

TOP 20 PHARMA

Eli Lilly & Co.
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HEADCOUNT	40,600
YEAR ESTABLISHED	1876
PHARMA REVENUES	\$17,638 +19%
TOTAL REVENUES	\$18,634 +19%
NET INCOME	\$2,953 +11%
R&D BUDGET	\$3,487 +11%

DRUGS APPROVED/LAUNCHED

Drug	Indication
cialis	erectile dysfunction (once daily)
cymbalta	maintenance major depressive disorder, fibromyalgia
evista	reduce invasive breast cancer risk in postmenopausal women with osteoporosis and those at high risk for invasive breast cancer

DRUGS CANCELLED

Drug	Indication
AIIR Inhaled insulin	type 1 and type 2 diabetes (in collaboration with Alkermes)

DRUGS PENDING APPROVAL

Drug	Indication
olanzapine	adolescent schizophrenia and bipolar disorder
olanzapine-fluoxetine	treatment-resistant depression
pemetrexed disodium	first-line treatment of NSCLC
efficient (prasugrel)	prevention/reduction of atherothrombotic events in patients with acute coronary syndromes who undergo percutaneous coronary intervention (PCI)
ruboxistaurin mesylate	diabetic retinopathy
teriparatide	glucocorticoid-induced osteoporosis
cymbalta	pain

DRUGS IN PHASE IIB AND BEYOND

Drug	Indication
arxozifene	prevention and treatment of osteoporosis and breast cancer risk reduction
duloxetine	chronic pain
enzastaurin	poor prognosis patients with diffuse large B-cell lymphoma
exenatide	once-weekly dosing
mhb8208	secondary progressive multiple sclerosis and relapsing-remitting multiple sclerosis (in collaboration with BioMS Medical)

teplizumab	type 1 diabetes (in collaboration with MacroGenics)
a-beta antibody	Alzheimer's disease
anti-cd20	NHL
asap	solid tumors
factor Xa inhibitor	venous thromboembolism prophylaxis, treatment and atrial fibrillation stroke
glp-fc analog	type 2 diabetes
hy10275	insomnia
il-1 beta antibody	rheumatoid arthritis
mgu2/3 prodrug	schizophrenia
opra II	alcohol dependence
trpv1 antagonist	treatment for various pain conditions, (in collaboration with Glenmark Pharma)

EARLY RESEARCH PROJECTS

Drug	Indication
neri IV	ADHD
ly2405319	type 2 diabetes
enzastaurin	leukemia, lymphocytic

TOP SELLING DRUGS

Drug	Indication	\$	(+/- %)
Zyprexa	schizophrenia	\$4,761	9%
Cymbalta	anxiety, depression, diabetic peripheral neuropathic pain	\$2,103	60%
Gemzar	pancreatic cancer	\$1,592	13%
Humalog	diabetes	\$1,475	13%
Cialis*	erectile dysfunction	\$1,144	430%
Evista	postmenopausal osteoporosis	\$1,091	4%
Humulin	diabetes	\$985	6%
Alimta	cancer	\$854	40%
Forteo	osteoporosis	\$709	19%
Strattera	ADHD	\$569	-2%

Account for 87% of total pharma sales, up from 83% in 2006.

* First year of full share of Cialis sales, which were previously recorded by the Lilly-ICOS joint venture

LILLY POSTED THE BIGGEST SALES growth among our top 10, and did so without the benefit of exchange rates. One of the keys to its 19% revenue growth was the incorporation of full Cialis revenues, which were previously split with Icos. But even dropping Cialis' revenues to 2006 levels would leave Lilly with 13% annual growth, better than anyone but

Roche, which benefited from the strong Euro.

So how did Lilly do it? By marketing the heck out of Cymbalta. The depression treatment zoomed past the \$2.0 billion mark at 60% growth last year. It slowed down to a phenomenal 37% increase in 1Q08, helping offset deteriorating Zyprexa sales. Lilly needs to strike while Cymbalta's iron

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is hot; the drug will lose patent protection in the U.S. in 2013, according to Lilly's regulatory filings.

To that end, Lilly is trying to get Cymbalta cleared in a whole mess of indications. John Russell of the *Indianapolis Star* recently asked whether the drug had become a "Swiss Army knife," after it was submitted to treat chronic knee and low back pain. Perhaps the new indications will help Lilly extend its patent protection for another year or two.

Zyprexa's key patents will expire in 2011, but that drug is already slowing down, partly over concerns with side effects. Meanwhile, the company continues to face legal issues over off-label marketing of Zyprexa. Lilly has settled more than 30,000 lawsuits about diabetes complications arising from Zyprexa for \$1.2 billion, and the company is allegedly negotiating with the U.S. government to make a \$1.0 billion settlement for criminal and civil charges related to marketing. The FDA recently gave Zyprexa Injection a "not approvable" letter in its application to treat schizophrenia. Still, \$4.7 billion in 2007 sales is nothing to sneeze at.

The company's best hope for replacing that revenue in a few years lies with would-be Plavix-buster Effient (generic name prasugrel). Lilly and development partner Daiichi Sankyo had great (but still a little mixed) results in a head-to-head study of Effient and Plavix, so the companies had their symbolic fingers crossed in late June 2008 as their PDUFA priority review deadline crept up.

Unfortunately, the agency declared that it needed an additional three months to evaluate Effient's NDA, putting a decision off until September 2008. The FDA made no mention of sending the application to an advisory committee, which is supposed to be a good omen, if you're into agency tea leaves. Every day it's delayed is another day fewer to convince doctors

to shift patients from away from Plavix.

Lilly saw a big change at the top this year, as John Lechleiter ascended to the chief executive officer suite, replacing Lilly lifer Sidney Taurel. Dr. Lechleiter, a chemist by training reorganized management in May 2008 in an attempt at streamlining the company's structure. In the Lilly Research Laboratories, the company has created a combined global regulatory, medical and patient safety organization. In International Operations, European infrastructure has been cut from four areas to two; Africa, the Middle East and the CIS have been combined with Asian markets (not including China and Japan); U.S. operations have been reorganized with two main groups: healthcare professionals and institution-based customers; the company's global and international marketing organizations were also consolidated.

These changes notwithstanding, the company hasn't made any new restructuring announcements. Restructuring costs dropped significantly in last year, at the tail-end of multi-year program that saw 5,500 employees fired and several facilities closed.

That said, Lilly announced in April that it will cut as many as 500 people from its manufacturing operations in Indianapolis. The affected site makes the API for Humalog, Humulin and Forteo. Dr. Lechleiter pointed out that most of the previous cuts took place through attrition, but that the Indy workers would be offered packages to leave the company. No word yet on the charge that Lilly will incur for this move.

A few weeks after that announcement, Lilly completed the final phase of its new biotech facility in Indianapolis. The site consists of a 250,000-sq.-ft. pilot plant, a 10,000-sq.-ft. research support facility, and the recently completed 475,000-sq.-ft. R&D laboratory. The company also just broke ground on a \$600 million expansion of a commercial biomanufacturing facility in Kinsale, Ireland.

THE LOWE DOWN

FOR ONE REASON OR ANOTHER, Eli Lilly seems to always have a balanced-looking portfolio of drugs across several therapeutic areas. I'm sure that they wouldn't say "No" to a gargantuan blockbuster that would ruin the aesthetic effect, but for now, not being dependent on one has to be sold as a feature, not a bug.

The closest thing they have currently is Zyprexa, which is going to be facing a lot of cheaper competition, and the best candidate coming on is prasugrel, yet another anticlotting therapy with huge financial hopes. But as I write this, no one's sure when that one is going to be approved, and how extensive its labeling will be. Safety concerns have been so much in the news that everyone, including the FDA, is extremely jumpy these days. Eli Lilly may find itself unwillingly — kicking and yelling, even — with a balanced drug portfolio again. They should look around the industry and remind themselves that there are worse problems.

—Derek Lowe

Exhaling To Wait

Lilly made its name in insulin, and it still has a major presence in that arena. But the company is fortunate it didn't get too far ahead of the curve in insulin delivery. Like several other of our top companies, Lilly was co-developing inhaled insulin. After Pfizer's fiasco with Exubera, Lilly cut its losses and bailed on the AIR Insulin project with partner Alkermes. AIR was in Phase III, but Lilly chose to close out the program at a cost between \$90 and \$120 million.

Announcing the decision, the company stated that it was "not a result of any observations during AIR Insulin trials relating to the safety of the product, but rather was a result of increasing uncertainties in the regulatory environment, and a thorough evaluation of the evolving commercial and clinical potential of the product compared to existing medical therapies."

Effient represents a huge question mark for Lilly. The company contends that its pipeline has never been this good, with 16 NMEs moved into trials in 2007. Lilly plans to bring two new drugs to market each year from 2011 to 2014, then three new ones per year after 2014, but it's that stretch from now to Cymbalta's 2013 expiration that they have to worry about. ■