

## NEUROSCIENCE MEDICINES

MARKETED PRODUCTS<sup>1</sup>

**Seroquel** (quetiapine fumarate) is an atypical anti-psychotic drug. It is approved for the treatment of schizophrenia, bipolar mania and bipolar depression. Its overall clinical efficacy and tolerability profile helped make it the leading atypical anti-psychotic in the US.

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

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

**Naropin** (ropivacaine), with its safety and mobility profile, is the world's best-selling, long-acting local anaesthetic, replacing the previous standard treatment of bupivacaine.

**Xylocaine** (lidocaine) continues to be the world's most widely used short-acting local anaesthetic after more than 50 years on the market.

## 2007 IN BRIEF

- > **Seroquel sales up 15% to over \$4 billion.**
- > **Seroquel XR major depressive disorder and generalised anxiety disorder clinical study data presented for the first time. US and EU regulatory submissions planned in 2008.**
- > **Seroquel XR approved in nine countries, including the US, and progressed through the mutual recognition procedure in the EU, for acute and maintenance treatment of schizophrenia.**
- > **US regulatory submissions for Seroquel XR for the treatment of bipolar depression and bipolar mania.**
- > **AZD3480 entered Phase IIb testing in Alzheimer's disease and cognitive disorders in schizophrenia.**
- > **Patent infringement actions commenced against two generic drug manufacturers in the US following abbreviated new drug applications relating to Seroquel.**
- > **Numerous personal injury actions in the US and Canada involving Seroquel being defended vigorously.**

## PERFORMANCE

	2007			2006			2005	2007 compared to 2006		2006 compared to 2005	
	Sales \$m	Growth underlying \$m	Growth due to exchange effects \$m	Sales \$m	Growth underlying \$m	Growth due to exchange effects \$m		Growth underlying %	Growth reported %	Growth underlying %	Growth reported %
Seroquel	4,027	526	85	3,416	655	-	2,761	15	18	24	24
Zomig	434	18	18	398	47	(1)	352	5	9	13	13
Diprivan	263	(53)	12	304	(62)	(3)	369	(17)	(13)	(17)	(18)
Local anaesthetics	557	(6)	34	529	24	(6)	511	(1)	5	5	4
Other	59	(1)	3	57	(8)	(1)	66	(2)	4	(12)	(14)
<b>Total</b>	<b>5,340</b>	<b>484</b>	<b>152</b>	<b>4,704</b>	<b>656</b>	<b>(11)</b>	<b>4,059</b>	<b>10</b>	<b>14</b>	<b>16</b>	<b>16</b>

## PIPELINE

Compound	Mechanism	Areas under investigation	Phase			Estimated filing date	
			I	II	III	Europe	US
<b>NCEs</b>							
PN400	naproxen + esomeprazole	signs and symptoms of OA, RA, and AS	■	■	■	1H 2009	1H 2009
AZD3480	neuronal nicotinic receptor agonist	cognitive disorders in schizophrenia	■	■		2011	2011
AZD3480	neuronal nicotinic receptor agonist	Alzheimer's disease	■	■		2011	2011
AZD6765	NMDA receptor antagonist	depression	■	■			
AZD2327	enkephalinergic receptor modulator	anxiety and depression	■				
AZD5904	inhibitor of myeloperoxidase (MPO)	multiple sclerosis	■				
AZD3241	inhibitor of myeloperoxidase (MPO)	Parkinson's disease	■				
AZD0328	selective neuronal nicotinic receptor agonist	Alzheimer's disease	■				
AZD1940	CB receptor agonist	nociceptive and neuropathic pain	■				
AZD2624	NK receptor antagonist	schizophrenia	■				
AZD1386	vanilloid receptor antagonist	chronic nociceptive pain	■				
AZD2066	metabotropic glutamate receptors	chronic nociceptive pain	■				
AZD7325	GABA receptor subtype partial agonist	anxiety	■				
AZD6280	GABA receptor subtype partial agonist	anxiety	■				
TC-5619 (Targacept)	neuronal nicotinic receptor agonist	cognitive disorders in schizophrenia	■				
<b>Line extensions</b>							
Seroquel XR	D <sub>2</sub> /5HT <sub>2</sub> antagonist	schizophrenia	■	■	■	Approved	Launched
Seroquel	D <sub>2</sub> /5HT <sub>2</sub> antagonist	bipolar maintenance	■	■	■	2Q 2008	Filed
Seroquel	D <sub>2</sub> /5HT <sub>2</sub> antagonist	bipolar depression	■	■	■	1Q 2008	Launched
Seroquel XR	D <sub>2</sub> /5HT <sub>2</sub> antagonist	generalised anxiety disorder	■	■	■	4Q 2008	2Q 2008
Seroquel XR	D <sub>2</sub> /5HT <sub>2</sub> antagonist	major depressive disorder	■	■	■	3Q 2008	1Q 2008
Seroquel XR	D <sub>2</sub> /5HT <sub>2</sub> antagonist	bipolar mania	■	■	■	1Q 2008	Filed
Seroquel XR	D <sub>2</sub> /5HT <sub>2</sub> antagonist	bipolar depression	■	■	■	1Q 2008	Filed

For discontinued projects see page 30.

<sup>1</sup> In 2006, we sold our range of US branded anaesthetics and analgesic products to Abraxis BioScience, Inc.. These included Xylocaine™, Polocaine™, Naropin™, Nesacaine™, Sensorcaine™, Astramorph™, EMLA Cream™ and Diprivan™.

## NEUROSCIENCE MEDICINES CONTINUED

**PIPELINE**

Our product pipeline and life cycle management work is focused on the important areas of pain control, psychiatry, analgesia, neurology and anaesthesia. In 2007, we have significantly strengthened the early development pipeline by progressing 10 additional compounds into clinical testing. Although it was decided in 2006 not to start new discovery work in Parkinson's disease (PD), multiple sclerosis (MS) and neuroprotection in stroke, current projects in development for PD and MS continue as planned.

**Pain control**

PN400 is a fixed-dose combination tablet of naproxen and esomeprazole which uses proprietary technology licensed from POZEN Inc. through a partnership established in August 2006. It is being developed for the relief of signs and symptoms of osteoarthritis, rheumatoid arthritis and ankylosing spondylitis in patients at risk for developing non-steroidal anti-inflammatory drug (NSAID)-associated gastric ulcers. At least 50% of the 60 million osteoarthritis patients in the US and the five largest European countries are at risk of developing NSAID-associated ulcers.

A phase III trial programme, which was initiated in the third quarter of 2007, is evaluating the incidence of gastric ulcers in at-risk patients with chronic pain taking PN400 versus the ulcer incidence in those taking naproxen alone. A regulatory submission for PN400 in the US is currently planned for the first half of 2009.

**Psychiatry**

We progressed four compounds, AZD6765, AZD2624, AZD6280 and AZD7325, into clinical development for the treatment of anxiety, schizophrenia and/or depression. We also entered into a collaboration with the University of Texas Southwestern Medical Center at Dallas, US to accelerate scientific discovery and therapeutic advancement for depression.

**Analgesia**

We have progressed three compounds, AZD2066, AZD1940 and AZD1386 into phase I clinical development for the treatment of nociceptive (caused by tissue damage) and/or neuropathic (caused by nerve damage) pain.

In October 2007, by mutual agreement with NPS Pharmaceuticals, Inc. we decided to end our collaborative efforts to discover and develop drugs targeting metabotropic glutamate receptors (mGluRs). As part of this agreement, we have acquired certain know-how, intellectual property and technology rights from NPS Pharmaceuticals for our exclusive use.

We have established a partnership with the University of Texas M. D. Anderson Cancer Center to develop platforms and clinical targets for new drugs in chronic pain.

**Neurology**

We continue to expand our research capabilities in positron emission tomography (PET) through our collaboration with the Karolinska Institute in Sweden, providing early signalling of potential efficacy for our Alzheimer's compounds. In addition, we have established two Alzheimer's alliances with key US centres, the Banner Alzheimer's Institute in Phoenix, Arizona and Washington University in St. Louis. Both approaches are focused on the identification and progression of Alzheimer's disease. We currently have eight development programmes, of which six are in clinical evaluation, in Alzheimer's disease, cognitive disorders in schizophrenia (CDS) and specific segments of other neuro-degenerative diseases, multiple sclerosis and Parkinson's disease.

AZD3480, the neuronal nicotinic receptor agent that we licensed from Targacept, Inc. in 2005, has successfully progressed into phase IIb clinical testing in both Alzheimer's disease and cognitive disorders in schizophrenia (CDS). We have exercised a right to acquire an option from Targacept to take a licence of TC-5619, which Targacept is developing in CDS.

**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.

**Underlying performance**

On a constant exchange rate basis, Neuroscience sales grew by 10%. Annual *Seroquel* sales exceeded \$4 billion for the first time in 2007, with full year sales of \$4,027 million, up 15% over last year. In the US, *Seroquel* sales increased by 15% to \$2,863 million. Total prescriptions increased by 10% for the year, more than twice the market rate. Market share of total prescriptions in the US antipsychotic market increased to 31.8% in December 2007, up 1.3 percentage points in the last 12 months, with a third of the increase attributable to *Seroquel XR* in the five months since launch in August. *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 by 5% in the US (to \$177 million) and 4% in other markets, totalling \$434 million.

**PERFORMANCE 2006****Reported performance**

Neuroscience sales grew by 16% to \$4,704 million in 2006 from \$4,059 million in 2005 with growth in all geographic areas, driven chiefly by *Seroquel*.

**Underlying performance**

After excluding exchange effects of \$11 million, underlying growth was 16%.

*Seroquel* sales reached \$3,416 million (up 24%). In the US, *Seroquel* sales were up 24% to \$2,486 million. Total prescriptions increased by 12%, well ahead of the market. The *Seroquel* share of total prescriptions in the US anti-psychotic market increased to 30.2% in December, up 1.7 percentage points over last year. In other markets, sales were up 23%, on good growth in Europe (up 25% to \$619 million) and in Asia Pacific (up 15% to \$149 million).

*Zomig* sales increased by 13% to \$398 million. *Zomig* sales comparisons in the US for the full year as compared with 2005 are affected by the resumption of full responsibility from MedPointe, Inc. for US commercialisation in April 2005. Sales for *Zomig* in the US were up 39%, although total prescriptions declined by 6%. Sales of *Zomig* in other markets were unchanged.