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banking on biotech

The industry has made major breakthroughs, but the best is yet to come

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BIO BIOTECHNOLOGY INDUSTRY ORGANIZATION

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Industry champion: As president of the Biotechnology Industry Organization, Carl B. Feldbaum has given biotech companies a strong voice in Washington.

Biotechnology drugs, vaccines, and diagnostics today benefit more than 350 million people worldwide and are part of the medical mainstream. They are used to treat emergencies such as heart attacks, and to slow the progression of diseases such as cancer, rheumatoid arthritis, and multiple sclerosis.

This year marks several milestones for the biotechnology industry. The double-helix structure of DNA, which we now take as much for granted as the structure of our solar system, was discovered 50 years ago in 1953. Recombinant DNA, the biotech industry's foundation technology, was invented 30 years ago in 1973.

Another anniversary takes place June 21–25 in Washington, D.C., as the Biotechnology Industry Organization (BIO) celebrates its first 10 years. Since 1993, BIO has grown from a fledgling outfit in a manner and scale that mirrors the almost geometric growth of the industry we represent.

Over BIO's first decade, our industry's impact on health care and the economy has soared. We've gone from 22 medicines and vaccines on the market to 155, and from a public biotech market capitalization of $39 billion to more than $200 billion, impressive even at today's depressed values. The U.S. biotech industry has also created tens of thousands of new jobs since BIO's inception.

The business of biotechnology is to provide the next generation of new therapies and cures for unmet medical needs. Our industry has made dramatic progress in a relatively short time, but it has only just begun. Driven by revolutionary advances in genomics, the best is yet to come.

–Carl B. Feldbaum, President
Biotechnology Industry Organization (BIO)

LAST MONTH, SUSAN FROSHAUER, an entrepreneurial CEO with a Ph.D. in microbiology and molecular genetics, made a significant breakthrough on the dollars-and-cents front—she convinced a group of savvy venture capitalists to invest $64 million in Rib-X Pharmaceuticals, a two-year-old biotech company that is working on a new group of antibiotics designed to fight pneumonia, tuberculosis, malaria, and other infections that are no longer fazed by today's line up of drugs.

Since investors have developed a bad case of risk aversion when it comes to anything remotely resembling biotech, this was a newsworthy accomplishment. But if its R&D efforts are successful, Rib-X will make even bigger news one day when it introduces a new class of drugs that stamp out antibiotic-resistant illnesses for good.

"My real pleasure is bringing scientists together to create new medicines," says Dr. Froshauer, a Harvard graduate who did her post doctoral research at Yale. "At Rib-X we assembled what I like to call a Noah's Ark of people and

disciplines—pharmaceutical drug hunters, crystallographers, biochemists, geneticists, computational and medicinal chemists, and ribosomologists."

This last group is the center of attention. Rib-X's new antibiotics are designed to shut down the ribosome, a fundamental part of the genetic machinery in all organisms. The ribosome takes instructions from genes and translates them into proteins that guide cellular functions. Because Froshauer's scientists understand the ribosome's atomic structure, they can computer-design a unique chemical compound that disables it in bacteria, kills the infection, and makes resistance futile.

"We have a very focused mission," Dr. Froshauer says. "You have to be respectful of investors' money. And you have to deliver on your goals." Although Rib-X is at least a year away from human testing, and it may be another six to ten years before Dr. Froshauer's gets pills into the hands of patients, these are the kind of words investors like to hear.

Nothing Short of Spectacular

William Rutter, an inventor of the hepatitis B vaccine and a cofounder of Chiron, one of the world's most successful biotech companies, is convinced the future of the biotech industry is nothing short of spectacular. He bases his enthusiasm on the leadership being provided by people like Dr. Froshauer and on the new therapies the genomics revelations of the past few years are making possible.

Dr. Rutter is one of the pioneers who started the biotech revolution. During the past 25 years, Dr. Rutter says, the industry deserves high marks for scientific innovation, but the former university professor isn't as generous when it comes to grading product development and business acumen. "On the technology side," he says, "the industry deserves an A and on the product and business side, a low B to C."

The grades, however, are improving, thanks to a combination of technological advances and more mature management. "In the beginning," he says, "there was overly aggressive development of products. There was also a naiveté, so the failure rate of products was higher than it should have been. But there has been a gradual development of sophistication in the industry in the past ten to 15 years."

Dr. Rutter was chairman of the biochemistry and biophysics department at the University of California at San Francisco before he co-founded Chiron in 1981. Five years later, in 1986, he and his colleagues successfully invented the world's first genetically engineered vaccine for hepatitis B. They went on to produce another vaccine for pertussis (whooping cough) and begin development of vaccines for HIV and hepatitis C.

Dr. Rutter has some advice for today's biotech CEOs. "Look for collaborations or mergers to decrease costs and increase effectiveness," he says. "Any move to boost capital and further development of products brings significant value to a company. Any indication of weakness will bring a severe reaction from investors." For his achievements, Dr. Rutter will receive the Heritage Award at the Biotechnology Industry Organization's BIO 2003 International Convention and Exhibition this month in Washington, D.C.

Leading the Way

As the biotech sector rallies back from the bear market of the past three years, several of the industry's pioneering enterprises founded in the late 1970s and 1980s are leading the way. Amgen is the world's largest biotech company, and Genentech was the first

biotech company. Both have achieved rival status with traditional pharmaceutical companies and are innovation leaders.

Amgen, founded in 1980, attained its status as the world's biggest biotech company on the strength of two drugs that have annual sales in excess of $1 billion: Epogen, a red blood cell booster for anemia, and Neupogen, a white blood cell booster for reducing the risk of infections in cancer patients undergoing chemotherapy. Last year Amgen purchased the third-largest biotech company, Immunex, acquiring another billion-dollar medicine, Enbrel, for rheumatoid arthritis. Only three pharmaceutical companies sell more blockbuster drugs than Amgen.

Genentech was co-founded by one of two scientists who in the mid-1970s invented recombinant-DNA technology—the science of genetic engineering that kick-started the biotechnology industry and made possible products like Dr. Rutter's hepatitis B vaccine. Genentech's achievements include completion of the first initial public offering in 1980, the 1982 development of the first recombinant biotech protein drug, insulin, for diabetes, and development of the first monoclonal antibody for cancer in 1997.

Therapeutic Scalpel

Biotechnology's promise lies in this power for innovation. Take the case of Alnylam, which is trying to harness one of the human body's own mechanisms, RNA interference (RNAi), as a therapeutic scalpel. RNAi is dispatched naturally by the human genome to cut down viruses, which it does by intercepting genetic instructions in the form of messenger RNA. It also can be made to destroy instructions from human genes whose proteins are linked to diseases such as cancer, arthritis, and obesity.

"RNAi represents the broadest new class of biologics since therapeutic proteins and monoclonal antibodies," says Alnylam CEO John Maraganore. "But there's still a lot to do to make a drug. It will take two to three years before we will begin clinical testing and it could take another six years to get the drug approved."

Dr. Maraganore, a Ph.D. in biochemistry and molecular biology from the University of Chicago, is one of the new generation of entrepreneurial scientists who inspires confidence in the biotech industry's future. He left the university for a stint at UpJohn, then joined Biogen, where he invented a drug for use as a blood anticoagulant. The medicine, in the last stage of human testing before market approval, failed to meet full efficacy requirements, and Biogen scrapped the drug.

"I was disappointed when it didn't work in Phase III," he recalls. "It showed efficacy, but it was not good enough." Biogen sold the drug to another company, which continued development and won market approval. It is now considered among the most effective anticoagulants used in angioplasty procedures. The experience will help Dr. Maraganore in his role as CEO. "I learned what it takes to make a drug," he says.

"Introducing early marketing strategies and clearly defining clinical development requirements are critical."

Global Momentum Building

In about three decades, biotech companies have brought more than 150 first-of-a-kind drugs, vaccines, and diagnostics to market for some of the most life-threatening illnesses, including heart disease, cancer, Alzheimer's disease, diabetes, multiple sclerosis, AIDS, and hepatitis. Hundreds more medicines are in the later stages of clinical development and many will reach patients within the next five years, which suggests the best is yet to come.

Not surprisingly, the U.S., where biotech was born, dominates the global biotech industry. The U.S. accounts for more than 70% of the revenues and R&D spending, and about 75% of the employees.

But biotechnology development is expanding rapidly worldwide, in Canada, Europe, Australia, and Asia. The European biotech industry, primarily located in Germany, the U.K., France, Sweden, and Switzerland, is the second biggest in terms of revenues, R&D spending, and employees.

The world's pharmaceutical companies are increasingly looking to biotechnology for innovation. They are, in many ways, becoming biotech companies themselves, integrating genomics into their research and development efforts and forging relationships with university researchers to take advantage of the latest advanced technology.

Switzerland-based Novartis, for example, one of the world's largest pharmaceutical companies, has recently shifted its R&D headquarters to Cambridge to be near the city's extensive university biomedical community. In May 2001, Novartis won market approval of Gleevec for chronic myeloid leukemia. It is one of the first cancer medicines developed through rational drug design, based on a genetic understanding of how some cancer cells work. The drug targets a specific component of cells, created by a genetic abnormality that causes their growth to become cancerous. In 2002, Gleevec also was approved for gastrointestinal stromal tumors. Its effectiveness against both a blood cancer and a solid-tumor cancer may indicate it has broad applications in other forms of cancer.

Banking on Biotech

Governments, another key driver of biotech expansion, are banking on biotechnology as the next big economic-development opportunity. Japan, Singapore, China, India, and Malaysia are pouring billions into programs to support basic research, stimulate formation of biotech startups, and attract Western R&D and manufacturing operations.

In the U.S., the National Institutes of Health budget has doubled over the past five years to $23 billion for basic research. More than 40 states have aggressive biotech-development programs to help startup companies commercialize the fruits of that research. Of the more than 200 new biotech drugs in late-stage clinical development in the U.S., as many as 50% could reach the market over the next several years, creating a sharply escalating demand for manufacturing.

Puerto Rico, a pharmaceutical manufacturing center for more than 30 years, has a head start on many U.S. states for this business. Sixteen of the top 20 bestselling drugs in the U.S. are manufactured in Puerto Rico. The island's government has targeted biotechnology as a key development area for research and manufacturing. Companies are attracted to Puerto Rico by the island's skilled workforce, economic incentives offered by the government, and lower operational costs.

Applications Beyond Medicine

Biotech involves more than medicine. The technology is a major force for innovation in agriculture, industrial production, and environmental management. In 2002, total acres planted worldwide in biotech crops increased 12% to 145 million acres. The U.S., Argentina, Canada, and China lead the world in applying this technology.

Some six million farmers in 16 countries now plant biotech crops that are grown from transgenic seeds. This means genes from other organisms have been spliced into the plants' genomes to achieve desired traits, such as protection against destructive pests or tolerance for herbicides. In many instances, transgenic crops allow farmers to reduce applications of chemical pesticides and herbicides, lower costs of production, and increase crop yields.

Soybeans, corn, cotton, and canola account for most of the transgenic crops planted globally. Although the application of biotechnology to agriculture has generated controversy, proponents are confident their critics eventually will recognize the benefits far outweigh any risks.

On the forefront of utilizing biotechnology to increase the quality, quantity, and safety of the global food supply is DuPont. The company's wholly owned subsidiary Pioneer Hi-Bred International is the world's leading seed company, with more than 200 hybrids that help growers get the maximum yield. DuPont also is using genetics-based technology to identify bacteria and pathogens with better than 99% accuracy and fast results and is making inroads in other areas such as new fibers from renewable resources like corn.

The expansion of biotechnology to the industrial production of chemicals, textiles, pulp and paper, and plastics has been called the science's third wave. Industrial production traditionally has relied on petroleum, a nonrenewable resource that generates pollution and solid waste, for material and energy. Biotechnology substitutes biomass (agricultural refuse) for petroleum, creating cleaner production processes and in most cases generating less waste.

A good example would be making plastic fibers from corn stalks instead of petroleum. The plastic material is used in clothes, packaging, upholstery, and bedding. In addition to reducing reliance on oil, the green plastic is biodegradable.

In environmental management, biotechnology enlists microbes to gobble up hazardous wastes, reducing the need for incineration and huge dumping sites. A fungus, for example, can clean up a noxious substance discharged in making paper. Other naturally occurring microscopic bugs can turn dangerous polychlorobiphenyls (PCBs) into harmless compounds.

Biotechnology also is being used to diagnose environmental problems and assess normal environmental conditions. Monoclonal antibodies can detect harmful organic pollutants in the soil, while antibody-based biosensors are being studied as a way of finding explosives at old munitions sites. These methods are cheaper and faster than traditional laboratory detection procedures that require large and expensive instruments. The biotech approach also is portable. Rather than gathering soil samples and sending them to a laboratory, the level of contamination is measured on-site and results are available immediately.

April 2003 marked the 50th anniversary of the discovery of the double-helix structure of DNA, which holds the instructions for life in each organism's genome. The discovery launched the modern era of biology. Another milestone this April was the completion of the map of the sequence of human genes on the double helix. Knowing where genes are located within the genome will accelerate the pace of discovering how they work. Although these anticipated revelations will take years to unfold, the enormous promise they hold for improving human health and quality of life is why the first 100 years of this new millennium have been dubbed the biotech century.

—**Charles Craig**