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BIOTECH BONANZA: PROSPECTS FOR TEXAS

"Biotech will be to the coming century what electronics has been for the one now passing." [1]

THIS IS A bold claim to make about an industry identified as having approximately 1,300 companies, 153,000 employees and market capitalization of $97 billion.[2] The entire biotech industry is dwarfed by just one pharmaceutical behemoth like Merck, which employs 53,800 at a market capitalization of $162 billion.[3] But pharmaceutical and agrochemical giants sense biotech's potential to transform their industries and actively seek partnerships with biotech innovators. Last year, biotech firm Millennium Pharmaceuticals signed a $465 million genomics deal with Bayer and a separate deal with Monsanto worth up to $218 million.[4] Just consider what has happened in agriculture since the first genetically modified tomato went on the market in 1994. In 1999, nearly half of the total U.S. corn, soybean and cotton acreage will be planted with genetically modified crops.[5] More than 65 biotech drugs and diagnostics are on the market, with hundreds more in development. Biotech supporters sense a bonanza.

Biotech may or may not live up to predictions, but it is attracting media attention. Although most biotech companies in the news are far from the Lone Star State, recent headlines confirm biotech activity in Texas. Austin-based Introgen Therapeutics made the *Wall Street*

INSIDE

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Journal and *Business Week* short lists of biotech companies with promising cures for cancer. The *Forbes ASAP* May 1999 biotech special listed Houston's LifeCell Corp. as a major player in tissue engineering.

Before the Biotech Century begins in earnest, this article investigates biotech's presence in Texas and potential for growth.

Biotech: Innovation and Industry

Biotech is a set of innovations revolutionizing health care, food and agriculture, even manufacturing and environmental cleanup. Biotech, the applied knowledge of biology, is not new. Throughout history, the production of foods such as wine, cheese and bread and the breeding of animals and plants depended on rudimentary biotech. Twentieth century advances in scientists' understanding of molecular and cellular biology, genetics and ways the human immune system fights disease, coupled with computer technology, have enabled companies to launch revolutionary products.

Biotech: The Innovations. The ability to recombine genetic fragments and the computer-enabled deciphering of genetic code are key tools of modern biotech. A 1973 experiment to insert a gene from an African clawed toad into bacterial DNA marked the beginning of genetic engineering and eventually led to the first Food and Drug Administration approval of a genetically engineered drug: bacteria-produced human insulin. The international Human Genome Project, using sophisticated gene-sequencing computers, plans to map and sequence all human DNA by 2003. Meanwhile, Celera Genomics Corp. plans to do for biotech what Bloomberg did for financial data: develop and sell access to a comprehensive, cutting-edge database. Genetic engineering enables scientists to change what cells do, deciphering of the genetic code reveals what changes to make and access to genetic information inspires innovation.

Biotech products today blur boundaries between industrial categories. Biotech in health care harnesses the human body's own tools to fight disease through medicines, vaccines, tissue engineering and gene therapy and to detect disease through new and improved diagnostic tests. Biotech foods already engineered for higher quality and nutritional content will soon be able to deliver vaccines and hemoglobin. Biotech increases crop yields without the use of chemicals by making plants immune to herbicides and toxic only to pests—launching a second green revolution. In manufacturing, cotton grown in blue or khaki eliminates the need for chemical dyes, and microbes grow super-resilient polyester. Plants that produce biodegradable plastics and bacteria engineered to clean up toxic chemical spills are under development. And as silicon microchips approach their processing-speed limit, engineers are constructing the next generation of computer chips from DNA.

Biotech: The Industry. Because biotech's dramatic advances are relatively new, we can still distinguish companies that are using biotech to develop pharmaceutical, agricultural or industrial products from those that are not. In that respect, we can discuss biotech as an industry. Over time, competition forces all firms to adopt the best technologies. Just as most companies today use information technologies and are "high-tech," most firms in the near future could be "biotech," and discussing biotech as an industry will be less meaningful. A new industry name—life sciences—has already been proposed, but for now, we can talk about biotech.

Industry characteristics. Biotech's complex innovation process characterizes the industry. The lifeblood of biotech companies is knowledge, labor and capital capable of enduring the time-consuming, risky process of taking a product to market. (See the box, "Biotech's Innovation Process.") A new biotech drug takes about 10 years to develop, and just one drug in 10 successfully completes clinical trials.[6] Thirty biotech agriculture products currently in development will take up to six more years to reach the market.[7] Biotech companies rely on the latest scientific advances and require personnel who can interpret and apply those results. Proximity to universities is typical as companies attempt to attract biologists—

Biotech's Innovation Process

Taking a biotech innovation from discovery to market is slow and expensive. Biotech innovations rely heavily on patent protection and undergo rigorous testing by federal agencies before they can be marketed. The diagram outlines the biotech innovation process for health care, which is similar to the pharmaceutical industry's drug discovery process. Note the entire biotech process typically takes 15 years, over half of which is spent acquiring approval from the Food and Drug Administration (FDA). Biotech applications in other industries also must comply with federal regulations. The U.S. Department of Agriculture regulates biotech food and agriculture innovations, and industrial and environmental innovations are often subject to regulations of the Environmental Protection Agency.

Despite facing considerable time and expense, companies endure biotech's innovation process because of the potential for profit. Ernst & Young identifies why companies may be willing to be patient and persistent.

> "The environment in which a biotechnology product is launched is quite distinct from that of typical high-technology markets. Most products are developed upon a strongly defensible base of intellectual property, and consequently the vast majority of new products occupy highly specialized or even unique niches in the marketplace."[1]

Serving unique niches enables a company to attain a sustainable competitive advantage and thus profits. So even though patent filings and FDA approvals take time, they arguably strengthen an innovation's commercial viability.

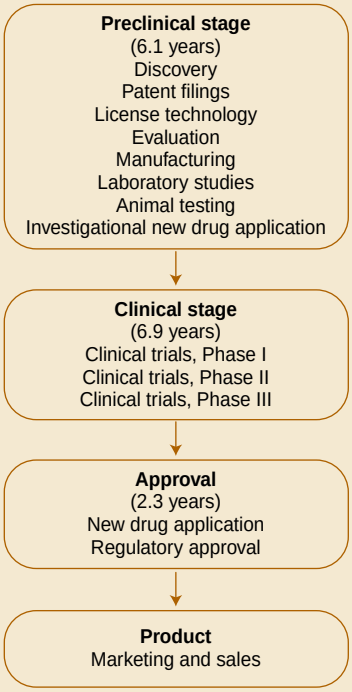
Biotech and Patent Policy. The U.S. Constitution, Article I, section 8, states that "Congress shall have power…to promote the progress of science and useful arts, by securing for limited times to authors and inventors the exclusive right to their respective writings and discoveries." The Biotechnology Industry Organization advocates strong patent protection for biotech inventions:

> "Because biotech companies depend on private investments, patents are among the first and most important benchmarks of progress in developing a new biotechnology product. Patents offer limited protection against commercial use of a company's invention by a competitor. In biotechnology, patents are critical to raising capital to fund the research and development of products."[2]

Two key court cases extended patent protection to biotech innovations, but currently biotech agriculture patent protection is under fire. Patent attorney William Warren explains, "Paradoxically, biotechnology-related inventions are patentable in the United States only if obtained through a non-biological process, defined as one in which the 'hand of man' has intervened."[3] Courts established this principle in 1980 by ruling General Electric could patent a genetically engineered oil-eating bacterium. Recently the Federal Circuit Court of Appeals reversed a Patent Office decision and ruled that DNA sequences that code for particular proteins are patentable. Plant patents, however, are being challenged, as a federal appeals court has taken up the issue of plant patent legality.

Biotech and FDA Regulation. The FDA, part of the U.S. Department of Health and Human Services, pursues a single objective: consumer protection by ensuring that food, drugs, biological products and medical devices are safe. The FDA has existed since 1931, though some law enforcement functions began in 1906 under the Food and Drug Act. The FDA's Center for Biologics Evaluation and Research coordinates with the Center for Drug Evaluation and Research to approve biotech health care products. The approval process for biotech medicines is estimated to cost between $200 million and $350 million and take from seven to 12 years.[4]

Innovation Process: Biotech Health Care Applications



SOURCES: Introgen Therapeutics; Texas Healthcare and Bioscience Institute; author's research.

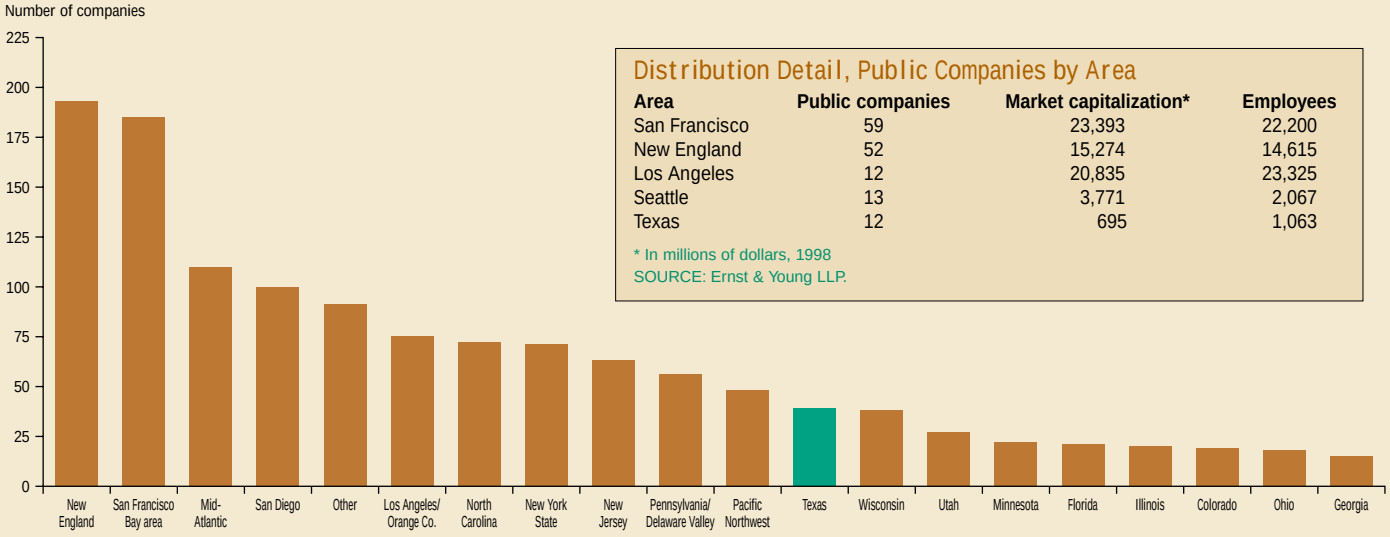
The Biotechnology Industry Organization lobbied for the 1997 FDA Modernization Act and achieved reforms liable to lop 19 months off total drug development times. Other changes include implementing fast-track approval designation to drugs for serious or life-threatening conditions and allowing one biologics license to cover both a product and a facility.

[1] Ernst & Young LLP, *13th Biotechnology Industry Annual Report*, p. 38.
[2] Biotechnology Industry Organization, *The 1998–99 BIO Editors' and Reporters' Guide to Biotechnology*, www.bio.org.
[3] William L. Warren, "Developments in Biotech Patent Law," Jones & Askew LLP.
[4] Biotechnology Industry Organization.

academics not usually involved in business. Finding investors who will wait out the product development phase is particularly challenging for biotech companies today. Many investors abandoned biotech in the mid-1990s for higher- and quicker-return tech stocks. In the meantime, biotech firms have funded themselves by tapping smaller, informed investors and licensing their technology to larger firms.[8]

Industry clusters. Biotech companies, like those in other industries, tend to cluster around essential resources, eventually attracting more such resources to the region. A cluster is not simply a geographic concentration of companies; clusters include suppliers, customers, manufacturers of complementary products and even governmental and other institutions such as universities, standards agencies and vocational training providers. Cluster growth is a self-reinforcing cycle. As a single company's success brings new suppliers or inspires cooperation with local institutions, other companies that can bene-

Chart 1
Distribution of U.S. Biotech Companies
(Public and private, mid-1998)



Distribution Detail, Public Companies by Area

Area	Public companies	Market capitalization*	Employees
San Francisco	59	23,393	22,200
New England	52	15,274	14,615
Los Angeles	12	20,835	23,325
Seattle	13	3,771	2,067
Texas	12	695	1,063

* In millions of dollars, 1998
SOURCE: Ernst & Young LLP.

SOURCE: Ernst & Young LLP.

fit from those resources are drawn to the area. Because company growth is easier in a good business environment, which itself is developed by the presence of other companies, clustering enables companies to gain competitive advantage they could not acquire in isolation.[9]

Biotech's Presence in Texas and Beyond

Traditional statistics often overlook industry clusters, and biotech's relative newness makes its industry presence even less visible to standard measures. In the following paragraphs I assess the presence of biotech companies by region and compare Texas statistics with those of other areas in the United States. I then discuss two large regional biotech clusters and the emergence of such clusters in Texas.

Biotech Companies in U.S. Regions. No database tracks all publicly traded and privately held biotech companies, but industry sources reveal the most important identities and locations of biotech companies. Ernst & Young has tracked public and private biotech companies for 13 years. Chart 1 shows the distribution of biotech companies across the United States. Table 1 lists the seven largest biotech companies. The chart and table show that not only do California and New England have the most companies, they also have the biggest companies. Texas has enough companies to register on Ernst & Young's biotech radar, but the entire Texas public biotech contingent is comparable to just one Seattle company, Immunex Corp., in terms of employees and market capitalization.

Ernst & Young's database is comprehensive but not exhaustive; yet an alter-

Table 1
Biotech Big Seven

Company	Location	R&D as percent of sales	Market capitalization (millions of dollars)	Employees	Selected products and uses
Amgen	Los Angeles	26	19,108	5,308	Procrit, red blood cell enhancement
Genentech	San Francisco	46	8,801	3,242	Humulin, manufactured insulin; hepatitis B vaccine
Biogen	Boston	34	4,912	797	Intron, cancer and viral infections
Alza Corp.	San Francisco	34	3,474	1,532	Advanced controlled dosage release for medicine
Chiron Corp.	San Francisco	32	3,312	6,842	Betaseron, multiple sclerosis
Genzyme Corp.	Boston	13	2,536	3,500	Tissue repair, cancer treatment and diagnostics
Immunex Corp.	Seattle	58	2,228	886	Treatments for cancer, immunological disorders

NOTE: Data as of November 1998. In comparison, pharmaceutical giant Merck employs 53,800 at a market capitalization of $162 billion and devotes only 7 percent of sales to research and development.
SOURCE: Ernst & Young LLP.

Table 2
Biotech Hotbed Communities in the United States

Community	Number of companies
Biotech Bay and Beach (N. and S. Calif.)	308
Pharm Country (N.Y., N.J., Conn., Pa.)	196
Genetown (Mass.)	127
BioCapital (Md., D.C., Va.)	95
Research Triangle (N.C.)	76
BioForest (Wash., Ore., Mont., Idaho)	60
BioTechxus (Texas)	45

SOURCES: Institute for Biotechnology Information; Biospace.com.

native assessment confirms those results. Biospace.com, an industry web site, identifies "hotbed communities" for biotech. The Institute for Biotechnology Information maintains a corporate directory of public and private companies by state. Combining the two sources gives a regional picture of biotech. The numbers in Table 2 differ slightly from Ernst & Young's but provide similar results. California and Massachusetts have the highest concentrations of companies, but Texas has enough to warrant identification and tracking.

Biotech Clusters in California and Massachusetts. California and Massachusetts have developed large numbers of biotech companies. These two states are home to the nation's biotech leaders because they have biotech clusters—companies surrounded by sources of innovation and supporting institutions—that can be traced to historical circumstances.

California's—and the nation's—first biotech company, Genentech, was founded in 1976 in San Francisco by venture capitalist Robert Swanson and Dr. Herbert Boyer of the University of California at San Francisco. The company's genetic engineering capabilities stemmed from recombinant DNA technology developed by Boyer and Stanford's Stanley Cohen in 1973.

Massachusetts' Genzyme Corp. initially benefited from the strength of the region's universities, medical centers and venture capital firms. Eventually, Genzyme required a manufacturing facility. Genzyme's president could have moved the company to the pharmaceuticals cluster in New Jersey and Philadelphia that already had a strong manufacturing base, but chose instead to cooperate with city contractors and develop manufacturing capability in Boston. Genzyme also has worked with the city government to improve the labor pool by offering scholarships and internships to local youth.

Biotech Clusters in Texas Cities. Texas shows signs of nascent biotech clusters. Nearly all Texas biotech companies focus on health care and concentrate in four metropolitan areas. Of the 39 public and private Texas biotech companies tracked by Ernst & Young, 18 are located in Houston, seven in Dallas, five in Austin and three in San Antonio. Table 3 details 20 Texas biotech companies.

Like companies in California and Massachusetts, Texas biotech companies benefit from proximity to educational institutions through research and technology transfer. Technology transfer occurs when a university licenses its technology or sells it outright to com-

Table 3
Texas Biotech Companies

Company	Location	Employees	Focus
Publicly traded			
Access Pharmaceuticals	Dallas	18	Cancer and canker sore therapeutics
Amarillo Bioscience	Amarillo	8	Human and animal disease therapeutics
Aronex Pharmaceuticals	Houston	91	Cancer and infectious disease therapeutics
Carrington Laboratories	Dallas	278	Custom molecular biology services
Cytoclonal Pharmaceuticals	Dallas	20	Cancer and infectious disease therapeutics
Energy Biosystems	Houston	84	Petroleum industry processes
Gamma Biologicals	Houston	134	In vitro diagnostics
GeneMedicine	Houston	109	Gene therapy for cancer
ILEX Oncology	San Antonio	180	Cancer therapeutics
LifeCell Corp.	Houston	95	Tissue engineering
Texas Biotechnology Corp.	Houston	81	Vascular disease therapeutics
Zonagen	Houston	50	Human reproductive system therapeutics
Privately held			
Ambion	Austin	100	Molecular diagnostic products
Bio-Synthesis	Dallas	70	Custom DNA synthesis
Diagnostic Systems Laboratories	Austin	100	In vitro diagnostics
Genosys Biotechnologies	Houston	165	Custom DNA synthesis
Introgen Therapeutics	Austin	60	Gene therapy for cancer
Lexicon Genetics	Houston	83	Functional genomics
Midland Certified Reagent Co.	Midland	45	Custom molecular biology services
Tanox	Houston	55	Immune system therapeutics

NOTES: This table lists public companies of all sizes and private companies with over 40 employees. GeneMedicine has merged to form Valentis; LifeCell has announced plans to move to New Jersey.

SOURCES: Ernst & Young LLP; Texas Healthcare & Bioscience Institute; Biotechnology Industry Organization.

Table 4
Texas Biotech Innovators

University	Affiliated technology transfer organization
Baylor College of Medicine, Houston	BCM Technologies
University of Texas Southwestern Medical Center, Dallas	Dallas Biomedical Corp.
University of Texas Health Science Center at Houston	Institute for Technology
University of Texas M.D. Anderson Cancer Center, Houston	Office of Technology Development
University of Texas Health Science Center at San Antonio	University–Industry Cooperative Research Center
University of Texas at Austin	Center for Technology Development and Transfer
Texas A&M University Texas Engineering Experiment Station	Technology Business Development Division

SOURCE: Texas Healthcare and Bioscience Institute.

Texas biotech companies benefit from proximity to educational institutions through research and technology transfer.

panies for commercial development.

Table 4 lists Texas institutions and their technology transfer organizations. BCM Technologies, Baylor University's technology transfer organization, has a portfolio of spinoffs including three of Texas' 12 publicly traded biotech companies. The University of Texas at San Antonio is responsible for another. Privately held Introgen Therapeutics acquired its core technologies through licensing agreements with the University of Texas M.D. Anderson Cancer Center. Technology developed by the University of North Texas Health Science Center and the University of Texas Southwestern Medical Center enabled the recent launching of ManTex Biotech, funded by Canadian incubator Genesys Venture. Of Texas biotech companies surveyed by the Texas Healthcare and Bioscience Institute, 55 percent say university ties create or help growth and 34 percent report research agreements with Texas universities.[10]

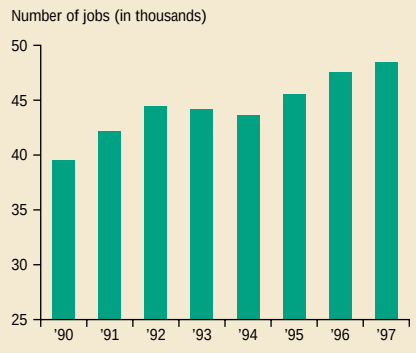
Biotech's Potential for Growth in Texas

Texas is home to some exciting biotech developments, but as an industry, biotech is still very small. For biotech to gain prominence in the Texas economy, the budding biotech clusters must grow. Clusters develop spontaneously in the right business environment, often in the presence of complementary industries. Biotech clusters grow when surrounded by the right resources; knowledge, specialized labor and capital enable companies to expand and new ventures to form. Government and institutions cannot force biotech clusters to grow, but they can remove barriers to growth.

Complementarities with Existing Industries. Biotech complements Texas' growing health care technology industry, which employed 49,000 people in 1997 (*Chart 2*). The Texas health care technology industry includes research laboratories, pharmaceutical manufacturers, and medical device and equipment manufacturers. At an annual industry employment growth rate of 3 percent from 1990 to 1997, Texas is above the national industry average of 1.7 percent.[11]

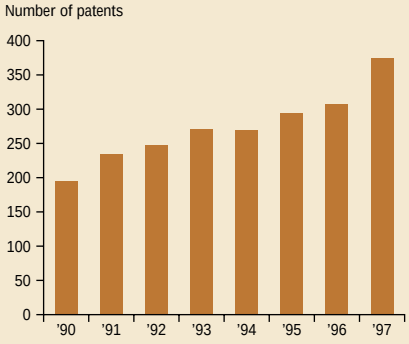
Knowledge. Biotech demands a stock of innovations, and Texas institutions supply a substantial number. The state's patent activity in health care technology suggests Texas innovations initiate in-state product development. The number of health care technology patents issued to Texas residents increased from 195 in 1990 to 375 in 1997 (*Chart 3*). Texas health care technology patents cite Texas research at nearly 3.5 times the expected rate, while California patents cite California research at 1.6

Chart 2
Texas Health Care Technology Employment



SOURCE: Texas Healthcare and Bioscience Institute.

Chart 3
Health Care Technology Patents Issued to Texas Residents



SOURCE: Texas Healthcare and Bioscience Institute.

times the expected rate.[12] Texas' health care patent activity reveals the state as an important source of university research that results in Texas patents.

Labor. Biotech requires a highly specialized labor force, and although regions can attract workers from elsewhere, a local trained workforce is important. Signs that Texas is developing its own biotech labor force include more life science graduates and new academic programs. Between 1989 and 1995, the number of life science degrees awarded in Texas increased 56 percent, from 11,306 to 17,645 (*Chart 4*). Austin Community College recently became one of six regional biotechnology centers funded by the National Science Foundation as part of Bio-Link. Like the regional centers at colleges in Madison, Wis., Portsmouth, N.H., Seattle, Baltimore and San Diego and the national center in San Francisco, Austin Community College will begin a biotech certification program in the fall of 1999, offering both one-year certification and two-year associate's degree programs.

Capital. As biotech companies across the nation feel a capital crunch, Texas companies are combining forces to attract investor attention. Texas biotech and medical/health-related companies received $80 million in venture capital in 1997—2.7 percent of the U.S. total—recovering from a drop to $11 million in 1995 (*Chart 5*).[13] In March 1999, San Mateo, Calif., biotech communications firm Russell-Welsh organized the Second Annual Texas Biomedical Investment Conference in Houston. And in May, the First Texas Life Sciences Stocks Forum was held, also in Houston.

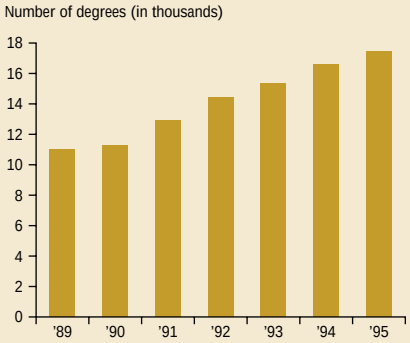
Institutional Support. Texas biotech receives support not only from its educational institutions, but also from other public and private institutions. The Texas Healthcare and Bioscience Institute is a two-year-old private consortium of biotech, medical device and pharmaceutical companies, universities and private research institutions. The institute tracks an index of the Texas health care technology industry and coordinates statewide industry initiatives and educational seminars. Cities like Houston, Fort Worth and Dallas are developing technology business incubators to address the unique needs of emerging biotech firms.

Conclusion

Although Texas biotech is still small, biotech clusters in metropolitan areas appear to be emerging in an improving business environment. Biotech complements the state's growing health care technology industry. The knowledge, labor and capital biotech needs to grow are being cultivated in Texas. Support is also developing from educational institutions, local governments and industry organizations. Whether biotech will grow clusters in Texas comparable to those in California and Massachusetts is impossible to predict, but the necessary conditions for growth are increasingly evident. Texas is a source of biotech innovations and already has a noticeable biotech presence. The biotech bonanza, whether a mother lode or just another strike, indeed has prospects for Texas.

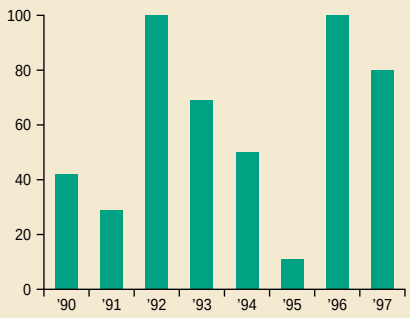
—Meredith M. Walker

Chart 4
Life Science Degrees Awarded by Texas Institutions



SOURCE: Texas Healthcare and Bioscience Institute.

Chart 5
Venture Capital Investment in Texas Biotechnology and Medical/Health-Related Companies



SOURCE: Texas Healthcare and Bioscience Institute.

Notes

Many thanks to Lori Taylor for constructive comments.

1 Michael Gruber, "Map the Genome, Hack the Genome," *Wired*, October 1997, p. 154.

2 Scott Morrison and Glen Giovannetti, "Biotech 99: Bridging the Gap," *Ernst & Young's 13th Biotechnology Industry Annual Report*, p. 4.

3 Ibid., p. 65.

4 Ibid., p. 10.

5 Steve Weinstein, "Biotech: The Third Wave," *Progressive Grocer*, April 1999, p. 22.

6 Larry Fisher, "Money Walks," *Forbes ASAP*, May 31, 1999, p. 77.

7 Biotechnology Industry Organization, *The 1998–99 BIO Editors' and Reporters' Guide to Biotechnology*, www.bio.org.

8 Larry Fisher, "Money Walks," *Forbes ASAP*, May 31, 1999, p. 77.

9 Michael Porter, "Clusters and the New Economics of Competition," *Harvard Business Review*, November/December 1998, p. 78.

10 Texas Healthcare & Bioscience Institute, *A Profile of Progress: The Texas Healthcare Technology Industry*, Spring 1998.

11 Texas Healthcare & Bioscience Institute, *Index of the 1998 Texas Healthcare Technology Industry*, p. 3.

12 Ibid., p. 12.

13 Ibid., p. 21.