



Health, Education and Human Services Division

B-232863

December 15, 1994

The Honorable Tim Valentine, Chairman
The Honorable Tom Lewis, Ranking Minority Member
The Honorable Peter I. Blute
Subcommittee on Technology, Environment and Aviation
Committee on Science, Space, and Technology
House of Representatives

Members of Congress have expressed concern that cost containment efforts such as those considered in the recent health care reform debate could adversely affect the biotechnology sector's ability to finance research and development (R&D) for new pharmaceutical products. In the pharmaceutical industry as a whole, similar concerns have been expressed by both industry representatives and independent analysts. These anxieties may be heightened for the biotechnology sector because it consists primarily of young research firms that depend heavily on outside financing from investors and pharmaceutical companies.

In light of these concerns, you asked us to describe the current state of biotechnology financing and to assess the potential impact of health care reform on the biotechnology sector. This letter contains the results of our review based on the literature on biotechnology financing and biotech and pharmaceutical R&D, and on interviews with industry experts.

We found that the firms that constitute the biotech industry typically are small, have few or no products on the market yet, and are heavily dependent on outside financing for their continued existence. As the industry matures, however, biotech companies are developing alliances with the pharmaceutical industry to provide both financial and technical support. The increasing financial links between biotech companies and pharmaceutical firms mean that legislation that affects the prescription drug market may affect the biotech industry first directly, and then indirectly through its influence on the pharmaceutical industry.

Should comprehensive health care reform legislation-- similar to the proposals considered during the 103rd Congress--be enacted, two major effects on the prescription drug market are likely. First, the demand for drug products could increase if health care legislation were to expand prescription drug insurance coverage. This would enhance profits for both the pharmaceutical and biotech industries. Second, provisions to contain costs could result in reduced revenues for drug products, and this would dampen profits for both industries. Overall, the prospects for both industries under health care reform, whether positive or negative, will depend on the relative strengths of these countervailing forces.

BACKGROUND

The term biotechnology (or biotech) refers to a collection of technologies that can help companies develop products from living cells. Companies are applying biotechnology in diverse areas, including agriculture, the environment and health care. The following are examples:

- In agriculture, biotech products are used to stimulate milk production, extend the shelf life of tomatoes, and to protect crops against pests.
- Environmental uses of biotechnology are largely directed at hazardous waste treatment and at oil spill cleanups (such as the 1989 Exxon Valdez oil spill off the coast of Alaska).
- In the health care field, biotechnology-derived products can aid in diagnosis and treatment--for example, erythropoietin (EPO) is used for treating dialysis anemia.

Of these areas, health care (and pharmaceuticals in particular) has received the most resources, especially as public acceptance of genetically-engineered agricultural products has lagged. About 68 percent of biotechnology companies are concentrated in human health care.¹ Companies emphasize health care products because market rewards appear greater--for example, this year EPO is expected to bring about \$1.8 billion in sales to Amgen, Inc., and its partner Johnson and Johnson. As

¹See "Biotech 94: Long-term Value, Short-term Hurdles," Ernst and Young, 1994; and Biotechnology in a Global Economy, U.S. Office of Technology Assessment, 1991.

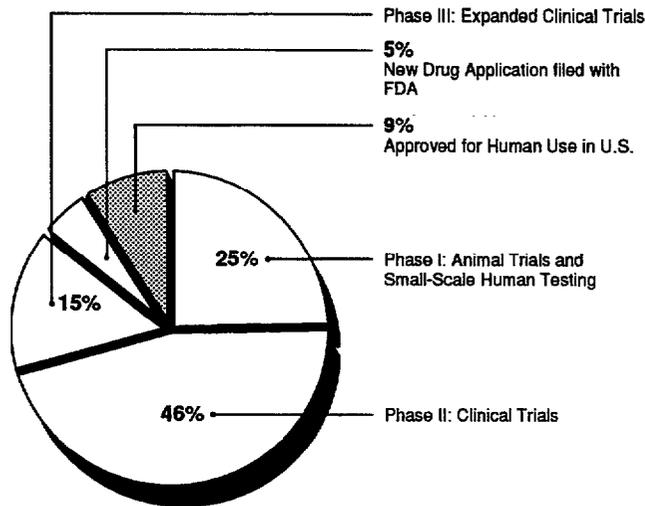
pharmaceutical companies become more competitive through consolidation and downsizing, industry experts and financial analysts expect biotechnology to become more important as a source of innovative new products.

Although large pharmaceutical companies are using biotechnology to supplement traditional drug-discovery techniques, most biotechnology companies are small. In 1993, 75 percent of biotechnology companies had 50 employees or fewer; only 10 percent had over 135 employees. In the United States, a large number of small, research-based firms have generated most of the new biotechnology products and promising discoveries. Most of these firms are located on the east and west coasts, particularly in the San Francisco and New England areas.

The biotechnology industry is growing steadily and rapidly. According to the accounting firm of Ernst and Young, since 1986 the number of biotechnology companies in the United States has grown by at least 50 percent (from 850 to 1,272), and in 1993 estimated employment topped 97,000, compared with 60,000 in 1986. Even after adjusting for general inflation, total sales increased from approximately \$714 million in 1986 to \$7 billion in 1993, and R&D spending also increased--to \$5.7 billion in 1993 from approximately \$475.6 million in 1986.

The biotech sector is relatively young, with 74 percent of biotech firms founded after 1980. For the most part, these young firms have yet to complete the long drug discovery process. R&D to discover new products, rather than marketing and selling existing drugs, is currently the main focus of these biotech companies. Relatively few biotech drugs have reached the pharmaceutical market, but many more are in the research, development, or testing phases. (Fig. 1 shows the stage of development for products of the top public biotech companies.)

Figure 1: Pharmaceutical Products in Development at Top Public Biotech Companies



Source: Ernst and Young, "Biotech 94: Long-term Value, Short-term Hurdles," 1994.

Because of the industry's youth, most biotechnology companies have no sales, and even larger and more established biotech companies may find their sales revenues insufficient to fully fund their research agendas. Some biotech R&D is funded by the federal government; basic and applied research in biotechnology received approximately \$3.4 billion in federal support in 1990. Industry spending continues to grow. As a result, companies must be able to raise substantial amounts of cash to complete the drug-development process.

BIOTECH COMPANIES NEED
EXTENSIVE OUTSIDE FINANCING

To bring a new pharmaceutical product to market, both biotech and traditional pharmaceutical companies must endure a time-consuming process of product development and regulatory approval. This process is also a risky one. Researchers at Tufts University's Center for the Study of Drug Development have estimated that of the many potential

drugs that are tested in humans, only 23 percent will be approved by the Food and Drug Administration (FDA).^{2,3}

Although the process of bringing a drug to market is common to the biotech and pharmaceutical firms, biotech companies face some unique financial challenges. The largest difference between the two sectors is clearly how research for new drugs is financed. Large pharmaceutical companies finance their R&D largely through sales of their current products. The Pharmaceutical Research and Manufacturers' Association estimates that the pharmaceutical industry generated \$56.4 billion in sales in 1993 and returned 18 percent (\$10.3 billion) to R&D. According to Fortune magazine, 15 of the 16 largest U.S. pharmaceutical companies returned profits to stockholders in 1993.⁴ By contrast, only 18 percent of biotechnology companies showed a profit in 1993.⁵ Small, relatively young biotech companies may have no current products or profits, and even more established biotech companies may find their sales insufficient to fully fund their research agendas. As a result, the biotech industry overall takes in less than it spends, depending on investor capital for continued operations. To fund the drug-development process, biotech firms may rely on a variety of funding sources, including venture capital, stock offerings, individual investors, and arrangements with large pharmaceutical companies.

Venture capital has been an important source of funding for biotechnology companies, especially brand-new firms. At the very early stage of a company's development, venture capital may be the only available source of "seed money" or start-up financing. Equity (selling stock) continues to be

²See Joseph DiMasi, Ronald Hansen, Henry Grabowski, and Louis Lasagna, "Cost of Innovation in the Pharmaceutical Industry," Journal of Health Economics, 1991.

³The risk in new drug development is more concentrated for the small biotech firm that may be devoting all its resources to developing a single drug. By contrast, large firms with greater R&D budgets can diversify their research portfolios, spreading the financial risk if any one individual product fails to pay off.

⁴Amgen, a biotechnology-based pharmaceutical company, is among this group of large and profitable companies.

⁵See "Biotech 94: Long-term Value, Short-term Hurdles," and Biotechnology in a Global Economy.

an important means of financing for biotech companies. Young private companies may "go public" by selling their stock in an initial public offering (IPO). After the IPO, the firm's shares can be publicly traded, and the company can raise additional capital in follow-on offerings if there is investor interest in its shares. Firms' ability to raise money by selling equity is subject to the ups and downs of the stock market as a whole, and of investors' expectations of biotech in particular. The weakness in biotech stock in 1993 and 1994 has left investors reluctant to buy new shares until companies make additional gains in the drug-development process, so follow-on stock offerings (after the IPOs) have become considerably less successful. In a 1993 survey, 34 percent of biotech companies that were planning a stock offering retreated because of the poor investment outlook.⁶

Some companies have been able to raise start-up capital from wealthy individual investors. However, this type of financing is limited in availability. Biotech companies that have conducted significant R&D on a product, but lack the money to fund clinical trials and marketing, can team up with large pharmaceutical companies that have the necessary resources. Biotech/ pharmaceutical deals can take several forms--equity arrangements, joint ventures, licensing and marketing agreements, and R&D contracts. For the biotech company, these arrangements may provide critically needed cash, and may also offer access to manufacturing or marketing capacity. However, strategic alliances can be an expensive financing method, because they may require a company to forfeit some control over its most crucial assets--the potential new products.

FINANCIAL ANALYSTS REPORT
A BIOTECH "CASH CRUNCH"

According to many financial analysts, biotech firms' increasing need for cash and investors' lukewarm response combined to produce a biotech "cash crunch" in 1993 and 1994, making it more difficult for biotech firms to get financial backing, especially from Wall Street. As the biotech sector has matured and more products have reached clinical trials, drug development expenses have risen dramatically and firms require additional funding. However, investors' response to biotech has been less

⁶Robert Goldberg, "Price Controls and the Future of Biotechnology: The Results of a Survey," Gordon Public Policy Center, Brandeis University, 1993.

enthusiastic than in the past. Like securities in many health care industries, biotech stock prices have fallen in the past year, and reports indicate that venture capitalists have also become more selective. Industry observers attribute the resulting cash crunch to a number of factors, including the following:

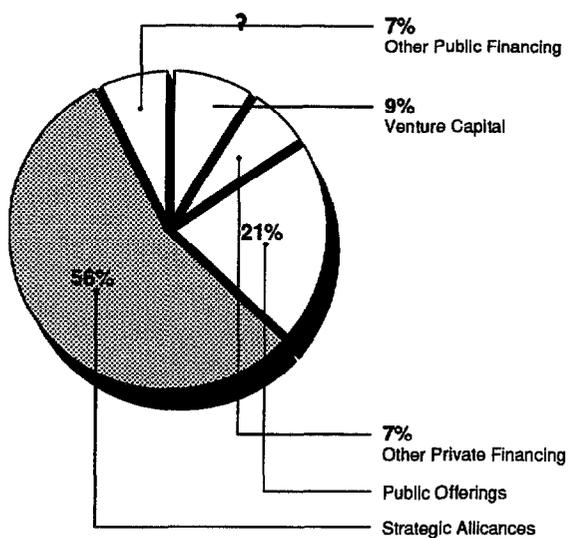
- Disappointing clinical results for several once-promising biotech products have led analysts and investors to revise their expectations, underscoring the inherent risks in new drug development. Three new drugs to treat septic shock were shelved after clinical trials showed that the drugs were either ineffective or caused serious negative side effects. Other, more successful biotech drugs have had narrower applications--and thus less profit potential--than industry backers had hoped. For many financial analysts, the initial excitement over the possibility of discovering cures for such major diseases as cancer and acquired immune deficiency syndrome (AIDS) has given way to the harsher reality that selling an idea is easier than developing a product.
- Uncertainty over biotechnology patent law has made investors more wary. Biotechnology products create special problems for patent regulators, who must determine if the product is both new and useful. Recently, the Patent and Trademark Office has been requiring more data on the potential usefulness of biotech products. In addition, costly and unpredictable patent infringement litigation has heightened the uncertainty over the future profits of biotech drugs. For example, the patent dispute between Genetics Institute and Genentech was first decided in favor of Genentech, but then the court overturned a previous ruling and found for Genetics Institute. Similarly, the long legal battle between Centocor and Xoma--a "mutual kamikaze strategy," according to Xoma's former chief executive officer--damaged both companies severely.
- In 1993 and early 1994, investors were worried that the health care reform proposals being considered would impose price controls, which could limit biotech companies' future profitability.

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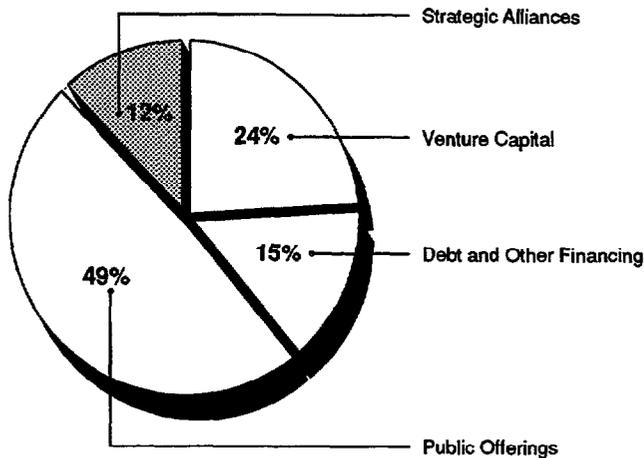
BIOTECH FIRMS TURN TO
ALLIANCES WITH
PHARMACEUTICAL COMPANIES

Accompanying the overall contraction in available capital has been a change in where that capital comes from. The sources of financing for biotech research have shifted in favor of more strategic alliances with pharmaceutical companies, with a decreased reliance on venture capital and the public equity markets. Although the figures are only roughly comparable because of methodological differences, figures 2 and 3 illustrate the change in biotech financing between 1986 and 1993. In 1986, public equity and venture capital provided most of the industry's financing; by 1993, strategic alliances had come to dominate the biotech industry's capital inflows.

Figure 2: Sources of Biotechnology Industry Financing, 1993



Source: Ernst and Young, "Biotech 94: Long-term Value, Short-term Hurdles," 1994.

Figure 3: Sources of Biotechnology Industry Financing, 1986

Source: Ernst and Young, "Biotech: At the Crossroad," 1986.

In large part, this change in industry financing reflects the maturing of the biotech industry. As a biotech firm's product development nears the clinical trials stage, the company needs an additional cash infusion to finance this costly process. Neither venture capitalists nor individual investors may be able or willing to fund a full-fledged clinical trial. In addition, the change in financing mechanism might reflect the decrease in enthusiasm for biotech in the financial markets. Pharmaceutical company alliances offer another, extremely important advantage: the technical expertise of the pharmaceutical company in planning and implementing clinical trials in a manner necessary to secure FDA approval. As a greater number of inexperienced biotech firms struggle with the regulatory process, this factor has taken on greater importance.

HEALTH REFORM AND CHANGING
MARKETPLACE COULD HURT OR HELP
BIOTECH AND PHARMACEUTICAL FIRMS

At both the state and federal levels, a number of proposals for health care reform would extend insurance coverage for prescription drugs to many individuals who are presently without such insurance. Because their out-of-pocket prescription drug expenses would fall, these individuals would be expected to demand more prescription

drugs.^{7,8} This increased demand would translate into greater revenues for pharmaceutical and biotech companies, increasing the potential reward for R&D investment.

However, in addition to increased coverage for prescription drugs, the reform proposals considered in the 103rd Congress also included cost containment mechanisms, which could dampen pharmaceutical industry revenues. Several health care reform proposals would impose prescription drug price controls or rebate requirements, limiting manufacturers' revenues and profits. These restrictions would reduce the profit potential for new drugs, making risky R&D investments less attractive.⁹ Downward pressure on prescription drug prices has already resulted from changes in the health care market, including the spread of managed care organizations.

If both cost containment and increased coverage come about, the effect on pharmaceutical company profits and research will depend on the relative strength of these two opposing forces.¹⁰ Again, profits and research could be either

⁷This increased demand for prescription drugs might also be fueled by individuals who would be newly eligible for medical insurance. Not only would these individuals have lower out-of-pocket expenses for drugs, but they would be likely to visit physicians more frequently and thus use more prescription drugs.

⁸A study by the Congressional Budget Office (CBO) estimated that the universal prescription drug coverage provisions of the Clinton administration's proposed Health Security Act would increase the total demand for all prescription drugs by 3 to 5 percent. See How Health Care Reform Affects Pharmaceutical Research and Development, June 1994.

⁹Estimates of the size of the relationship between pharmaceutical prices and firms' R&D expenditures are imprecise at best. For example, one study estimated that a 10 percent decline in pharmaceutical prices could lead to a decline in R&D spending of as little as 1 percent or as much as 12 percent. See Prescription Drugs: Spending Controls in Four European Countries (GAO/HEHS-94-30, May 17, 1994).

¹⁰CBO estimated that under the Clinton administration's proposed Health Security Act, estimated profits from drug development would rise by less than 3 percent. However, CBO's estimate applies only to the particular provisions of

encouraged or discouraged by health reform provisions, including the level of copayments, limitations on coverage, and the severity of price controls or rebate requirements.

Given the countervailing effects of increased coverage and cost containment, the initial set of reform provisions might be designed to achieve some objective, such as encouraging or discouraging industry R&D. If, however, the initial consequences are later determined to be inconsistent with congressional intent, then it may be possible to change the results by recasting the provisions or by incorporating additional ones such as tax credits or assessments.

EFFECT ON BIOTECH COMPANIES
HEIGHTENED BY FINANCIAL TIES TO
PHARMACEUTICAL INDUSTRY

Not only would health care reform affect firms' incentives to conduct R&D, but it might have a secondary effect on the cost of financing R&D. To fund their in-house R&D investments, and also their investments in biotech firms, pharmaceutical companies typically use their current profits, rather than borrow the money or issue additional stock. This type of financing is likely to be cheapest for the pharmaceutical firm, which is in a better position to evaluate the expected costs and benefits of an R&D project than potential outside investors. A reduction in these profits may limit the cash on hand that pharmaceutical firms use to invest in both their in-house R&D and in the R&D efforts of biotech firms. While external capital markets could supply a greater share of funds to make R&D possible, the likely result would be an increase in the cost of financing new drug development.

Therefore, as relationships between biotech and pharmaceutical companies become stronger, changes in the pharmaceutical market--from health care reform or from market forces--will have a greater impact on biotechnology. If pharmaceutical products become more profitable, then biotechnology companies will see enhanced profits and also may be able to obtain financing from pharmaceutical

the Health Security Act for which quantitative estimates could be calculated. As a result, CBO cautions that the combined effect of the administration's proposal on the future profitability of pharmaceutical R&D remains highly uncertain. See How Health Care Reform Affects Pharmaceutical Research and Development.

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companies at a lower cost than would have been possible in a less favorable market. Similarly, biotech firms may be more vulnerable to a reduction in pharmaceutical profits because for them this could mean both lower future revenues and costlier R&D financing.

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We are also sending copies of this correspondence to Representative Tom Lewis, Ranking Majority Member, and to Representative Peter I. Blute. Please contact me on (202) 512-7119 if you or your staff have any questions. Major contributors to this letter include Scott Smith, Assistant Director; Sarah Glavin, Senior Economist; and Claude Hayeck, Evaluator.

Sincerely yours,



Sarah F. Jaggar
Director
Health Financing and Policy Issues

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