

TOP 20 PHARMA

10 Wyeth
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HEADCOUNT	50,527
YEAR ESTABLISHED	1926
PHARMA REVENUES	\$22,399 +10%
TOTAL REVENUES	\$22,399 +10%
NET INCOME	\$4,616 +10%
R&D BUDGET	\$3,257 +5%

DRUGS APPROVED/LAUNCHED

Drug	Indication
pristiq	major depressive disorder
xyntha	hemophilia A
torisel	renal cell carcinoma
lybrel	low-dose combination oral contraceptive
protonix	GERD, delayed-release oral suspension
relistor	subcutaneous for opioid-induced constipation in advanced medical illness (EU)

DRUGS PENDING APPROVAL

Drug	Indication
lybrel/anya	continuous contraception (EU)
pristiq	vasomotor symptoms of menopause
viviant	postmenopausal osteoporosis prevention, treatment
relistor	subcutaneous for opioid-induced constipation in advanced medical illness
tygacil	community-acquired pneumonia (approvable)
refacto AF	hemophilia A (EU)
torisel	mantle cell lymphoma (EU)
bazedoxifene	postmenopausal osteoporosis

DRUGS IN PHASE IIB AND BEYOND

Drug	Indication
lybrel/anya	premenstrual dysphoric disorder
aprela	postmenopausal osteoporosis, vasomotor symptoms of menopause
bapineuzumab	Alzheimer's disease (with Elan)
tygacil	diabetic foot infections
prevnar 13	prevention of pneumococcal disease, pediatric, high-risk individuals and adults over 50
inotuzumab	follicular NHL, diffuse large B-cell
ozogamicin	lymphoma
rapamune	liver transplant
bosutinib	chronic myeloid leukemia

IN ANOTHER YEAR OR TWO, Wyeth may move off of our Top 20 Pharma list. This isn't (necessarily) a sign that the company is in free-fall; rather, it's an indication of how well its Biopharma unit is performing. With vaccine and Enbrel revenues still climbing, Wyeth may soon gain more than half of its pharma sales from biologic products.

The company's biggest success is its Prevnar pediatric vaccine. A recent study determined that, since the introduction of Wyeth's 7-valent vaccine against invasive pneumo-

acc-001	Alzheimer's disease
pristiq	neuropathic pain
vabicaserin	schizophrenia
meningococcal B vaccine	prevention of meningococcal disease in adolescents
moxidectin	river blindness (collaboration with WHO)
anrukinzumab	asthma
bosutinib	breast cancer

EARLY RESEARCH PROJECTS

Drug	Indication
oral methylnaltrexone	opioid-induced constipation
sra-444	Alzheimer's disease
pra-027	fibroids
ilv-094	psoriasis
sbi-087	rheumatoid arthritis
gap-134	arrhythmia

DRUGS COMING OFF PATENT

Drug	Indication
effexor/venlafaxine	antidepressant (2008)
zosyn	antibiotic (2007)

TOP SELLING DRUGS

Drug	Indication	\$	(+/- %)
Effexor	depression	\$3,794	2%
Prevnar	pediatric vaccine	\$2,439	24%
Enbrel	rheumatoid arthritis	\$2,045	36%
(outside N.A.)			
Protonix	GERD	\$1,911	6%
Zosyn/Tazocin	antibiotic	\$1,137	17%
Premarin	HRT	\$1,055	0%
Alliance revenues*		\$1,294	-3%

Account for 80% of total pharma sales, up from 79% in 2006.

* Alliance revenues include revenues from Amgen's sales of Enbrel, King Pharma's sales of Altace, and J&J's sales of the Cypher drug-eluting stent, for which Wyeth makes the API of the eluted drug.

coccal disease (IPD) in 2000, incidents of IPD in infants and young children dropped 77% by 2005. The company anticipates that its 13-valent version, fast-tracked by the FDA, will file for approval early next year. Prevnar passed the \$2.4 billion mark in 2007 and posted revenues of \$706 million (+14%) in 1Q08.

Meanwhile, Wyeth's non-North American sales of Enbrel (Amgen handles the market and pays Wyeth royalties) reached \$2.0 billion and were up 36% to \$606 million in 1Q08.

TOP 20 PHARMA: *Wyeth*

Amgen's royalties helped account for a 21% bump in Wyeth's 1Q08 alliance revenues, which reached \$369 million.

Rapid Transition

Despite that success, the company is in a transition year, in more ways than one. In September 2007, Bernard Poussot was named president and chief executive officer of Wyeth. He replaced Robert Essner, who retained his position as chairman until June of this year, when he retired and Mr. Poussot was elected to that role.

In April 2008, Robert R. Ruffolo, Jr., Ph.D., 58, announced his retirement as president, Wyeth Research and senior vice president, Wyeth. Dr. Ruffolo will be replaced by Mikael Dolsten, M.D., Ph.D., who previously served as executive vice president of Pharmaceutical R&D/Medicine at Boehringer Ingelheim. Dr. Ruffolo received a lot of press in recent years for his metrics-based "shots on goal" concept for R&D, but the value of that strategy isn't clear. This is partly because of the length of the R&D cycle, but the company also seems to have had a series of setbacks with new products lately.

In fact, delays and rejections by the FDA led Mr. Essner — near the time of his departure from Wyeth — to give an interview in which he lambasted the approval process and complained that the FDA's efficacy assessments now keep products off the market and establish de facto monopolies for first-in-class drugs. His frustration was understandable, after the agency delayed approval for Viviant (osteoporosis) and Pristiq (depression) and flat-out rejected bifeprunox (schizophrenia).

Major Depression

Without those new products on the market, Wyeth went into 2008 with a major question unanswered: How would it replace

more than \$1 billion in Protonix revenues? In 1Q08, the Protonix family of GERD treatments went generic (at risk), leading to a sales collapse. Teva, Sun and Wyeth's own generic version stripped branded sales from \$474 million to \$159 million in the quarter.

The loss of Protonix sales is just a warmup. Further down the road, Wyeth faces the prospect of losing its top seller, Effexor. There's already a limited generic competitor in the form of Sun Pharma's tablet version of the product, which exploits patents that expired in June 2008. In 2010, Wyeth will likely lose most of the \$3.8 billion kit-and-kaboodle, the most widely prescribed antidepressant in the world.

Given that prospect, you can understand why Mr. Essner fumed as much as he did about the FDA's delay on Pristiq, which was intended to help Wyeth's transition from Effexor revenues. Pristiq received its first approval in February 2008, and was launched in May for treatment of major depressive disorder in adults. It had received an approvable letter from the FDA in that indication 13 months earlier. The company is trying to expand its label to cover hot flashes from menopause, for which it also received an approvable letter.

Some contend that Pristiq's slow approval was due in part to its me-too nature; the drug is chemically similar to Effexor, so it's possible that the agency perceived Pristiq as more of a brand extension/life-cycle management product than a unique new product with solid benefits. If I can get someone at FDA to answer that question, I'll let you know.

Springboard to Impact!

So how is Wyeth dealing with the potential loss of two drugs that combined for one-third of its 2007 pharma revenues? Same way that every other drug company is doing it: by restructuring!

In 2008, Wyeth transitioned from its open-ended and somewhat ambiguous Project Springboard productivity plan into Project Impact. While "springboard" followed by "impact" may evoke images of Wile E. Coyote smashed flat against a cliff face, this new initiative is intended to "adjust down our infrastructure and reduce our operating costs in response to loss of Protonix sales in 2008 [and] to facilitate long-term growth, as well as to address short-term fiscal challenges," according to the company's 10-K statements.

The first impact of Project Impact was a \$185.6 million charge in 1Q08 for severance costs, primarily for Protonix-related personnel. The company plans to cut its total workforce by around 6% in 2008, which would add up to 3,000 employees laid off. Staff reductions may ultimately reach 10%, but a company spokesman insisted that no number is etched in stone.

The productivity initiatives for Project Springboard, which will wind down in the next several years, may incur total charges of \$850-950 million.

It's not all doom and gloom at Wyeth. Several of those FDA-delayed products are beginning to reach market. Pristiq launched in May 2008, while Relistor (opioid-induced constipation) was approved in April 2008, and Xyntha (hemophilia-A) in February 2008. Sure, Viviant is still in "approvable" limbo, but you can't replace more than \$5 billion in expiring products without getting some marketable "shots on goal." ■

THE LOWE DOWN

WYETH HAS HAD A LOT of disappointments over the years, but the company keeps pitching. They and Elan have been going after an immune-based therapy for Alzheimer's for many years now, and (for now) it looks like they may eventually have one with bapineuzumab. There's room to argue about how much benefit it'll show under real-world conditions, but the field is large, and the current options so poor, that anything could come in and presumably do well. And here's hoping that they come up with a ridiculously catchy brand name, because that's about the ugliest generic name I've ever seen.

The problem is, there doesn't seem to be enough to pick up the slack until (alien-language-swear-word) arrives. Their existing drugs will all be getting a bit silver-haired by then, which means that if anything bad happens in the Alzheimer's trials, things will get nasty very quickly. Add the near-term worries about Enbrel's safety profile, and it's going to be tense over there for a few years yet.

—Derek Lowe