

08 | F. Hoffman - La Roche

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HEADCOUNT	74,372
YEAR ESTABLISHED	1896
PHARMA REVENUES*	\$19,300 +16%
TOTAL REVENUES*	\$33,572 +18%
NET INCOME	\$7,324 +33%
R&D BUDGET	\$5,262 +15%

DRUGS APPROVED/LAUNCHED

<i>Drug</i>	<i>Indication</i>
avastin	NSCLC first line
herceptin	early stage breast cancer
mabthera/rituxan	rheumatoid arthritis
tarceva	pancreatic cancer
xeloda	advanced stomach cancer

DRUGS PENDING APPROVAL

<i>Drug</i>	<i>Indication</i>
mircera	anemia associated with chronic renal failure
xeloda	metastatic colorectal cancer (first and second line combo)
avastin	metastatic breast cancer (first line combo with taxol), metastatic colorectal cancer (first line combo with oxaliplatin)
herceptin	HER2 metastatic breast cancer (hormonal therapy combo) (EU approval)
antevas	subarachnoid haemorrhage (Japan approval)
epogin	chemotherapy-induced anemia (Japan approval)
sigmart	acute heart failure (Japan approval)
xelox	advanced colorectal cancer

DRUGS IN PHASE IIB AND BEYOND

<i>Drug</i>	<i>Indication</i>
r105	rheumatoid arthritis DMARD inadequate responders
actemra	rheumatoid arthritis, juvenile idiopathic arthritis
r1594	rheumatoid arthritis
cellcept	lupus nephritis, pemphigus vulgaris
mabthera / rituxan	chronic lymphocytic leukemia (first line, relapsed), NHL (first line)
tarceva	non-small cell lung cancer (first line, second line combo with Avastin)
xeloda	adjuvant colon cancer combo oxaliplatin, adjuvant breast cancer
herceptin	advanced gastric cancer

valcyte	CMV in transplantation
avastin	pancreatic cancer, metastatic breast cancer, prostate cancer, ovarian cancer, NSCLC
ed-71	osteoporosis
xolair	pediatric asthma

EARLY RESEARCH PROJECTS

<i>Drug</i>	<i>Indication</i>
r1646	pain
r1295	multiple sclerosis
r3421	autoimmune diseases / transplantation
r1511	type II diabetes
r1663	anticoagulant
r1450	Alzheimer's disease
r1647	depression
r7090	anxiety
r7118	schizophrenia
r1507	solid tumors
r7204	malignant melanoma
r7025	HCV

TOP SELLING DRUGS

<i>Drug</i>	<i>Indication</i>	<i>\$</i>	<i>(+/- %)</i>
tamiflu	influenza	\$2,098	67%
herceptin*	breast cancer	\$1,902	94%
mabthera/rituxan*	non-Hodgkin's lymphoma	\$1,793	19%
neorecormon/epogin	anemia	\$1,778	-2%
cellcept	transplantation	\$1,471	7%
pegasys/copegus	hepatitis C	\$1,171	-20%
xeloda	oncology	\$775	21%
avastin*	oncology	\$619	200%
xenical	weight loss/management	\$553	8%
rocephin	antibiotic	\$332	-55%

Account for 63% of total pharma sales, up from 59% in 2005.

* Figures only include Roche's portion, not those of Genentech, which is 60% owned by Roche and co-markets several major products.

WERE ALL AFRAID OF CANCER, and we're all afraid of a flu pandemic, so it looks like Roche is set for another strong year. The company's oncology drugs posted huge sales growth, with Herceptin's total numbers blasting past the \$3 billion mark (Genentech booked \$1.2 billion of that, leaving Roche's

"share" at \$1.9 billion) and Avastin adding \$1 billion to reach a total of \$2.4 (Roche's share of that was \$619 million, while Genentech booked \$1.7 billion).

The company has filed sNDAs in new oncology indications for both of these drugs. First approved for treatment of

colorectal cancer, Avastin is showing plenty of potential in other fields, including kidney, lung (approved in October 2006) and breast cancers. Roche is ramping up its supply of both Avastin and Herceptin with new biomanufacturing facilities in Basel and Germany. In May 2007, the company announced completion of the Avastin API site, in Basel while the facility for Herceptin is due for completion in July. Validation and certification are expected to be wrapped up in 2009, at which point Avastin commercial manufacturing will commence. Roche has taken pains to insist that the Basel facility isn't dedicated to Avastin, but hasn't said what other programs it may accommodate.

Total Avastin sales grew 44% to \$749 million in 1Q2007 (\$216 million sans Genentech's portion), while Herceptin was up 43% to \$947 million in the quarter (\$636 million for Roche). And that's not even mentioning Roche and Genentech's biggest seller, MabThera/Rituxan, which was up 16% in 2006 to \$3.8 billion (\$2.0 billion of which was booked by Genentech), and posted \$1.1 billion in 1Q2007 sales (\$527 million of which were booked by Roche).

It looks like the only thing that can slow Avastin down is the fact that it's too effective! In May, the company reported results from a clinical trial that showed a low dosage of Avastin was as effective as a higher dose when used in combination with a particular chemotherapy program to treat advanced lung can-

cer. The trial could lead to doctors prescribing lower doses of Avastin, but we'll see if that really offsets the increase in overall prescriptions, as Avastin's effectiveness against other types of cancer is established. In all the company plans to make 20 oncology filings in the next five years, including sNDAs.

Infectious

Tamiflu, meanwhile, didn't match up to 2005's jump of 371%, but it still added \$845 million in sales to reach \$2.1 billion in 2006. Governments continue to stockpile the flu medication as a bulwark against an H5N1 outbreak. At its 1Q2007 announcement, Roche contended that it "successfully established and tested a supply capacity capable of annually producing 400 million treatment courses, well in excess of government orders received to date," noting that 80 nations have ordered stockpiles so far.

Roche and Chugai announced in June 2007 that they will conduct new clinical trials for their flu medication, after reports of suicides by teenage Japanese Tamiflu users. The companies contend that there's no causal link between Tamiflu and the urge to jump off buildings, but will conduct both clinical research on the drug's influence on sleep and a review of its preclinical animal tox studies. The FDA required psychiatric warnings on Tamiflu's label last fall.

Buy Small, Think Big

In April, the company made a series of small acquisitions, topping out with the \$600 million purchase of BioVeris. Chairman and chief executive officer Franz Humer ruled out making any major acquisitions with Roche's cash reserves, which reached nearly \$20 billion before the April spree. In an interview with SwissRadioInternational, he remarked, "The money is there for small and medium-sized acquisitions. A big acquisition makes no sense for us. The cash is not burning a hole in our pocket."

Instead, it looks like some of that cash will be used to buttress Roche's R&D efforts. In February 2007, the company announced a restructuring of its global R&D, centered on Disease Biology Areas (DBA). Each DBA will be managed by a "cross-functional leadership team with representatives from Discovery, Clinical Research and Exploratory Development, Clinical Development and Strategic Marketing co-located at one site," according to Roche. DBAs were established for the following therapeutic areas:

- Oncology - Nutley, NJ
- Virology - Palo Alto, CA
- Inflammation - Palo Alto, CA
- Metabolism - Basel, Switzerland
- Central nervous system - Basel, Switzerland

The company is going great guns in several of those areas, and with Actemra (rheumatoid arthritis) giving a strong Phase III performance, Mircera's approvable ruling in renal anemia (pending FDA review of its entire class), and new oncology indications for its top drugs, Roche and its "partners" are poised for serious growth. ■

THE LOWE DOWN

ROCHE IS A DIFFICULT COMPANY TO IGNORE, if you know the industry. They're strong in many different therapeutic areas, and they've come up with some very interesting ideas over the years. They're also active on an unusually broad front: small molecules, peptides, antibodies, diagnostics: they do them all. They also do deals with everyone from the big players down to companies that you'd swear that someone just made up for the press release. You wonder if anyone actually sleeps over there.

But like a couple of other companies on this list, they keep a low profile with the broader public, which is probably a good idea in the current climate. I'm not looking for a Roche vehicle on the stock car racing circuit any time soon, for example.

They've been strong in cancer, which has been a good market to be strong in the last few years. Their current move into arthritis could be a big one, since they're off to the side of the vicious anti-TNF market space. But since it's a new mechanism, here's hoping that they don't end up joining the Colossal Clinical Failure Society, which they've so far dodged. I don't see any reason for any bad news, but the whole problem with joining the CCFS is that you never see it coming.

—Derek Lowe