

## 01 | Amgen

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<b>HEADCOUNT</b>	20,000+
<b>YEAR ESTABLISHED</b>	1980
<b>BIOPHARMA REVENUES</b>	\$13,858 +15%
<b>TOTAL REVENUES</b>	\$14,268 +15%
<b>ROYALTY REVENUES</b>	\$410 flat
<b>NET INCOME</b>	\$2,950 -20%
<b>R&amp;D BUDGET</b>	\$3,366 +45%

### DRUGS APPROVED/LAUNCHED

Drug	Indication
aranesp	chemotherapy-induced anemia, anemia assoc. with chronic kidney disease
vectibix	metastatic colorectal cancer

amg 714	psoriasis
amg 745	muscle wasting disorders
apo2L/TRAIL	cancer
amg 220	Crohn's disease
amg 557	systemic lupus erythematosus
amg 837	type 2 diabetes
sclerostin Ab	bone loss

### DRUGS IN PHASE IIB AND BEYOND

Drug	Indication
amg 531	immune thrombocytopenic purpura
darbepoetin alfa	anemia in heart failure, cardiovascular disease in patients with chronic kidney disease and type 2 diabetes
denosumab	bone loss induced by hormone ablation therapy for breast cancer or prostate cancer, postmenopausal osteoporosis, prevention of cancer-related bone damage, prevention of bone metastases
cinacalcet HCl	cardiovascular disease in patients with secondary hyperparathyroidism and chronic kidney disease undergoing maintenance dialysis
panitumumab	first- and second-line colorectal cancer

### TOP SELLING DRUGS

Drug	Indication	\$	(+/- %)
aranesp	chemotherapy-induced anemia	\$4,121	26%
enbrel	rheumatoid arthritis, psoriatic arthritis	\$2,879	12%
neulasta	chemotherapy-induced neutropenia	\$2,710	18%
epogen	anemia	\$2,511	2%
neupogen	chemotherapy	\$1,213	0%

Account for 97% of total biopharma sales, down from 98% in 2005.

### EARLY RESEARCH PROJECTS

Drug	Indication
amg 221	type 2 diabetes
amg 317	asthma
amg 379	pain
amg 386	cancer
amg 403	pain
amg 479	cancer
amg 623	systemic lupus erythematosus
amg 655	cancer

### KEY PERSONNEL

Kevin Sharer  
*chairman, chief executive officer, president*

David Lacey  
*senior vice president, head of research*

Fabrizio Bonanni  
*senior vice president, manufacturing*

Laurel Junk  
*vice president, supply chain*

Jim Daly  
*senior vice president, North America commercial operations*

Dave Tillett  
*vice president, quality*

**A**NEMIA HAS LEFT AMGEN WEAK in the knees. After years of fantastic growth and a minimum of controversy, the world's biggest biopharma finds its key franchise under siege.

In March 2007, the FDA determined that erythropoiesis stimulating agents (ESAs) — anemia treatments like Amgen's Aranesp and Epogen and J&J's Procrit — should carry "black box" warnings. Soon after, a Congressional committee called on both Amgen and J&J to suspend DTC advertising and "personal income incentives to prescribers" of these anemia drugs until an FDA safety review is complete.

In May, an FDA panel declared that use of these drugs should be limited in cancer patients, and recommended new

trials be conducted to determine whether they could be decreasing survival rates and/or promoting tumors. The Center for Medicare and Medicaid Services soon proposed cutting reimbursement for those uses.

Come June, the House Ways and Means Committee held hearings on dosing regulations and Medicare reimbursement of the drugs; it spent \$2 billion on them (including Procrit) in 2005. In calling for the hearings, chairman Pete Stark (D-CA) noted, "The existing Medicare payment system incentivizes higher doses in certain circumstances, with resulting health risks and higher costs for beneficiaries and taxpayers." (Yes, a U.S. Representative used the word "incentivizes.")

At press time, Amgen hadn't announced a revised financial guidance for the rest of 2007 or beyond, but it's obviously going to take a sizeable hit from this controversy. Aranesp and Epogen totaled nearly half of Amgen's \$13.9 billion in 2006 biopharma revenues. One analyst referred to the FDA panel's recommendations as "devastating" for Aranesp. 1Q2007 sales were up 14% worldwide, to \$1.0 billion, but only rose 10% in the U.S., to \$654 million, as the safety issues first broke.

The best Aranesp safety news Amgen generated during this time was that it didn't pose a greater risk of death in a trial of lung cancer patients. The worst news? Another trial involving patients with cancer-induced anemia (rather than chemotherapy-induced anemia) showed no reduction in the need for transfusions and a 45% increase in deaths.

## Hit Me One More Time

Meanwhile, Amgen's anemia franchise is under attack from another front. In May 2007, Roche gained preliminary approval for Mircera, its own ESA for anemia, from Europe's Committee for Medicinal Products for Human Use (CHMP). The EC usually follows CHMP's recommendations within 90 days, so there's a good chance that Mircera will be approved in Europe this summer. The FDA recently delayed its ruling on Mircera, pending the resolution of the ESA studies.

## THE LOWE DOWN

SOME PEOPLE AT AMGEN MUST FEEL as if the Devil has finally come to collect. The company has been coining money for many years with its protein drugs, and (like the rest of the biotechs), smiling at the patent expiration difficulties of the small-molecule world. But it's been one bucket of bad news after another recently: questions about side effects, investigations into marketing practices, and (even more troubling in the long term) talk of guidelines for biologics. What to do?

In Amgen's case, one thing they've been doing is funding a rather large small-molecule discovery effort. That's probably a smart move, in the same way that many small-molecule houses have been branching out into proteins. But it's really hard to say what they're getting for the money, because those folks hardly ever publish a word. I'm not sure what it means when things are done that quietly. Eventually we'll find out.

For now, the company has a real shock to its culture to deal with. I'm not sure how many people there have gone through something like this, or how they'll react. For their sake, Nietzsche had better have been right about whatever doesn't kill you making you stronger.

—Derek Lowe

Amgen has vigorously opposed Roche's product, contending that it violates Amgen's patents (a claim Roche denies, of course). Their suit will go to court in the U.S. in September 2007. A week or so before the CHMP ruling, the U.S. Supreme Court refused to hear Amgen's appeal in a trial against Shire and Sanofi-Aventis over an Epogen patent. That trial's been going on so long, it's actually referred to as Amgen v. Hoechst-Marion-Roussel and Transkaryotic Therapies, but that's the wheel of justice for you.

## Euro Trashed

Europe hasn't been too friendly to Amgen. In addition to giving Mircera a positive recommendation, the CHMP also shot down Vectibix for advanced colon cancer treatment in May 2007. The committee noted that there wasn't sufficient evidence of benefit, due to the design of the key clinical trial. Amgen is appealing the decision, and hopes to sell Vectibix in Europe as a monotherapy after a combination with approved cancer treatments stops working.

Vectibix was a bright spot for Amgen in 2006, the fruit of a long collaboration between two companies that Amgen acquired over the years, Immunex and Abgenix. Approved in September 2006, Vectibix marked Amgen's first cancer drug. It posted \$39 million in 4Q2006 sales and \$51 million in 1Q2007. In April 2007, the company received positive news from a Phase III trial of Vectibix, demonstrating an improvement in progression-free survival for patients with metastatic colorectal cancer when chemotherapy has failed.

Unfortunately, in another trial designed to test Vectibix in combination with those earlier chemotherapies, the drug seemed to fail miserably. Amgen pulled the plug on a trial that combined chemotherapy, Genentech's Avastin, and Vectibix. Adding Amgen's drug to the approved chemotherapy-plus-Avastin regimen led to increased toxicity (more deaths) but no increase in efficacy.

## Little Help Over Here?

It's not like all of Amgen's trials have led to failure. The company got positive results from AMG 531, a treatment for immune thrombocytopenia purpura (ITP) and myelodysplastic syndromes (MDS). Around 10,000 to 20,000 people get diagnosed with MDS annually in the U.S. AMG 531, which stimulates platelet growth, may be filed by the end of the year for treatment of ITP.

Denosumab is another moderately bright spot for Amgen. The MAb finished one Phase III trials for postmenopausal osteoporosis (PMO) and is in the midst of another in breast cancer patients. Amgen recently published data that Denosumab may be effective in treating rheumatoid arthritis. According to a Phase II study, the drug reduced bone erosion in patients with RA, even though it didn't reduce pain and inflammation. Unfortunately, Denosumab may get trumped in the PMO indication by Novartis' Reclasta, so the company will likely have to push the oncology studies.

All these late-stage trials helped contribute to Amgen's massive \$3.4 billion R&D expenditure in 2006, up 45% from 2005.

The pace kept up in 1Q2007 as the company spent \$803 million, up 29%. Quarter-to-quarter, R&D spend actually dropped 20%, since 4Q2006 expenditure was \$1.0 billion, needed in part to support nine mega-trials (trials with more than 200 sites).

### Pickup Game

All of which would lead me to write, "Amgen can't buy a break," but it turns out that they're trying to do just that. In June 2007, the company made a pair of "small" company acquisitions, getting into the DPP-4 diabetes arena with Alantos Pharmaceuticals and enhancing its kidney offerings with Ilypsa's lead drug, ILY101. Neither initiative will bear fruit for a few years (if ever, given the vagaries of R&D).

In past years, I wondered when Amgen would finally slip under 20+%

revenue growth. Looks like I got my answer. Now I'm just hoping it doesn't fall under 10+% in 2007. Amgen's still almost twice the size of its two closest competitors on this list, but it's definitely lost any aura of invulnerability it once had.

Or, as an April 2007 profile in the *Wall Street Journal* put it, "Amgen has arrived as a big pharmaceutical company — and now confronts some of the same problems as Pfizer or Merck . . . heavy reliance on a few blockbusters, an uncertain pipeline of new drugs despite heavy research spending, questions about safety and marketing and, recently, the prospect of competition from generics makers."

Oh, yeah, I forgot to mention: the federal government is working on guidelines to allow biosimilars on the U.S. market. ■

## ACQUISITIONS

**Target:** Alantos Pharmaceuticals

**Price:** \$300 million

**Announced:** June 2007

**What they said:** "We are pleased to add this clinical stage DPP-IV inhibitor to our growing portfolio of therapeutics for the treatment of metabolic diseases."

—Roger M. Perlmutter, M.D., Ph.D.,  
executive vice president for R&D, Amgen

**Target:** Ilypsa

**Price:** \$420 million

**Announced:** June 2007

**What they said:** "Ilypsa and ILY101 are a strategic fit for Amgen's nephrology portfolio and further demonstrate our commitment to explore, develop and commercialize promising therapies that help in the fight against kidney disease and its complications."

—George J. Morrow, executive vice president of  
Global Commercial Operations Amgen

**Target:** Avidia

**Price:** \$290 million, plus \$90 million in milestones

**Announced:** September 2006

**What they said:** "Avimers may have several advantages as therapeutic products in terms of biological activity, tissue distribution, reduced immunogenicity and improved manufacturing efficiencies."

—Roger M. Perlmutter, M.D., Ph.D.,