

TOP 10 BIOPHARMA



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HEADCOUNT	17,500	
YEAR ESTABLISHED	1980	
BIOPHARMA REVENUES	\$14,311	+3%
ROYALTY REVENUES	\$460	+4%
TOTAL REVENUES	\$14,771	+12%
NET INCOME	\$3,166	+7%
R&D BUDGET	\$3,266	-3%

DRUGS APPROVED/LAUNCHED

<i>Drug</i>	<i>Indication</i>
vectibix	(EGFr) expressing metastatic colorectal cancer (EU)
aranesp	anemia associated with chronic renal failure in pediatric patients (EU)

amg 853	asthma
amg 827	rheumatoid arthritis
amg 811	systemic lupus erythematosus
amg 477	type 2 diabetes
amg 745	muscle wasting disorders
amg 714	psoriasis
amg 379	pain

DRUGS PENDING APPROVAL

<i>Drug</i>	<i>Indication</i>
enbrel	pediatric psoriasis

KEY PERSONNEL

Kevin W. Sharer
chairman, chief executive officer, president

Fabrizio Bonanni
executive vice president, operations

George J. Morrow
executive vice president, global commercial operations

Roger M. Perlmutter
executive vice president, R&D

DRUGS IN PHASE IIB AND BEYOND

<i>Drug</i>	<i>Indication</i>
panitumumab	head and neck cancer, colorectal cancer
cinacalcet HCl	cardiovascular disease in patients with secondary hyperparathyroidism and chronic kidney disease undergoing maintenance dialysis
romiplostim	immune thrombocytopenic purpura
motesanib diphosphate	first-line NSCLC
denosumab	prevention of bone metastases, bone loss in breast cancer or prostate cancer, prevention of cancer-related bone damage, postmenopausal osteoporosis
darbepoetin alfa	anemia in heart failure, chronic kidney disease, type 2 diabetes

TOP SELLING DRUGS

<i>Drug</i>	<i>Indication</i>	<i>\$</i>	<i>(+/- %)</i>
Aranesp	chemotherapy-induced anemia	\$3,614	-12%
Enbrel	rheumatoid arthritis, psoriatic arthritis	\$3,230	12%
Neulasta	chemotherapy-induced neutropenia	\$3,000	11%
Epogen	anemia	\$2,489	-1%
Neupogen	chemotherapy	\$1,277	5%

EARLY RESEARCH PROJECTS

<i>Drug</i>	<i>Indication</i>
sclerostin Ab (amg 785)	bone loss

Account for 95% of total biopharma sales, down from 97% in 2006.

LAST YEAR, I NOTED THAT AMGEN had turned in its first year of sub-20% revenues growth. I blithely wrote, "I'm just hoping that it doesn't fall under 10+% in 2007." Turns out I didn't know the half of it. Amgen's drug revenues last year were up an anemic (ha-ha) 3%, actually dropped 2% in 1Q08, and don't look like they're going to get better for the rest of this year.

The collapse was triggered by restrictions on Aranesp and Epogen. Safety studies revealed previously unknown risks in erythropoietin stimulating agents (ESAs) last year, leading to "black box" warning labels, reduced Medicare reimbursement, dosage restrictions, and a whole lot of lost sales. The safety issues continue to unfold.

In March 2008, Amgen changed the label for Aranesp and Epogen to explicitly warn doctors against using high doses of the drugs for patients with early-stage breast, non-small cell lung, head and neck, lymphoid and cervical cancers, after studies showed increases in mortality and tumor progression. Not what you want in a drug used by cancer patients.

Aranesp sales plummeted 25% in 1Q08 to \$761 million, with a 38% drop in U.S. sales. Epogen revenues dropped 11% \$554 million in that span. Those are awful numbers, keying the company's 2% decline in the quarter, but the new warning label is sure to hammer the company's revenues further.

Amgen's ESA issues haven't been confined to the label. The company has also been involved in a lengthy court bat-

TOP 10 BIOPHARMA: Amgen

tle with Roche over the Swiss company's ESA drug Mircera, a pegylated-erythropoietin (peg-EPO) product. Roche received FDA approval for the drug, but the U.S. Patent & Trademark Office ruled that Roche's process infringes on numerous Amgen patents. Negotiations are ongoing, but Amgen seems adamant in not permitting a kindasorta biosimilar on the market, especially if it offers an improvement on dosing cycles.

Phthisis Ridiculous

Did I mention that Amgen's #2 seller, Enbrel, might be linked to tuberculosis? The drug carried a warning about that topic previously, but a "black box" was added in March 2008 to highlight the risk of TB and other infections in patients. Other drugs in the TNF-alpha inhibitor class carry the same warning, so this wasn't as horrible a set of circumstances as Amgen's ESA collapse, but it can't make the company happy.

Neither can the news that the FDA is looking into whether TNF-blockers may increase the risk of cancer in children. The agency announced it was looking into it in June 2008, the same time that an advisory panel narrowly recommended Enbrel for use in children's psoriasis.

Enbrel has actually performed pretty well in its tough category (although there are some questions about Amgen's marketing practices with the drug), and will take over as Amgen's top seller next year.

Rationalizing

What's a company to do when it faces this much lost revenue? Restructure! For the first time in its history, Amgen last year began a program of mass layoffs and cost cutting. The initial announcement in August 2007 targeted 2,200 to 2,600 firings, or 12-14% of the company's total headcount. In addition, the company planned to "rationalize" its manufacturing network, hold off on new capital expenditures, and rethink its R&D plans.

The plan is designed to cut \$1.0 to \$1.3 billion from Amgen's expenses by this year. As part of the plan, Amgen revised its expansion in Puerto Rico, delayed construction of a new facility in Ireland indefinitely, closed down bulk Enbrel operations in West Greenwich, RI earlier than planned and shuttered a clinical manufacturing site in Thousand Oaks, CA. Restructuring costs in 2007 added up to \$739 million.

The company also reported in its SEC filing that it is implementing an enterprise resource planning system to "support our increasingly complex business and business processes."

I'm not sure if this is a "duh" move for them, similar to Jeff Bezos' admission that Amazon was still doing its accounting on Quicken when it was approaching \$100 million in revenues.

Still Spending

All this restructuring doesn't mean Amgen's in a no-spend mode. Shortly before the announcement was made last year, the company made a pair of acquisitions (covered in the 2007 edition of this issue), spending \$720 million to pick up Alantos and Ilypsa. The Alantos acquisition gives Amgen entree into the DPP-4 inhibitor arena, which is fraught with regulatory peril (especially now that the FDA is ready to ask for CV risks for any new diabetes treatment) and one dominant player in Merck's Januvia, but can help the company make headway in the metabolic field.

In March 2008, Amgen made a \$520 million deal (\$100 million upfront, plus milestones) with Kyowa Hakko Kogyo for a CCR4 inhibitor (think inflammation and oncology) headed toward Phase II. Amgen will have commercialization rights outside of Japan, South Korea, China and Taiwan.

Eastern Promises

Along with cost-cutting measures, Amgen also decided to license out some of its drug programs, bringing in cash and reducing R&D expenses. In February 2008, Amgen signed a deal with Takeda to give allow that Japanese pharma company to develop and commercialize as many as 13 Amgen molecules for the Japanese market. According to an Amgen statement, "the collaboration includes early to mid-stage clinical-stage candidates across a range of therapeutic areas, including oncology, inflammation, and pain."

It also includes money. Takeda paid Amgen \$200 million upfront for the deal, will cover as much as \$340 million in development costs, and may pay as much as \$362 million in milestones, as well as royalties.

A separate deal allowed Takeda to buy into late-stage cancer treatment motesanib diphosphate. This deal makes Takeda a worldwide partner on the Phase III drug for \$100 million upfront, \$175 million in milestones for the first two indications, double-digit royalties on sales in Japan, and 60% of ongoing development costs outside Japan. The companies will split profits outside Japan down the middle.

Their partnership also covers Vectibix, the colorectal cancer MAb that Amgen got approved in 2006. It posted sales of \$170 million in its first full year, but dropped 33% to \$34 million in

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1Q08, on lack of demand. The company is engaged in a number of trials to expand the drug's label, and has also gained several new markets in Canada and Australia for Vectibix.

Good to the Bone?

Much of Amgen's pipeline hopes are pinned on denosumab, a bio-treatment that will be submitted for postmenopausal osteoporosis, but is also being investigated against a number of indications, including treatment-induced bone loss, bone metastases, rheumatoid arthritis, and multiple myeloma, according to the company.

The drug (no commercial name yet) has been touted as a \$2.0 billion+ blockbuster for Amgen, with some estimates

THE LOWE DOWN

AMGEN USED TO SEEM INVULNERABLE, floating around on a golden cloud of revenue from its untouchable biologics. But concerns about erythropoietin use have hit them but good, making them the best example of a big biotech in real trouble. Even Carl Icahn decided that Biogen/Idec was the place to go for more upside. Amgen will no doubt have company, though — after all, it's the drug industry, there's always potential trouble coming from somewhere. In this area, it'll eventually be from biogenerics. Those are coming slowly, but they're coming, and everyone is preparing for the day when the barbarians come over the wall.

Amgen has been trying to hedge its bets by working on small molecules, but to no apparent avail. They do have some more promising biologics well along in the clinic, and if the erythropoiesis bombs would just stop dropping for a bit, the company might well right itself. Recent troubles and all, their finances are still the envy of most of the rest of the industry.

—Derek Lowe

reaching \$3.3 billion/year, based on strong results against existing treatments. There have been some concerns with rates of infection among clinical trial patients, but Amgen has stressed that these are not out of the norm, based on the trial's population group. The company plans to have all data in and analyzed by the end of this year, leading to a submission in early 2009.

Amgen isn't devoid of hope, but the company has a very tough road. There are rumors that a second round of layoffs is pending, with the total goal of dropping the workforce numbers by 20%, not the 12-14% of the original plan. I hope that's not the case, but this company's prospects look bleak for the next several years, and that's assuming denosumab is an instant hit (and that there's a nice boost from Nplate, a platelet-boosting drug that just got delayed three months by the FDA). ■