory inhalation drug that helps prevent symptoms and improves the control of asthma.

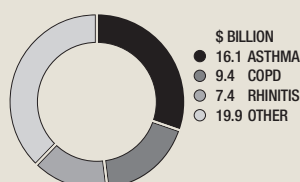
***Pulmicort Respules*** (budesonide inhalation suspension) is the first and only nebulised corticosteroid in the US for the treatment of asthma in children as young as 12 months.

***Rhinocort*** (budesonide) is a nasal steroid treatment for allergic rhinitis (hay fever), perennial rhinitis and nasal polyps.

***Oxis*** (formoterol) is a fast onset, long-acting beta-agonist for treating asthma and COPD.

***Accolate*** (zafirlukast) is an oral leukotriene receptor antagonist for the treatment of asthma.

## THERAPY AREA WORLD MARKET (MAT/Q3/08)



The prescription Respiratory world market value is \$53 billion.

The World Health Organization estimates that 100 million people worldwide suffer from asthma and more than twice that from chronic obstructive pulmonary disease (COPD), which is currently the fourth leading cause of death in the world with further increases in the prevalence and mortality of the disease predicted for the coming decades.

## OUR STRATEGIC OBJECTIVE

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

## COPD AND ASTHMA

COPD is expected to become the world's third biggest health threat by 2020. Current treatment has recently demonstrated some survival benefit but the prognosis of the COPD patient remains poor. In asthma, morbidity and mortality remain important issues and disease normalisation is not achieved by any treatment.

The typical treatment across COPD and asthma is a fixed-dose combination of an inhaled corticosteroid (ICS) with a long-acting beta-agonist (LABA) or for COPD specifically, inhaled long-acting muscarinic agonist (LAMA). Other major asthma treatments include oral leukotriene receptor antagonists and oral steroids for severe disease and (in combination with antibiotics) for exacerbations. Significant new product classes impacting the asthma market up to 2015 are unlikely. First novel anti-inflammatory compounds aimed mainly at prevention and/or treatment of COPD exacerbations, such as oral phosphodiesterase 4 inhibitors, may appear on the market before 2015.

*Symbicort SMART* flexible dosing introduced a step change to asthma care in Europe resulting in lower ICS and oral steroid use. Novel ICS/LABA combination products for this area are expected from 2009 and generic ICS/LABA combinations may be available from the early part of the next decade. Several companies are developing new biologics for severe asthma, including improved versions of anti-IgE and differentiated anti-cytokine antibodies. Post-2015, immune response modifiers could deliver intermittent therapy for moderate to severe asthma.

A number of novel COPD combinations in industry pipelines may change the way in which COPD is managed. Combinations of LABAs, LAMAs and triple-combinations with existing and new anti-inflammatories, may become future treatments of choice. There are also agents in early development with the potential to change the course of the disease by targeting the immune and inflammatory response that results in lung damage.

## OUR FOCUS

### Our key marketed products

*Symbicort Turbuhaler* provides rapid, effective control of asthma and effective reduction of exacerbations, improving symptoms and providing a clinically important improvement in the health of patients with severe COPD.

*Symbicort Rapihaler* (pMDI) approved for the long-term maintenance treatment of asthma in patients 12 years of age and older, was launched in the US in 2007. Further information about the progress of *Symbicort* since its launch in the US is set out in the Geographical Review on page 49. In December 2008, the Joint Advisory Committees of the FDA completed a review of the benefits and risks of asthma medications containing LABAs. This concluded that the benefits of *Symbicort* outweigh the risks in adult and adolescent asthma patients.

*Symbicort SMART* provides increased asthma control and simplifies asthma management through use of only one inhaler for both maintenance and relief of asthma symptoms. It is also a cost-effective treatment option for many healthcare payers. *Symbicort SMART* is included in the Global Initiative for Asthma, the international treatment guidelines.

The US sNDAs for *Symbicort Rapihaler* (pMDI) in COPD and paediatric asthma in the US were submitted as planned during the second quarter of 2008. Our existing regulatory filings for *Symbicort Rapihaler* (pMDI) in the EU for asthma and COPD were supplemented with data supporting two additional strengths in the second half of 2008.

*Pulmicort* remains one of the world's leading asthma medicines and is available in several forms. *Pulmicort pMDI* is now approved in 98 countries.

Information about our settlement of the patent infringement action against IVAX in the US, which began in October 2005, in relation to IVAX's ANDA for a budesonide inhalation suspension is set out in Note 25 to the Financial Statements from page 154.

*Oxis* is added to the treatment regime when corticosteroid treatment alone is not adequate. *Oxis* is also indicated for symptom relief in COPD.

*Rhinocort* combines powerful efficacy with rapid onset of action and minimal side effects and is available as a once-daily treatment in the *Rhinocort Aqua* (nasal spray) and the *Turbuhaler* dry powder inhaler forms.

## OUR FINANCIAL PERFORMANCE

	2008			2007			2006	2008 compared to 2007		2007 compared to 2006	
	Sales \$m	CER growth \$m	Growth due to exchange effect \$m	Sales \$m	CER growth \$m	Growth due to exchange effect \$m	Sales \$m	CER growth %	Reported growth %	CER growth %	Reported growth %
<i>Pulmicort</i>	1,495	7	34	1,454	128	34	1,292	–	3	10	13
<i>Symbicort</i>	2,004	346	83	1,575	265	126	1,184	22	27	22	33
<i>Rhinocort</i>	322	(41)	9	354	(16)	10	360	(12)	(9)	(4)	(2)
<i>Oxis</i>	71	(21)	6	86	(9)	7	88	(24)	(17)	(10)	(2)
<i>Accolate</i>	73	(4)	1	76	(6)	1	81	(5)	(4)	(7)	(6)
Other	163	(9)	6	166	7	13	146	(5)	(2)	5	14
<b>Total</b>	<b>4,128</b>	<b>278</b>	<b>139</b>	<b>3,711</b>	<b>369</b>	<b>191</b>	<b>3,151</b>	<b>7</b>	<b>11</b>	<b>12</b>	<b>18</b>

**Clinical trial developments**

In the latter part of 2008, data from one of the pivotal US COPD studies were published (SHINE), confirming the efficacy and tolerability of *Symbicort Rapihaler* (pMDI) in COPD.

**In the pipeline**

Our monoclonal antibody (MAb) programmes for asthma treatments focus on targeting interleukins which appear to play a role in the regulation of inflammatory and immune responses and, therefore, may improve the treatment and/or prevention of asthma. Most of these MAbs are in Phase II to assess their potential to affect the significant remaining unmet medical need in the disease including uncontrolled asthma and moderate to severe persistent asthma. Concurrent Phase I activity is supporting our understanding of the impact of these large molecules on asthma biology.

MEDI-563 is an investigational approach that may treat or help prevent asthma by targeting the interleukin-5 (IL-5) receptor to neutralise the binding of IL-5 and deplete the cells expressing the IL-5 receptor, typically eosinophils, as both IL-5 and eosinophils are thought to play key roles in the pathology of asthma. In 2008, the results of a Phase I study presented at the European Respiratory Society meeting showed that MEDI-563 exhibited an acceptable safety profile and showed pharmacological activity in mild asthmatics. In addition, a Phase I study to measure the depletion of eosinophils in the airways of asthmatics and a Phase II study with this anti-IL-5 receptor MAb to assess whether it can reduce the incidence of asthmatic relapse in subjects following an asthmatic episode that required hospitalisation have been initiated.

Also in 2008, we completed two out of three ongoing Phase IIa studies evaluating the potential for MEDI-528 (anti-IL-9 MAb) to treat or prevent symptomatic, moderate to severe persistent asthma, and a fourth Phase IIa clinical trial, designed to assess its effectiveness in patients with stable asthma and exercise-induced bronchoconstriction, was initiated.

CAT-354 targets interleukin-13 (IL-13). In 2008, we initiated two new studies with CAT-354: a Phase II trial in Europe and Australia designed to assess the potential of this MAb in patients with uncontrolled asthma despite optimal treatment, and a US Phase I study to assess pharmacokinetics in healthy adult patients.

The early pipeline has been reshaped to focus more on COPD, looking for novel strategies to inhibit exacerbations in COPD which include regulation of inflammatory cell migration and activation with MAbs directed to antigen. These include CXCR3, as well as inhibition of molecules involved in both viral and bacterial mediated exacerbations. A number of small molecule approaches for the treatment of COPD are in development. AZD1236 is a potent MMP inhibitor currently in Phase II, the expression of these proteins are associated with key pathological features of the disease including bronchiolitis, vasculitis and emphysema. Human Neutrophil Elastase (HNE) is a key factor in cigarette smoke induced inflammation, lung injury and emphysema and AZD9668, a potent and selective oral, reversible inhibitor of HNE, also in Phase II, is expected to reduce the progression and severity of COPD.

Alongside these novel approaches and building on our capabilities in combinations and device development demonstrated through our experience with *Symbicort*, we are aiming to improve further the symptom relief delivered by on-market bronchodilators, the mainstay of treatment for all COPD patients. By combining two enhanced bronchodilators in one inhaler, patients should benefit from improved symptom control, as well as reducing the complications of multiple dosing or inhaler devices.

Strategic collaboration activity makes a key contribution to our respiratory pipeline. AstraZeneca and MAP Pharmaceuticals announced in December 2008 an exclusive worldwide agreement to develop and commercialise Unit Dose Budesonide (UDB), MAP Pharmaceuticals' proprietary nebulised formulation of budesonide. This agreement

is subject to review in the US under the Hart-Scott-Rodino Act and becomes effective after the waiting period has ended. UDB is being developed by MAP Pharmaceuticals as a potential treatment for paediatric asthma and is currently in Phase III clinical development. UDB has the potential to be nebulised more quickly and at a lower nominal dose than the commercially available product. AstraZeneca and Daiippon Sumitomo have a well-established alliance to discover and develop small molecules directed towards toll-like receptor 7 and the first compound from this alliance has entered early stage development.

The partnership with Dynavax Technologies Corporation, which began in 2006, continues to pursue opportunities in the field of toll-like receptors. Dynavax has unique competence in generating immunostimulatory DNA sequences that activate toll-like receptors. The alliance should enable us to expand our portfolio of small molecule and biological drugs to treat asthma and COPD.

Our 2007 discovery alliance with Argenta Discovery Limited aimed at identifying improved bronchodilators to treat COPD continues.

Our three-year research collaboration with Silence Therapeutics, established in 2007, is continuing. In 2008 we entered into a new collaboration with this company focused on the development of a range of novel approaches for the delivery of siRNA molecules, which allows both Silence Therapeutics and AstraZeneca to commercialise the novel delivery systems we develop together.

**RHEUMATOLOGY**

Rheumatoid arthritis (RA) is currently treated with generic disease-modifying anti-rheumatic agents and, where the relevant criteria are met, biologic disease-modifiers. There remains a need for novel effective treatments since only about a third of patients treated with biologics achieve their treatment goals.

The RA market has grown from \$1.3 billion in 1998 to over \$10 billion in 2008, driven largely by the introduction of biologic tumour necrosis factor alpha (TNF $\alpha$ ) blockers (first Amgen/Wyeth's Enbrel™, followed by Centocor/Schering-Plough's Remicade™ and Abbott's Humira™), which together account for over \$8 billion in this disease alone. Launches of additional TNF blockers are imminent, and use of other biologic approaches, currently reserved for TNF failures, is expected to increase. Targeted novel oral drugs aimed at patients that currently choose not to take, are ineligible for or don't respond to biologics, are in development to provide anti-TNF-like efficacy with safety benefits and more convenient dosing.

Current treatment of systemic lupus erythematosus (SLE) focuses on controlling disease flares, preventing renal failure and suppressing symptoms to an acceptable level while minimising toxicity. Despite considerable recent development activity, no targeted disease-modifying agents have yet been successfully launched for SLE. Most emerging biologic agents will likely be used initially in combination with corticosteroids or immunosuppressants to provide incremental benefit and/or allow reduced doses or numbers of these agents.

## OUR FOCUS

### In the pipeline

In 2008, we invested in several novel multi-functional MABs that allow simultaneous inhibition of either two secreted proteins or surface receptors. Our first disease being studied is RA, where TNF inhibitors with other molecules may improve both the efficacy and prevent the establishment of TNF refractory disease while maintaining an acceptable safety profile.

MEDI-545 is a MAB targeting interferon-alpha, which regulates processes involved in autoimmune diseases. In 2008, we initiated a Phase IIa trial in patients with SLE and a Phase I study in patients with active dermatomyositis.

CAM-3001 is a MAB with potential to help patients with RA. The antibody targets the alpha sub-unit of the granulocyte-macrophage colony stimulating factor receptor. In September 2008, preliminary results were reviewed from the first Phase I study of CAM-3001, which had been initiated to evaluate the safety profile and tolerability of single doses in patients with RA. AstraZeneca, through its acquisition of MedImmune, acquired exclusive development rights to the CAM-3001 programme from CSL Limited in 2007.

AZD9056 and AZD5672 are novel oral compounds being primarily developed as a new generation of disease modifying anti-rheumatoid arthritis drugs. Currently in Phase IIb, their different mechanisms of action (a P2X7 antagonist and a CCR5 antagonist) provide multiple chances of success to provide significant new choice in the management of RA.

We also have an ongoing alliance with Bayer Schering in respiratory and rheumatology indications with the objective of identifying novel compounds without steroid side effects.

## FURTHER INFORMATION

Patent infringement litigation filed by AstraZeneca against IVAX Pharmaceuticals (a wholly owned subsidiary of Teva Pharmaceuticals USA (Teva)) following the submission of an ANDA with the FDA for generic *Pulmicort Respules* was settled in November 2008. Under the terms of the settlement, Teva concedes that the patents asserted by AstraZeneca in the litigation are valid and enforceable and that its generic version of *Pulmicort Respules* infringes AstraZeneca's patents. See Note 25 for further details.

## FINANCIAL PERFORMANCE 2008/2007

### PERFORMANCE 2008

#### Reported performance

Sales in Respiratory and Inflammation therapy area (R&I) increased by 11% to \$4,128 million from \$3,711 million in 2007.

#### Performance – CER growth rates

R&I sales grew by 7% at CER.

Sales of *Symbicort* grew by 22% to \$2,004 million. In the US, sales of the product were \$255 million, up 410%. Product trial rate among target specialist physicians is now approaching 90%; these specialists are now starting more than 30% of patients new to combination therapy on *Symbicort*. More than half of target primary care physicians have prescribed *Symbicort*, and share of new patient starts is just under 18%. Overall, *Symbicort* share of new prescriptions for fixed combinations reached 11.7% in the week ending 16 January, with market share among patients newly starting combination treatment at 18.3%. *Symbicort* sales in other markets in the year were \$1,749 million, up 9%. *Symbicort SMART* has now been approved in 91 markets.

*Pulmicort* sales were flat at \$1,495 million, with US sales up 2% as the generic competition from the Teva product affected quarter four sales. US sales for *Pulmicort* were down 15% to \$260 million in the fourth quarter and *Pulmicort Respules* sales were down 18% as a result of the "at risk" launch of generic budesonide inhalation suspension (BIS) on 18 November. The patent litigation between Teva and AstraZeneca was subsequently settled on 26 November. The agreement allows Teva to commence sales of BIS under an exclusive licence from AstraZeneca beginning 15 December 2009. The agreement also provided that any product already shipped by Teva would remain in the market to be further distributed and dispensed. As a result, Teva products accounted for nearly 15% of total prescriptions for BIS products dispensed during the fourth quarter, including a 40% share in December 2008. US sales for *Pulmicort* for the full year were \$982 million. *Pulmicort Respules* accounted for around 90% of total *Pulmicort* sales in the US. Sales of *Pulmicort* in Rest of World were down 2% for the full year to \$513 million.

### PERFORMANCE 2007

#### Reported performance

Continued growth from *Symbicort* drove the increase in reported sales for R&I, which grew by 18% from \$3,151 million in 2006 to \$3,711 million in 2007.

#### Performance – CER growth rates

Sales in R&I increased by 12% at CER.

*Symbicort* sales for the full year were up 22% to \$1,575 million. Sales in Western Europe were up 16%, with market share up another point in the last 12 months, aided by the roll-out of the *Symbicort SMART* regime. Good growth for the year was achieved in Canada (up 25%) and in Emerging Markets (up 26%). Sales in the US were \$50 million since launch at the end of June 2007. Specialist physicians rapidly adopted the product; nearly 75% of allergists and more than 60% of pulmonary specialists in our target audience have prescribed *Symbicort*. *Pulmicort* sales increased by 10% to \$1,454 million. US sales increased 15% for the full year to \$964 million. *Pulmicort Respules* sales in the US were up more than 20% for the full year, on estimated volume growth of 15%. Of the approximately six million children under the age of eight who are treated for asthma, more than one million benefit from treatment with *Pulmicort Respules*. Sales in other markets were unchanged for the year.

*Rhinocort* sales fell by 4% to \$354 million, with a 9% decline in the US being compensated by small gains elsewhere.