

# Back to the Future: Biotech Product Sales 1983-1993

The art of predicting which products will make it and when is a lot more difficult than we used to think

ARTHUR KLAUSNER

## 10 CELEBRATING A DECADE OF EXCELLENCE

With Amgen (Thousand Oaks, CA) likely to record close to a billion dollars in revenue for 1992 on the strength of a pair of blockbuster drugs, the days of wondering whether actual, marketable products would ever emerge from the new science of applied molecular biology seem far behind us. It's well worth remembering, however, that when *Bio/Technology* was launching its inaugural issue just ten years ago this month, the human insulin engineered by Genentech (S. San Francisco, CA) and marketed by Eli Lilly (Indianapolis, IN) was the only biotech-derived therapeutic on the market. In the decade that followed, more than a dozen rDNA products have been approved in the U.S., and total annual sales in this country now top \$2 billion (see Table 1).

### The "big four"

This is not to imply that the past ten years have been a casual stroll through the lab by any means. Back when *Bio/Technology* was first trying to figure out what it wanted to be when it grew up, the "Big Four" of the toddling biotech "industry" were Genentech, Cetus (Emeryville, CA), Biogen (Cambridge, MA), and Genex (Paris, France). Biogen and Genex dropped off this prestigious list early on as a result of business difficulties, while Genentech and Cetus eventually decided that there were more important things in life than being a free-standing company. Today's "Big Four" of independent biotech concerns would include the following:

- Amgen (which had been written off by many as virtually dead around 1985 and doesn't seem to have made a single mistake since then);
- Chiron (Emeryville, CA) (which acquired neighboring Cetus as part of its impressive rise toward the top);

*Arthur Klausner is director of research at Domain Associates (Princeton, NJ), a venture capital firm specializing in early-stage life sciences investments. From 1983-1988, prior to finding honest employment he toiled as an editor at Bio/Technology.*

- Synergen (Boulder, CO) (mostly on the strength of its interleukin-1 receptor antagonist, Anril, which has completed Phase III clinical trials—and whose status is keeping stockpickers across the biotech industry holding their collective breath); and

- Biogen (which has made a spectacular recovery under the leadership of Jim Vincent and now has the enviable responsibility of cashing more than \$100 million worth of royalty checks each year).

Back in the early 1980s, however, not only was it difficult to pick the winning companies, but even figuring out what *products* might be blockbusters was no simple task. Early articles in *Bio/Technology* touted tissue plasminogen activators (t-PA) for blood clot disorders (June, 1983), described an experimental enzyme therapy for a rare and little-known genetic disorder called Gaucher's disease (November, 1983), and even put alpha-interferon on trial (March, 1984). All of these products are on the market today.

### Biodog or superdrug?

Yet it was more than determining which products would work; even if eventual FDA approval was taken as a given for a particular product, estimates of total sales potential could vary all over the map. Take, for example, the drugs in the early Genentech product portfolio. Alpha-interferon was initially (and very naively) hailed as biotech's prototypical superdrug. When this lymphokine's development didn't set new clinical land-speed records, however, it languished for several years in biotech's doghouse. Today, with alpha-interferon boasting worldwide sales of over half-a-billion dollars [via the combination of Schering-Plough (Union, NJ) and Hoffmann-La Roche (Nutley, NJ)], one would be hard-pressed to call this drug a dog. Similarly, human growth hormone (hGH) was originally panned as having just a \$40 million U.S. market potential (unless it became widely sold to parents dreaming of being supported in their aging years by basketball-star offspring). Nevertheless, through short-stature applications alone, hGH now generates over half-a-billion dollars in annual worldwide sales. Finally, there is t-PA. Not too long ago, this clot-dissolving agent was supposed to be Genentech's billion-dollar blockbuster. Current an-

Biogen has made a spectacular recovery under the leadership of Jim Vincent and now has the enviable responsibility of cashing more than \$100 million worth of royalty checks each year.

nual (though declining) sales of close to \$200 million in the U.S. can't be considered peanuts, but t-PA certainly didn't become the caviar that high-paid market analysts thought they had ordered from biotech's tempting menu.

Turning to other companies and products, remember when Teena Lerner (then a biotech analyst for L.F. Rothschild; now a biotech analyst for Lehman Brothers) was almost laughed off Wall Street for predicting that Amgen's erythropoietin (EPO) had a greater than billion-dollar sales potential? Say hello to EPO, biotech's first billion-dollar drug. In another case, Genzyme's Ceredase, the enzyme replacement for victims of Gaucher's disease (U.S. population 2000-3000), was widely regarded as nothing more than a concept-proving niche product. But now that the price of this drug may range from \$58,000 to \$546,000 per patient per year (according to figures from the U.S. Office of Technology Assessment), Ceredase quickly becomes the only player in a potential \$100-million "niche."

These success stories, however, do not mean that biotech products have uniformly exceeded expectations. Cetus bet its future on interleukin-2, and although this product is now on the market it is not clear whether IL-2 will ever attain substantial sales. And don't forget the hype that surrounded tumor necrosis factor versus cancer, superoxide dismutase against ischemia-associated damage, and recombinant growth factors for wound healing. Further, while highly touted monoclonal antibodies have succeeded in revolutionizing the diagnostics industry and have begun to impact imaging as well, these "magic bullets" have thus far missed the mark in therapeutics.

### A new playing field

Clearly, biotech's playing field has changed greatly over the past ten years. Perhaps nowhere was this transformation more evident than at January's Eleventh Annual Hambrecht & Quist Life Sciences Extravaganza in San Francisco. No longer did presenting companies use the majority of their precious 25 minutes of fame to expound on the virtues of their "enabling technology platforms." Instead, for example, Chiron CEO Ed Penhoet spent the first 10 minutes of his speech defending the pharmaceutical industry — that's right, the *pharmaceutical* industry — and its aggressive pricing practices that have come under so much fire of late. Importantly, the majority of other speakers for so-called second- and third-tier companies succeeded in making comparable transitions from the technical lexicon of the 1980s (rDNA, GM-CSF, MAb) to biotech's modernized, product-oriented version of alphabet soup (IND, NDA, PLA). Can the days of PE ratios, ROI, and EBIT be far away?

So, what does the future hold? Data churned out annually by the Pharmaceutical Manufacturers Association (Washington, D.C.) indicate that biotech products are literally clogging up the FDA pipeline. (If only Genex's ill-fated microbial drain cleaner could have worked on *this* kind of log-jam. . .). As a result of all this clinical progress, publicly traded biotech companies are beginning to be valued less on science-based "hopes and dreams" and more on the timely accomplishment of commercially oriented milestones.

	1987		1992		1997	
	U.S.	World	U.S.	World	U.S.	World
Alpha-interferon	14	55	135	565	290	1020
Beta-interferon	—	5	—	20	10	35
CD4	—	—	—	—	30	45
Centoxin/E5 MAbs	—	—	55	75	115	220
Erythropoietin	—	—	600	1225	910	1845
Factor VIII	10	10	140	235	270	445
Gamma interferon	—	—	15	25	35	45
G-CSF	—	—	295	405	550	870
GM-CSF	—	—	50	70	155	305
Hepatitis B vaccine 50	100	105	260	105	275	—
Human growth hormone	95	130	270	575	225	660
Human insulin	65	175	245	625	405	1035
Interleukin-2	—	—	5	20	30	50
Orthoclone OKT3	5	10	55	90	95	160
T-PA	55	60	180	230	85	120
<b>TOTAL</b>	<b>294</b>	<b>545</b>	<b>2150</b>	<b>4420</b>	<b>3310</b>	<b>7130</b>

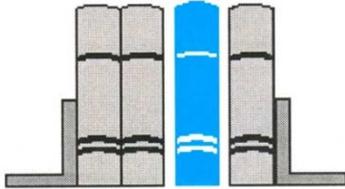
Source: Robin Rodgers, Decision Resources, Inc. (April, 1992). Note that these figures were derived prior to the difficulties encountered by Centoxin.

Surely this is a more mundane state of affairs than the previous ability to obtain lofty valuations based solely on far-off visions of technological wizardry. But in the long run, the winning biopharmaceutical companies will be the dull, plodding firms that succeed in putting actual products into the hands of practicing physicians to be administered to real patients. Suddenly, "boring" doesn't sound so bad after all.

**TABLE 1.** Estimated sales of selected biopharmaceutical products (in U.S. \$ millions).

**Antibodies?  
Neurochemicals?  
Peptides and proteins?  
DNA probes?**

for neuroscience  
signal transduction  
cell adhesion  
endothelium  
research



**AFFINITI's 1993-1994 Directory of  
Products and Services is now available.**

For a free copy  
call (+44/0) 602 436100 or  
fax (+44/0) 602 436300

AFFINITI Research Products Ltd., GPT Business Park,  
Technology Drive, Nottingham, NG9 2ND, UK.

Write in No. 510 on Reader Service Card