

## 03 Sanofi-Aventis

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<b>HEADCOUNT</b>	100,289
<b>YEAR ESTABLISHED</b>	2004
<b>PHARMA REVENUES</b>	\$35,643 +5%
<b>TOTAL REVENUES</b>	\$35,643 +5%
<b>NET INCOME</b>	\$8,844 +12%
<b>R&amp;D BUDGET</b>	\$5,527 +10%

### DRUGS APPROVED/LAUNCHED

<i>Drug</i>	<i>Indication</i>
acomplia	cardiometabolic risk factors (not U.S.)
taxotere	squamous cell carcinoma of the head and neck
xyzal	seasonal and perennial allergic rhinitis, uncomplicated skin manifestations of chronic idiopathic urticaria
actonel	osteoporosis
allegra	oral suspension
lovenox	most severe type of heart attack
actonel	osteoporosis, bone mass in men
allegra	seasonal allergies and chronic idiopathic urticaria in pediatric patients
plavix	reduce the rate of death from any cause and the rate of a combined endpoint of re-infarction, stroke or death in patients with acute ST-segment elevation myocardial infarction
taxotere	advanced stomach cancer

### DRUGS WITHDRAWN FROM FDA

<i>Drug</i>	<i>Indication</i>
zimulti	obesity (NDA withdrawn at press time)

### DRUGS PENDING APPROVAL

<i>Drug</i>	<i>Indication</i>
acomplia	smoking cessation
dronedarone	antiarrhythmic
apidra	diabetes in children

### DRUGS IN PHASE IIB AND BEYOND

<i>Drug</i>	<i>Indication</i>
ave1625	obesity
ave0010	type 2 diabetes
ave2268	type 2 diabetes
apidra	diabetes
ave5530	hypercholesterolemia
larotaxel	pancreatic cancer, breast cancer
xrp6258	hormone-resistant prostate cancer
alvocidib	chronic lymphocytic leukemia
vegfr trap	vascular endothelial growth factor
xaliproden	Alzheimer's disease, dementias, oncology, chemotherapy-induced neuropathies
saredutant	major depressive disorders, generalized anxiety disorders
amibegron	major depressive disorders, generalized anxiety disorders

eplivanserine	insomnia
volinanserin	insomnia
surinabant	smoking cessation
dianicline	smoking cessation
teriflunomide	multiple sclerosis
satavaptan	dilution hyponatremia and cirrhotic ascites
icatibant	pain
ferroquine	malaria
multaq	prevention of atrial fibrillation
celivarone	maintenance of sinus rhythm
xrp0038	peripheral arterial disease
llepatril	hypertension and diabetic nephropathy
taxotere	hormone-resistant prostate cancer

### EARLY RESEARCH PROJECTS

<i>Drug</i>	<i>Indication</i>
idraparin sodium	anticoagulant
biotinylated idraparin sodium	deep-vein thrombosis, pulmonary embolism
sr123781	acute coronary syndrome, deep-vein thrombosis
ave5026	prevention of venous thromboembolic events in cancer patients
otamixaban	acute coronary syndrome

### TOP SELLING DRUGS

<i>Drug</i>	<i>Indication</i>	<i>\$</i>	<i>(+/- %)</i>
lovenox	thrombosis	\$3,059	15%
plavix	heart attack, stroke	\$2,800	11%
ambien	insomnia	\$2,545	35%
taxotere	cancer	\$2,201	10%
eloxatin	colorectal cancer	\$2,127	9%
lantus	diabetes	\$2,093	38%
avapro	hypertension	\$1,275	15%
delix	hypertension	\$1,227	-2%
copaxone	multiple sclerosis	\$1,123	22%
allegra	allergic rhinitis	\$864	-48%
amaryl	diabetes	\$567	-33%

Account for 56% of total pharma sales, up from 54% in 2005.

### KEY PERSONNEL

Jean-François Dehecq  
*chairman*  
Gérard Le Fur  
*chief executive officer*

**S**ANOFI-AVENTIS SLIPPED BACK TO the #3 slot, but many pundits are predicting that the company will try for the #1 spot next year by acquiring Bristol-Myers Squibb. I don't think it's going to happen, which raises to 100% the likelihood that a merger will occur the day before this issue arrives on your desk.

Which isn't to say that SA doesn't have reason to go after BMS. SA's run of patent expirations and pipeline failures — reaching a nadir with Acomplia/Zimulti's unanimous "not approvable" recommendation by an advisory panel to the FDA — have left the company scrambling, and it's easier to buy one ready-made than to overhaul internal R&D. New CEO Gerard Le Fur is rumored to be against a mega-merger, contra chairman Jean-Francois Dehecq. Longtime readers know my bias against mega-mergers, which tend to boost short-term gains while solving few of the structural problems that led the acquiring company to seek out a partner (See "Notional Champions").

And, boy, are there a bunch of problems for SA.

The Acomplia ruling was devastating, wiping out billions in SA's share value. The panel contended that patients in clinical trials did manage to lose 5% more weight when dieting than the control group did, but also had twice the risk for suicidal thoughts and other mental problems. The Agency will make its final ruling by the end of July, but is likely to wait until the next major clinical trial is complete (around 2010) before reconsidering the one-time miracle drug. Will SA continue to incur the expense of a huge Phase III trial for a drug that may never

reach the U.S. market? Will management feel compelled to rein in costs or will it decide that there's too much money at stake NOT to continue to the end? SA had been projecting Acomplia's peak annual sales at \$3.0 billion, but that was all contingent on a strong U.S. demand.

In a snowball effect, the EMEA plans to publish the comments its safety committee has on Acomplia at its meeting in

## "NOTIONAL CHAMPION"

**T**HE MERGER OF SANOFI AND AVENTIS was portrayed as creating a "national champion," but in its annual report, the company admitted it "was more vulnerable than other pharmaceutical companies to the effects of government measures intended to limit healthcare expenditure in France and Germany, due to its long-standing presence in these markets." In October 2006, the company's French subsidiary announced layoffs of 500 staffers, 400 from the sales force. Hey, is that my own petard?

Speaking of national champions, one of SA's biggest shareholders (13% stake) recently announced plans to divest its holdings. That company is Total, formerly known as TotalFinalElf, which was implicated in the Iraqi Oil-for-Food scandal in a massive corruption investigation that spread to France's interior ministry. (The other large shareholder is L'Oreal, but they've stayed clean.) —GYR

## THE LOWE DOWN

**W**HAT TO SAY ABOUT SANOFI-AVENTIS? That things at least haven't been dull over there? They've had the Plavix business (from which no one is coming out looking well) hanging over them this whole time, which would be enough to bring on gray hairs. But the recent demolition of rimonabant (a.k.a. Acomplia) by the FDA has been the real story. Like Pfizer's torcetrapib disaster, this is just another reminder of what kind of business this is, and it's enough to make a person wish that the pace of said reminders would slow down a bit.

The really striking thing about rimonabant, to me, was always how extraordinarily tight-lipped the company was about the drug and its problems. Perhaps they felt that the hype and expectations had gotten out of hand a few years ago, and were resolved not to make a similar mistake in the other direction. But you can't help but think that the days have passed when companies could just roll down the storm shutters and wait for these things to go away.

Well, a lot of things aren't going away over at SA, unfortunately. It's too early to say what the company's reaction to the rimonabant story will be, but you know, they're probably not going to tell us, anyway. We'll just have to watch.

—Derek Lowe

July 2007, which may result in an immediate suspension of sales throughout the EU. For all the guff people give the FDA and its panels, I'd like to point out that they managed to identify the risk of suicide and psychoses, and also note that Acomplia is legal in the EU and is sold in several member countries, as well as in Brazil, Argentina, and Mexico. Overall, it was approved in 37 countries and marketed in more than half of them.

The FDA dealt SA another blow when it restricted use of antibiotic Ketek. The drug, approved in the U.S. in 2004, saw two of its three indications removed in February 2007 amid safety concerns. It's now approved only for mild to moderate community acquired pneumonia. Ketek's clinical trial data turned out to be flawed, and one doctor involved in the trials is serving a 57-month prison sentence for fraud. Once upon a time, Ketek's peak sales were projected above \$1.5 billion.

SA also took a hit in the Plavix debacle, losing out on royalties when Apotex's generic submarined BMS's sales of the drug. With the June court decision to uphold SA and BMS's patent, the companies can try to pursue damages for generic marketer Apotex (who is appealing the decision). However, at press time it was uncertain whether one of the stupidest points of the Plavix agreement is still in force: the waiver of triple damages. If this waiver applies, then SA and BMS can only try to gain back 40-50% of Apotex's net sales of Plavix. If it's overturned, as other parts of the deal were, then the companies can pursue some serious coin. BMS contended that it lost approximately \$2.0 billion in Plavix sales when wholesalers were flooded by Apotex's generic.

This wasn't the only Plavix problem for SA. The military-installed government of Thailand has determined that SA's price for Plavix was too high and, after fruitless negotiations, issued a compulsory license to acquire Plavix from Indian generic companies.

SA came out on the short end of the patent stick in the past year. The worst news is that SA lost a court case in February 2007 that may open the door for a generic of top seller Lovenox. SA is appealing a February 2007 decision that invalidated its patent and allowed Amphastar and Teva to file Lovenox ANDAs. This may not turn out to be damaging to SA, since some consider Lovenox to be a very difficult molecule to characterize and the ANDAs may not receive approval. SA did receive some good news in May 2007 when the FDA approved Lovenox to treat the most severe type of heart attack.

Sleep drug Ambien has rocketed along — +35% in 2006 and +32% in 1Q2007 — despite new competitors in its field. But the April 2007 expiration of the original version's patent — the CR version is still protected — will lead to a slowdown in sales growth. In total, SA lost protection on four products in the U.S. in 2006, including Allegra, which shed half its sales (around \$800 million) last year. Eloxatin, the company's #5 seller, is under generic pressure in Europe, which led to a 3% sales drop in 1Q2007.

On the bright side, SA had success with its vaccine unit, where sales rose 22% to \$3.2 billion in 2006. In April 2007, the company received a license for its vaccine against avian flu, and received an "approvable" recommendation for Pentacel, which immunizes against diphtheria, tetanus, pertussis, polio, and *Haemophilus influenzae* type b (Hib) in infants and young children. In June 2007, the Department of Health and Human Services awarded SA a \$77 million grant to retrofit a vaccine facility so it can make a rapid changeover for pandemic flu vaccine at HHS' request. SA produced 170 million doses of flu vaccine in 2006, nearly half the world's supply.

I've enumerated plenty that's gone wrong for SA. So what's going well? SA's insulin product, Lantus, remains the

leading brand in the world, posting \$2.0 billion in 2006 sales. In April 2007, the FDA approved a new pen-injector for Lantus, the Solostar. MS treatment Copaxone crossed the billion-dollar mark in 2006. Cancer treatment Taxotere keeps chugging along, adding new indi-

cations (head and neck cancer) and demonstrating greater survival benefits as time passes (breast cancer and prostate cancer). The company still has plenty of products in its mid-to-late pipeline, but none of them have "immediate blockbuster" written on them. ■