

## 05 | Novartis

Lichtstrasse 35, CH-4056, Basel (Switzerland)  
Tel: (41) 61324 1111 Fax: (41) 61324 8001  
[www.novartis.com](http://www.novartis.com)

<b>HEADCOUNT</b>	100,735
<b>YEAR ESTABLISHED</b>	1996
<b>PHARMA REVENUES</b>	\$23,532 +16%
<b>TOTAL REVENUES</b>	\$37,020 +15%
<b>NET INCOME</b>	\$7,202 +17%
<b>R&amp;D BUDGET</b>	\$5,364 +11%

### DRUGS APPROVED/LAUNCHED

<i>Drug</i>	<i>Indication</i>
optafly	influenza vaccine (EU)
exforge	hypertension
lamisil	fungal infection of the scalp, pediatric
focetria	influenza pandemic
sebivo	first-line treatment for chronic hepatitis B (EU, China)
reclasta	Paget's disease
tekturna	hypertension
lucentis	wet age-related macular degeneration (EU)

### DRUGS PENDING APPROVAL

<i>Drug</i>	<i>Indication</i>
galvus	type 2 diabetes
tasigna	chronic myeloid leukemia
comtan	Parkinson's disease (Japan)
exelon patch	dementia
certican	prevention of organ rejection
mycograb	severe fungal infections
aclasta	Paget's disease of the bone (approved EU), osteoporosis
prexige	osteoarthritis, acute pain, primary dysmenorrhea
tyzeka	hepatitis B (EU)

### DRUGS IN PHASE IIB AND BEYOND

<i>Drug</i>	<i>Indication</i>
diovan	prevention of new onset type 2 diabetes, cardiovascular mortality
lotrel	high risk hypertension
ptk787	colorectal cancer, solid tumors
gleevec	glioblastoma multiforme
epo906	ovarian cancer, solid tumors
lic477	bipolar disorder
ago178	depression
fty720	multiple sclerosis
qab149	COPD
mff258	asthma, COPD
zelnorm	functional dyspepsia
ldc300	hepatitis B
albuferon	hepatitis C
rad001	renal cell cancer, pancreatic tumors
lbh589	cutaneous T-cell lymphoma
as1404	squamous non-small cell lung cancer
cyt002-NicQb	smoking cessation
som230	Cushing's disease

xyotax	non-small cell lung cancer
pkc412	acute myeloid leukemia
qab149	asthma and COPD
tmb100	cystic fibrosis
tfp561	recombinant tissue factor pathway inhibitor
abf656	chronic hepatitis C
opc759	dry eye

### EARLY RESEARCH PROJECTS

<i>Drug</i>	<i>Indication</i>
crad001c2242	colorectal cancer
app018	atherosclerosis
lci699	hypertension
lbh589	hematological and solid tumors
aee788	melanoma
hcd122	CLL and multiple myeloma
raf265	melanoma
afq056	anxiety
baf312	multiple sclerosis
cad106	Alzheimer's disease
rsv604	RSV infection
aeb071	psoriasis
rki983	glaucoma
ain457	rheumatoid arthritis

### DRUGS COMING OFF PATENT

<i>Drug</i>	<i>Indication</i>
lamisil	antifungal (June 2007)

### TOP SELLING DRUGS

<i>Drug</i>	<i>Indication</i>	<i>\$</i>	<i>(+/- %)</i>
diovan	hypertension	\$4,223	15%
gleevec	chronic myeloid leukemia	\$2,554	18%
lotrel	hypertension	\$1,352	26%
zometa	bone metastasis	\$1,283	5%
lamisil group	fungal infections	\$978	-14%
neoral	immunosuppression	\$918	-4%
sandostatin group	acromegaly	\$915	2%
lescol	cholesterol	\$725	-5%
trileptal	epilepsy	\$721	17%
femara	breast cancer	\$719	34%
voltaren	inflammation/pain	\$690	0%
zelnorm	irritable bowel syndrome	\$561	34%
exelon	Alzheimer's disease	\$525	12%

Account for 69% of total pharma sales, down from 72% in 2005.

**B**OLSTERED BY THE \$1 BILLION ADDITION of a new vaccine and diagnostics unit, Novartis posted one of the biggest revenue gains in our Top 20 list, adding a total of \$3.3 billion to last year's results. The boost enabled Novartis to jump from the #7 spot into our top 5, and 1Q2007 results (pharma +17% to \$5.9 billion, vaccine/diagnostics +47% to \$231 million) show that it's not looking back. (As was the case last year, we're not including revenues from Novartis' generic unit, Sandoz. That group posted nearly \$6 billion in sales, up 27% in 2006.)

Novartis continued its diversification strategy in 2006, growing its vaccine business and getting approval for its first biogeneric (via Sandoz). The company's Consumer Health unit also received some attention for marketing a drug to treat separation anxiety in dogs. The drug, Clonicalm, is adapted from Anafranil, a human anti-anxiety treatment first marketed by Novartis predecessor Geigy back in the 1960s.

In December 2006, Novartis named a Cambridge, MA site as its vaccine and diagnostics headquarters and announced plans to begin construction of a cell culture-based vaccine facility in Holly Springs, NC in 2007. In June 2007, Novartis gained approval in the EU for Optaflu, a flu vaccine that doesn't use chicken eggs to produce viral antigens. "Optaflu marks the first major innovation in influenza vaccine manufacturing in over 50 years. This vaccine, which is based on our proprietary cell culture technology, would provide for a more flexible and reliable production process, so as to contribute to meeting the ongoing need for seasonal influenza vaccines and the potential need for influenza vaccines in the event of a pandemic," said Dr. Joerg Reinhardt, chief executive officer of Novartis Vaccines and Diagnostics. The group also received approval in May 2007 for Forcetra, a pandemic vaccine with an adjuvant technology intended to extend vaccine supply by requiring smaller doses.

## Pressure Pipeline

Novartis made a splash with the March 2007 approval of Tekturna, a daily hypertension drug. Tekturna is the first in its class of direct renin inhibitors, targeting an enzyme that can contribute to high blood pressure and providing blood pressure control for 24 hours, with reduced side effects. The approval marked the first new hypertension treatment in more than a decade. It received approval in Europe in June 2007 as Rasilez.

Several other companies have been pursuing renin inhibitors, including Merck and GSK, but Novartis' head start could turn into a billion-dollar lead by the time other drugs hit the market. One analyst predicted \$2 billion in Tekturna sales by 2011. In May, Novartis submitted a combo-pill of Tekturna and a generic diuretic, HCT, and has other combos in trials. This should help Novartis weather the patent expiration of top-selling Diovan, expected in 2012.

Of course, Novartis isn't taking Diovan's expiration lying down. In a curious example of lifecycle management, the company gained approval in June 2007 of Exforge, a combination of Diovan and the API of Pfizer's Norvasc. As it turns out, the patent on that API will remain protected for a few months, so it appears Novartis will hold off on marketing Exforge in the U.S. The combo is already on sales in nine countries in Europe. Diovan's top competitor, Norvasc posted \$4.9 billion in sales in

2006. With its initial approval, Exforge wasn't cleared as an initial treatment for high blood pressure, but rather in patients who can't control their blood pressure with any type of angiotensin receptor blocker or calcium channel blocker.

Further confusing the lifecycle, Novartis' #3 seller, Lotrel, is actually a combo of Lotensin and . . . Pfizer's Norvasc! The patent on Lotrel is supposed to expire in 2017, but Teva recently received court approval to market a generic version of Lotrel in the U.S. Novartis is suing Teva to stop the generic shipments, but is also hedging its bets by . . . selling its own generic Lotrel through Sandoz! (Cross-company combos can create confusion.)

## Rough Sailing

Despite its short-term growth, Novartis hasn't had the smoothest of sailing lately. In April 2007, the company withdrew Zelnorm, a treatment for irritable bowel syndrome (IBS), from the U.S. market. New analysis of 29 clinical trials revealed a slight increase in risk for heart attack, stroke or severe chest pain. Zelnorm racked up \$561 million in 2006 sales (+34%), so its recall will put a dent in the company's 2007 results.

In June 2006, Novartis acquired NeuTec, a Manchester, UK-based biopharma with unique antibody-based treatments for life-threatening infections. Novartis paid \$569 million for Neutec, only to see its lead product, Mycograb, get rejected by committee in the EU.

For what it's worth, the "negative opinion" was a result of manufacturing issues, not a question of efficacy. Mycograb's manufacture was handled by a third party, and Novartis is working to get these CMC issues solved and appeal the ruling

## THE LOWE DOWN

**W**HAT'S STRIKING ABOUT NOVARTIS is how calm things seem over there compared to many of their peers. They've had the normal portions of good and bad luck, but somehow the variance just doesn't seem as brutal. People forget that they had a COX-2 inhibitor ready to go when Vioxx imploded, for example. From one perspective, that was bad news – after all, they'd spent all that money. But it was probably better that way, since the compound never made it to market, and thus never made it as far as the tort lawyers. (Better still would have been to have had no COX-2 effort at all, but who would have known that?)

They're not a quiet company when it comes to publications and publicity, though. Their DPP-4 program was the one making all the noise in the literature, but wasn't the first one to market after all that. And the high profile of their Cambridge research center has pretty much erased the memory of them as one of the big NJ pharmas. Will it eventually supplant their reputation as a big Swiss one? If the pipeline holds up, the folks in Basel might find that a reasonable trade.

—Derek Lowe

by CHMP. Mycograb is intended to treat invasive candidiasis, a fungal infection.

No word on whether that acquisition — minor by large pharma standards — is what led chief executive officer Dan Vasella, M.D. to say, “[P]atiency pays off, because an acquiring company runs the risk of paying too much if it acts too agitated,” in an interview with Swiss paper *Le Temps*.

Novartis’ biggest headache is the ongoing application for diabetes drug Galvus. The FDA accepted the NDA for Galvus, a DPP-4 inhibitor, in January 2006, but has yet to gain approval. Novartis received an approvable letter from the FDA in February 2007, requesting a trial to demonstrate safety and efficacy in patients with kidney impairment. Meanwhile, Galvus competitor Januvia (from Merck) is on the market and rack-

Novartis faces plenty of challenges. It’s in position to prolong its hypertension franchise through the next decade, but its diabetes challenger may fall short. It’s making plenty of headway in vaccines, but that’s long been regarded as a lower-margin activity (even if it is starting to catch up to therapeutic

drugs). It’s poised to challenge the status quo in biogenerics with its Sandoz unit, but that may create a “follow-on arms race” that decimates the higher end of the biologics market. As Dr. Vasella put it in his letter to shareholders, “Business as usual is no longer a viable long-term option.” ■

## ON THE EDGE

**R**OGER FEDERER MAY FEED INTO THE impression that the Swiss are a tad dull, but I believe that any company that continues trials with a Cox-2 inhibitor is willing to live on the edge. Novartis is still trying to gain approval for Prexige, filed for osteoarthritis in the U.S. The company contends that the lack of a sulphur molecule in Prexige’s structure should eliminate the risk of skin reactions that sank another Cox-2 inhibitor. The drug reached the UK market in January 2006, and may get approved in the U.S. under a different name. —GYR

ing up new prescriptions, and Bristol-Myers Squibb and AstraZeneca are in mid-stage development of their own DPP-4 inhibitors.

At the June 2007 American Diabetes Association annual meeting, a Novartis spokesman commented that the company expects a decision from the EU on Galvus by the end of this year, but that conversations with the FDA were ongoing. The company projects \$1.0-\$1.5 billion in annual sales from Galvus, and hopes for a U.S. release by the end of 2008, once the company allays the FDA’s concerns over high-dose primate tests that resulted to skin lesions.