

TOP 20 PHARMA

AstraZeneca
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HEADCOUNT	67,000
YEAR ESTABLISHED	1999
PHARMA REVENUES*	\$28,713 +12%
TOTAL REVENUES*	\$29,559 +12%
NET INCOME	\$7,983 -7%
R&D BUDGET	\$5,162 +32%

* Revenues include seven months of MedImmune results

DRUGS APPROVED/LAUNCHED

Drug	Indication
crestor	atherosclerosis
nexium	GERD (EU) sachet formulation
seroquel XR	schizophrenia
symbicort pMDI	asthma
flumist	influenza (from MedImmune)
seroquel	bipolar maintenance

DRUGS CANCELLED

Drug	Indication
azd1283	thrombosis
azd3988	diabetes/obesity
azd3118	arrhythmias
crestor	outcomes CHF
nexium	NSAID GI side effects, symptom resolution, ulcer healing
azd9056	inflammatory bowel disease
azd3783	anxiety and depression
azd1080	Alzheimer's disease
azd6495	range of tumors
azd5180	solid tumors
hMPV MAb	respiratory infection
medi-552	leukemia/lymphoma
medi-555	solid tumors
cat-3888	hairy cell leukemia
azd9935	solid tumors
azd4992	breast cancer
medi-552	inflammation
azd6605	osteoarthritis

DRUGS PENDING APPROVAL

Drug	Indication
seroquel XR	bipolar mania, bipolar depression, generalized anxiety disorder, maintenance of schizophrenia
symbicort pMDI	COPD
iressa	locally advanced or metastatic Non-Small Cell Lung Cancer (NSCLC)
symbicort	treatment of asthma in pediatric patients

DRUGS IN PHASE IIB AND BEYOND

Drug	Indication
atacand	diabetic retinopathy
crestor	outcomes end stage renal disease
nexium	peptic ulcer bleeding

seroquel XR	major depressive, generalized anxiety disorder
faslodex	first line, adjuvant advanced breast cancer
iressa	NSCLC
azd6140	arterial thrombosis
saxagliptin	diabetes
dapagliflozin	diabetes
crestor/abt-335	dyslipidemia
pn400	signs and symptoms of osteoarthritis, rheumatoid arthritis
zactima	NSCLC
recentin	NSCLC and CRC, recurrent glioblastoma
zd4054	hormone resistant prostate cancer
motavizumab	RSV prevention (MedImmune)

EARLY RESEARCH PROJECTS

Drug	Indication
azd1175	diabetes/obesity
azd1305	arrhythmias
azd6370	diabetes
azd2066	GERD

DRUGS COMING OFF PATENT

Drug	Indication
losec/prilosec	acid-related diseases (2007)
toprol-X	hypertension, heart failure and angina (2007)
zestril	cardiovascular disease, hypertension (2007)
plendil	hypertension and angina (2007)
symbicort	COPD (2007 EU) (formoterol and budesonide)

TOP SELLING DRUGS

Drug	Indication	\$	(+/- %)
Nexium	peptic ulcer, acid reflux	\$5,216	1%
Seroquel	anti-psychotic	\$4,027	18%
Crestor	cholesterol	\$2,796	38%
Arimidex	oncology	\$1,730	15%
Symbicort	asthma	\$1,575	33%
Pulmicort	asthma	\$1,454	13%
Seloken/Toprol	hypertension	\$1,438	-20%
Casodex	prostate cancer	\$1,335	11%
Atacand	hypertension	\$1,287	16%
Losec/Prilosec	peptic ulcer, acid reflux	\$1,143	-17%
Zoladex	oncology	\$1,104	10%
Merrem	anti-infection	\$773	28%

Account for 83% of total pharma sales, down from 84% in 2006.

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ASTRAZENECA HAS BEEN HAUNTED by recent failures, as several late-stage crashes and commercial mishaps have left it vulnerable. Are things turning around? In the last three months, AZ has negotiated its way out of generic exposure for its top seller (Nexium) and won a court battle extending the patent protection for its #2 seller. Those products added up to more than \$9.0 billion in 2007 revenues, so their loss would have spelled doom for the company before its 10th anniversary.

Speaking of anniversaries, June 2008 marked one year since AZ closed on its \$15.5 billion acquisition of MedImmune. As I pointed out in GSK's profile, major pharma companies like to talk about how they're going to incorporate the entrepreneurialism and flexibility of biopharmas into their existing companies. AZ has been a bit more honest about employing MedImmune for its infrastructure and experience in developing biologics, rather than paying lip service to how they'll incorporate some sort of freewheeling maverick biotech spirit into a 67,000-employee company.

The acquisition had the immediate effect of bumping AZ's clinical projects (NMEs and line extensions) from 71 to 95, and doubled the number of projects in Phase III to 10. In February 2008, the company filed a BLA for Numax, a next-generation version of Synagis, a treatment for respiratory syncytial virus (RSV), so the purchase has generated some value.

Still, to my eye, there are moments when MedImmune looks like AZ's accidental poison pill, keeping unwanted suitors at bay. I'm sure that wasn't the key driver in acquiring MedImmune; I still take AZ management at face value when they said that MedImmune was intended to deliver a fully-formed biopharma infrastructure, capable of "accelerat[ing] delivery of its biologics strategy while lowering its execution risk," to quote AZ chief executive officer David Brennan.

That said, I can see how paying off that \$15.5 billion bill, on top of the standard problems involved with integrating a major pharma, would make takeover players back off. Especially now that the two top figures at MedImmune have moved on to greener pastures.

Less than two weeks after the acquisition's anniversary, MedImmune chief executive David Mott and R&D head James Young, Ph.D. chose to leave AZ. The *Wall Street Journal's* Health Blog noted that Mr. Mott — who's sticking around through July — and Dr. Young signed retention term sheets to stay with the company for one year after the merger.

Mr. Mott received a payment of around \$145 million from AZ's buyout, which must have made it awfully difficult to make it through the workday. I'd have set up my computer with a countdown clock to notch off the seconds until the one-year term expired, at which point I would run home and dive into a swimming pool filled with cash, but that's just me.

Not Dead Yet

I don't mean to imply that it's all doom and gloom at AZ. The company's LDL drug, Crestor, gained almost \$800 million in sales in 2007; FDA approval of asthma treatment Symbicort helped that drug reach \$1.5 billion in 2007 sales, and Seroquel is picking up new indications as it moves up to become AZ's top seller.

Crestor "only" increased 16% in 1Q08, but the company noted that it was the only branded statin to gain market share during that period. It'll likely perform even better in 2Q08, given the fallout from the Vytorin mess (see Merck and Schering-Plough's profiles for more on that). In November 2007, Crestor was approved by the FDA to treat atherosclerosis, and AZ recently began a trial to test Crestor against Lipitor in that indication.

In addition to that NuMax filing, AZ has two other NDA filings planned: Onglyza (saxagliptin), the diabetes drug it licensed from Bristol-Myers Squibb last year, and Zactima, a cancer treatment that received fast-track status from the FDA in 2006 for thyroid cancer.

In-or-Outsourcing?

For our readership, the most interesting event involving AstraZeneca last year was its on-again, off-again statements about its plans to outsource almost all of its manufacturing within the decade.

The kerfluffe began in September 2007. In a *London Times* article by Robin Pagnamenta, AZ's executive vice president of operations, David Smith, commented, "Manufacturing for AstraZeneca is not a core activity . . . AstraZeneca is about innovation and brand-building . . . There are lots of people and organisations that can manufacture better than we can."

He added that the company's priority was to outsource all API manufacturing, preferably to the far east, and eventually move drug manufacturing out of house, too. He remarked, "We would own the IP, the research, branding and the quality and safety issues . . . but [everything else] would be outsourced. The idea is to take out as many stages as you can." Mr. Smith's comments were almost immediately denied by AZ, which presented his remarks as hypotheticals.

THE LOWE DOWN

ASTRAZENECA'S BEEN CUTTING BACK its research this year — but then, you could substitute a lot of other company names and that statement would fit just fine. The research organization seems to be unafraid to try new things, if all those fragment-based drug design papers they're publishing are any measure. That may be a hopeful sign, because new things definitely seem to be needed around the industry. (Of course, the literature being what it is, those papers might only mean that they weren't afraid to try new things four years ago).

They'll be needing some new stuff soon. The Vytorin mess over at Schering-Plough has helped out AZ's statin sales, but you can't just live on other people's problems. The Nexium franchise is on the downward side of its life, and there aren't as many things to replace it as there looked to be a few years ago. The company seems to be doing the right things: here's hoping that that's enough.

—Derek Lowe

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When our online editor Joanna Cosgrove asked AZ to clarify things, Joan E. Pitt, AZ's director of communications, global operations, commented, "We currently outsource API production in Europe and India, and are currently looking at outsourcing intermediates from China. And, under the strategy we will continue to look at opportunities in both Europe and Asia."

A few months later, however, AZ performed another about face. In AZ's "authorized generic" agreement with Ranbaxy over Nexium, the two companies made an interesting side agreement. In addition to authorizing Ranbaxy to make a generic of the drug in 2014, with its 180-day exclusivity, AZ will also allow Ranbaxy to manufacture the API for Nexium in 2009 and formulate some of the U.S. supply of it around May 2010.

In a conference call about the Ranbaxy deal, Mr. Brennan said, "This move is absolutely consistent with our supply chain strategy . . . We have been looking to outsource our manufacturing where we can . . . we have long-term plans to exit all API production over the next five to 10 years."

Ms. Cosgrove called Ms. Pitt again, and she responded, "We have now stated our intent to outsource API manufacture over the next five to ten years . . . Please note this is only API manufacture [for Nexium] and not all manufacture. As noted . . . the full outsource of supply and manufacturing activities is not part of the AZ strategy."

THE NAME'S AL. ALBIREO.

ANOTHER INTERESTING ASPECT of AZ's restructuring efforts is its interest in licensing out development programs. Just last year, AZ put forth a huge investment to in-license Bristol-Myers Squibb's saxagliptin, which has a chance of being the third DPP-4 inhibitor to reach the U.S. diabetes market. A year later, AZ spun off some of its GI research to a new firm called Albireo. The company is funded by several growth capital firms (AZ still has a "significant minority interest" in it) and covers one clinical and several preclinical programs for GI disorders. The new company is located in AZ's old digs in Gothenburg, Sweden. Where it discovered Nexium.

I'll be interested to see if the agreement holds up, since there are several generic companies still suing to get the Nexium patents overturned. If it does, this may shed some light on how AZ plans to tackle the outsourcing of its mature products.

I'd love to see a major pharma company blow up the existing infrastructure and radically rethink its very nature. I just don't get how they plan to source their new compounds (and, yes, I'm assuming they *will* have new compounds). ■