The biotechnology bubble machine

David Rasnick

The Biotech Advisor newsletter[1] informs potential investors that biotechnology is "not the stuff of which bubbles are made." The reason biotechnology is so exciting, and such a great investment, we are assured, is because…

> *"[I]t's for real. It's substantial. It's not going away. Biotech companies aren't run by twenty-something MBAs with green hair whose lifelong goal is to cash in and retire by age 30. Biotechnology companies are managed by some of the smartest—and most ethical—people in the world: scientists, physicians, and top managers who have dedicated their lives to improving human health. These folks are smart enough to realize that the only way they're going to get rich is if the stockholders get rich. And the only way the stockholders are going to get rich is if their products work—if they pass five to eight years of testing that costs upwards of $800 million, culminating in approval by the toughest regulatory agency on earth, the US Food and Drug Administration."*

Even within the pharmaceutical industry, biotechnology is different. Unlike the 'meds' in your bathroom cabinet (pills, creams, tablets, etc.), which pretty much only treat your symptoms, biotechnology products offer the potential for effective, long-lasting treatment for the root causes of such chronic diseases as cancer, diabetes, and heart disease. In some cases, biotech products (e.g., gene therapy) could even *cure* certain illnesses. That's the hope and the promise—the reason large pharmaceutical companies like Merck and Pfizer continue to pour billions into biotechnology, through partnerships and through their own home-grown biotechnology efforts. And that's also why individual investors also need to give biotechnology stocks a hard look[1].

However, the depressing regularity of biotechnology failures has led to the realization that, "Far from delivering on its early promise of effective cures for exotic diseases, biotechnology has instead proved to be a complex endeavor, with high costs and long lead times requiring the financial stamina only big corporations can usually deliver"[2].

While biotech continues the Sisyphean effort to realize its promise, the healthcare industry as a whole appears to thrive in a period of economic malaise. In a recent article in the *New York Times*, Henry A. McKinnell, the chief executive of Pfizer, said that while "The telecom industry and the financial industry have crashed[,] [w]e're still growing"[3]. Some of the people who once worked in the Northeast's technology sector have found a refuge in the healthcare industry. The Northeast has a higher proportion of healthcare workers than any other region of the country. In New York City, for example, 40% of the largest private employers are medical institutions. In Philadelphia, the figure is 70%[2]. But this is a temporary refuge at best because the entire healthcare industry in the United States is set for a major fall and biotechnology will likely lead the way.

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There are 1,457 biotechnology companies in the United States, of which 342 are publicly held[4]. The total value of publicly traded biotech companies was $224 billion as of early May 2002. The biotechnology industry has more than tripled in size since 1992, with revenues increasing from $8 billion in 1992 to $35.9 billion in 2001 (ref. 5). The US biotechnology industry currently employs 179,000 people; that's more than all the people employed by the toy and sporting goods industries. Many biotechnology companies are small startups that disappear in a couple of years only to be replaced by a new crop of startups eager to recycle the highly skilled workforce.

Biotechnology is one of the most research-intensive industries in the world. The US biotech industry spent $13.5 billion on research and development in 2001 (ref. 5). The top five biotechnology companies spent an average of $89,400 per employee on R&D in 2000. Yet, in spite of its colossal size, favorable publicity in the popular media, and two decades of effort, biotechnology's real contributions to human health and economic growth are pitifully few. Only one of 16 regions in the United States where biotechnology has a significant presence showed net income for 1999 (ref. 6). And that income was largely due to Amgen (Thousand Oaks, CA) and a handful of other companies[5,6]. Overall, publicly held biotechnology companies showed a loss of more than $5.3 billion in 2001 (ref. 5).

Amgen's Epogen and Neupogen, which stimulate the bone marrow to produce more red and white blood cells, respectively, are biotechnology's biggest moneymaking drugs. One of the main uses of both drugs is to treat the toxic effects to the bone marrow caused by chemotherapy for cancer and AIDS. Developing drugs to treat the toxic effects of other drugs has become a growth industry. Since 1996, 11 such drugs were approved by the US Food & Drug Administration (FDA; Rockville, MD) (ref. 7).

Genentech (S. San Francisco, CA)—one of the companies that pioneered the biotechnology sector and produced such groundbreaking products as recombinant insulin and human growth hormone—also brought us tissue plasminogen activator (tPA), a recombinant human factor used to prevent blood clots after heart attacks. The company has spent massive amounts of money on clinical studies in an effort to demonstrate the superiority of tPA over its competition and to justify its high cost. Because tPA works no better than streptokinase, a bacterial enzyme used for the same purpose that costs ten times less[8], Genentech has spent millions of dollars marketing tPA aggressively.

Biogen, the world's oldest independent biotechnology company, is still trying to find a use for its otherwise highly profitable recombinant interferons, which have been sold for 17 different types of cancer, viral infections, hepatitis, hairy cell

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leukemia, Kaposi's sarcoma, AIDS, and multiple sclerosis.

These examples epitomize the triumphs of biotechnology. Most of the remaining 140 or so biotechnology products are not moneymakers either because FDA approval is for rare diseases with small markets or because they just plain don't work.

Because biotechnology had so little to show after two decades and billions of dollars spent, it used to puzzle me that most people working or investing in biotechnology companies never seemed to lose money. The reason for this, I came to realize, was the sector's incestuous nature. The way money is made is for certain biotechnology companies to merge with or acquire other biotech companies. Some bioscience companies are acquired by large pharmaceutical companies eager to obtain the special capabilities of the smaller fish. With each merger and acquisition, money and stock change hands. A recent example is Amgen's $16 billion acquisition of Immunex (Seattle, WA)[9]. A sure way to make money (though less glamorous) is by providing the technical reagents and equipment used by other biotechnology companies.

In order to forestall the eventual implosion, a new breed of biotechnology company has chosen to abandon the painstaking and often spotty laboratory approach to research in favor of using higher mathematics to exploit a genetic map of the human genome to 'better target' that research. The recent surge in bioinformatics companies may set a record for swiftness of disillusionment. Bioinformatics is gambling that the secrets to health and disease are waiting to be deciphered from the labyrinth of the human genome and proteome. The bioinformatics fad is based on the same misguided belief used partly to justify funding of the genome project: that complex human diseases, such as cancer and arthritis, are caused by 'bad' genes. Gene therapy—replacing bad genes with good—would be the logical solution to such diseases. But, the naive belief in gene therapy for complex diseases is inexplicable given that it has not even been attempted in a real, well-recognized gene disease, such as hemophilia.

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How long this self-referential, pyramid structure of the pharmaceutical/biotech industries will remain standing is anyone's guess.

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3. Leonhardt, D. Northeast Quietly Becomes a Health Care Corridor. *New York Times,* December 30 (2002).
4. http://www.bio.org/news/stats.asp
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7. http://www.bio.org/er/approveddrugs.asp
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