Business & Industry

A suburban San Francisco warehouse is where a new major industry is dawning—in the laboratories and offices of Genentech, the foremost of America's firms devoted exclusively to genetic engineering. And it is only fitting that such a company epitomizes a new way of doing business. Everyone shares the glory of company efforts, and no doubt will bask in the considerable financial rewards the genetic revolution is likely to bring. Like all revolutions, it has its visionary: Robert Swanson, a founder and the chief executive officer of Genentech, who realized first that now is the time to put aside the fears of DNA research. He believes that results are too important—not just for his company, but for mankind as well.

Robert A. Swanson, Chief Genetic Officer

He masterminded good science into big business

THE OFFICES OF GENENTECH INC., AMERICA'S premier biotechnology company, are in a constant state of expansion. A manufacturer of addressograph machines closes next door, and Genentech takes over the space. A cavernous warehouse becomes two floors of lawyers' offices crowding next to laboratories, salespeople working side by side with technicians. In one lab, a notice tacked to a bulletin board announces the impending visit of the king of Sweden. A sign warns: DO NOT PIPETTE BY MOUTH! Bright-orange letters on a locked door identify a room as P2, meaning that the work inside is a low-level biohazard.

The most prominent posters, however, are less threatening; taped to cubicle walls, they announce this Friday's Ho-Ho, the company's weekly beer bash. Bob Swanson, who wore a grass skirt to the Hawaiian Ho-Ho and a bumblebee outfit to the Halloween Ho-Ho, will probably wear a tie this time (unlike the scientists, who never wear ties). Friday's party is special, a celebration of the company's eighth anniversary. And Robert A. Swanson, this short, chunky, chipmunk-cheeked thirty-six-year-old, is not only Genentech's president, not merely the father of bioindustry. In an era when our "methodological promise," as sociologist Daniel Bell wrote in *The Coming of Post-Industrial Society*, "is the management of organized complexity," Swanson is the inventor of postindustrial management.

These are heady and volatile days in the world of biotechnology, the industry founded upon the technique of gene splicing. Only a decade removed from the basic scientific discovery that theoretically allowed for the commercial exploitation of genetic manipulation, products have begun to come to market. Aspartame, the artificial sweetener that has revolutionized the soft-drink industry, is made with phenylalanine, a genetically engineered amino acid. Newborn calves are being inoculated against scours, a deadly intestinal disease, with a vaccine developed in a Minnesota recombinant lab. More than $2.5 billion has been invested in biotech start-ups, and the Congressional Office of Technology Assessment estimates that by the end of the century the products created by virtue

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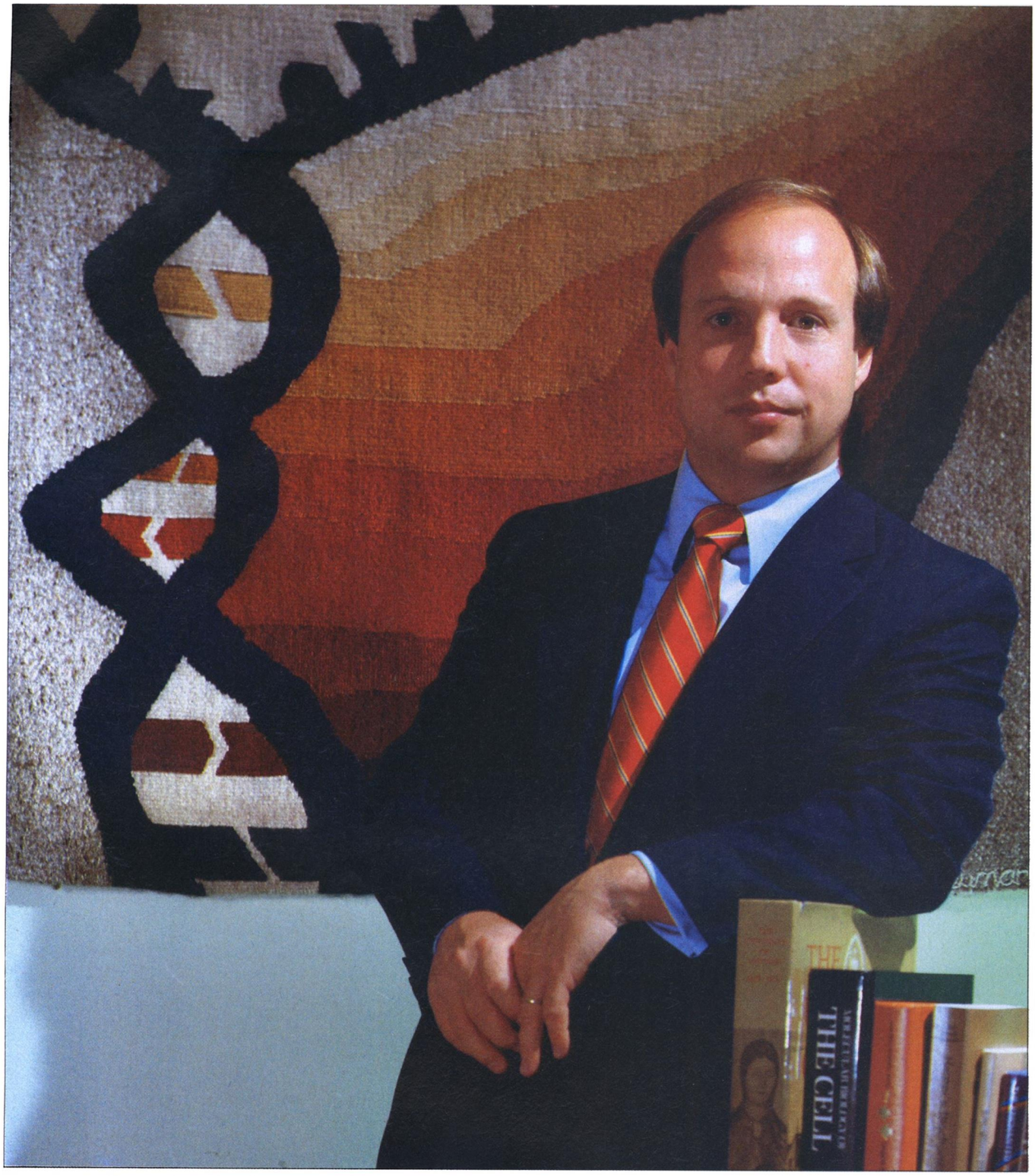
by Randall Rothenberg



PHOTOGRAPH • GEORGE HURRELL

Genentech's Robert A. Swanson before a tapestry of the molecule that started it all: eight years ago he decided to challenge God at his own game. Swanson had finally met his match.

of recombinant DNA will account for $15 billion a year in sales, the equivalent of the entire pharmaceutical industry's U.S. sales today.

Biotechnology's bridging of the gap from infant to industry is well represented by Genentech, the firm that started it all. Eight years ago Genentech was only the dream of Robert Swanson, a twenty-eight-year-old venture capitalist. In 1980 the company went public. Experts predicted Genentech's stock could trade as high as fifty dollars a share. When it peaked at eighty-nine dollars and closed at $71.25, Swanson was the first boy millionaire of biotech. Today the South San Francisco company is the most successful by far of the last decade's heralded biotechnology start-ups. Not only has Genentech weathered the general decline that has beset the rest of the industry, but 1984 will be its sixth straight profitable year. Genentech's first product, synthetic human insulin—the first genetically engineered ethical drug approved for distribution by the FDA—is on the market, licensed to pharmaceutical giant Eli Lilly and Company. Two other important drugs, tissue-type plasminogen activator, which can dissolve blood clots in heart attack victims, and human growth hormone, which may have uses beyond the curing of pituitary dwarfism, are in the final stages of clinical trials. Genentech, says Janice LeCocq, a biotech analyst at Montgomery Securities, is "the Hertz of the business."

But Genentech's importance goes beyond its products. In form and substance, it has been a model of the future. In fact, the tsunami of change wrought upon society by the advance of technology is best illustrated by the structural, economic, and ethical issues surrounding the commercialization of biotechnology. In each area Robert Swanson, "this untried, thoughtful person," in the words of a friend, was a pioneer. "There's no question about it," says the president of a competing firm. "He's the most significant figure in the industry.... The industry has got to be grateful to Swanson. He was the first one to identify and act upon the fact that basic science in molecular biology had progressed to the point where it could become a business.

"The rewards—money, prestige—the maximum, go to people like him," concludes the rival. "Swanson took the maximum risk."

THE THEORETICAL KNOWLEDGE AT THE center of biotechnology dates to 1866, when Austrian monk Gregor Mendel published research based on observations he had made while raising peas. Mendel theorized that single units he called genes might be the basic stuff of heredity. An American zoologist, Thomas Hunt Morgan, conducting experiments with fruit flies at Columbia University, took Mendel's work a step further, concluding that genes, these individual transmitters of heredity, are arranged in lines on chromosomes, the strands found in the nuclei of living cells. In 1944 Oswald Avery determined that genes are actually molecules of deoxyribonucleic acid, or DNA, and that DNA alone is the reason for, the foundation of, heredity, the inheriting of specific traits.

The 1953 discovery by James Watson and Francis Crick of the structure of DNA—the famed double helix—paved the way for the future processing of genetic information. The order of the rungs of a DNA molecule, a spiral ladder about ten atoms wide, actually determines the shape of life. These steps up the double helix comprise pairs of four nucleotide bases: thymine, adenine, guanine, and cytosine, usually represented by their initials, the DNA alphabet. The sequence of these letters *is* the genetic code. Genes are nothing more than long nucleotide chains. In the two decades after Watson and Crick's discovery, a series of epiphanies advanced the science of genetics to a critical point. The ability to "sequence" DNA—to determine the exact order of the nucleotides in a gene—was obviously one discovery. Another was the discovery of restriction enzymes, chemicals that can cut a strand of DNA at exact and predictable points along the chain. In 1973 Stanley N. Cohen of Stanford University and Herbert W. Boyer of the University of California, San Francisco, reported an event that antibiotech activist Jeremy Rifkin says "rivaled the importance of the discovery of fire itself." They took DNA strands from two different living organisms and glued them together, creating a bit of life that had never existed, and under "natural" circumstances never would exist, on earth. It was now possible to synthesize life.

The Cohen-Boyer discovery created a controversy that impinged upon, and threatened to halt entirely, further research with recombinant DNA. Fears that new life forms created in university laboratories might escape and indelibly contaminate the human race embroiled college towns on both coasts.

The scientists themselves created the crisis. Concerned that their work might lead to health or social problems, and aware of the criticism that had descended upon the scientific community for its "amorality" in helping to develop atomic weapons, the scientists took it upon themselves to police their work. The situation was confused. "Practically 99 percent of the scientists involved with the discussion at the time felt it was a very safe technology," recalls Herbert Boyer. But the fearmongering of a few and the susceptibility of others to a heightened sense of public responsibility held sway. "Having just come out of Vietnam and Watergate," says Boyer, "I think there was an attitude that one should try to bring everything into a public forum."

The scientists did—at the Asilomar Conference Center in Pacific Grove, California, where in February 1975, after listening to impassioned pleas from their brethren and philosophical meanderings from assorted legal scholars, molecular biologists from across the globe decided to regulate their own research. But instead of quenching the public's fears, the scientists' decision ignited them. The nation's press went wild with stories about the harmful potential of a technology that inspired fear even among its creators. These ruminations in turn lighted a fire under environmental groups, still laboring under the antitechnology fantasies developed in the late 1960s. All of a sudden biologists—not physicists or chemists, who had been subjects of past public ire—were the targets.

"There were just some wild things going on," recalls Boyer, the scientist whose work lay behind the controversy. "You have to learn—at least *I* had to learn—to deal with a lot of criticism.... But it's hard to take when you've led this sheltered life, and you have this image of yourself, and you feel you're doing something good and meaningful, and all of a sudden somebody tells you you're a warped scientist trying to destroy the world because you want to make money."

BOB SWANSON WAS NOT content with the idea of hiring *good* scientists. "'Get the best'—his famous words," says a scientist. "'Get the best! And get there before anybody else.'"

For Boyer, a large man with long curly hair and a hip sensibility, who considered himself then, as today, fairly liberal, the nadir was reached the autumn after Asilomar, when the *Berkeley Barb,* in its special Halloween edition, listed him among the ten biggest bogeymen in the Bay Area.

Then came Robert Swanson's telephone call. Boyer heard only the words "Well, there might be some money involved." At the time, his lab was struggling with its budget; there was not enough money to support the research, and the funding for a couple of postdoctoral assistants was running dry. "I was intrigued that there might be some money available through some agency or some source to help my lab." Herb Boyer offered Robert Swanson ten minutes on a Friday afternoon.

LEAVING THE UNIVERSITY was a wrenching experience for many of Swanson's scientists. They'd stepped off the Olympus of pure science just to make a buck.

Swanson had always been an impatient man. When he'd finished all the work toward his undergraduate degree in chemical engineering at MIT in three years rather than the usual four, he'd petitioned the school's administration to allow him into the Sloan School of Management to begin his graduate studies as a senior. Chemistry, he had decided, was too isolating; fiddling around in labs for a fourth year seemed unappealing. Swanson wanted to work with people.

Management of groups had long fascinated Swanson, and in business school he concentrated on organizational development. One of the things that had most impressed him at MIT was how the university's elders had managed the student unrest of the late 1960s. At one point an Army deserter had found his way to the MIT student center, and a large group of undergraduates kept a round-the-clock vigil there to protect him from the police. But the vigil was interfering with a spring dance planned for the facility. The school asked the protesters not to abandon their efforts but to move to another protected venue. "They worked to manage it, rather than bring in the storm troopers, the way others would," remembers Swanson. "MIT was a good place, where people were encouraged to go their own way."

In his last year at the Sloan School Swanson took the sole course offered on venture capital and found the subject exciting. Immediately upon graduating in 1970 he accepted a job at Citibank, which was one of the few organizations willing to take young people into venture capital. He made enough of a mark to be given the task of opening Citicorp Venture Capital Ltd.'s San Francisco office. After four years he was invited to become, at twenty-six, the youngest partner in Kleiner & Perkins, a successful and rapidly growing venture partnership. Kleiner & Perkins was dedicated to discovering high-tech entrepreneurs with high-growth potential and guiding them through every phase of the business cycle. Like the other partners, Swanson had a technical background; founder Eugene Kleiner had worked with Nobel laureate William Shockley in the early days of Silicon Valley, and Tom Perkins, who would become Swanson's mentor, was another MIT grad. However, unlike his colleagues, Swanson had no hands-on management experience; he had never been anything *but* a venture capitalist.

Yet something was gnawing at Swanson. "He was around venture capital, but I think he was very frustrated by venture capital," says Brook Byers, a fellow venture capitalist who shared an apartment with Swanson and who has himself since become a partner at what is now Kleiner Perkins Caufield & Byers. Swanson would frequently say that venture capital made him feel like a coach on the sidelines, when his real desire was to be on the playing field. Swanson claims, "There wasn't a frustration so much as a feeling of—I saw so many good ideas. I built up more confidence in my ability to make good decisions. It came down to a matter of 'If you're so smart, why aren't you doing it yourself?'" "Bob," explains an industry analyst who knew him during his venture days, "was looking for the ultimate."

Swanson had been following the Emeryville-based Cetus, the first of the decade's big biotech start-ups (1971). Cetus had lost money almost from the start. "They're not doing it right," Swanson announced at his office one day. He stopped, then mused, "What does 'doing it right' mean?" He took it upon himself to answer his own question.

Swanson went to local university libraries and, using his chemistry background, began reading technical monographs on the infant science of bioengineering. He compiled lists of the authors and started calling the scientists one by one for their opinions on commercializing gene splicing. Each call would elicit more technical information, but invariably the end response would be "It's a marvelous technology, but commercialization is many years off at the least." The major pharmaceutical companies agreed with the academics.

Swanson disagreed. Cetus was just going about things *the wrong way,* he reasoned. It was trying to employ the new technology merely to improve processes at client companies. It was not product-oriented. For a biotech company to be successful it would have to create products and bring them to the market. Swanson determined to accomplish just that goal. "The idea of building something is so important to me," says Swanson, explaining his motivation. "Creating something where there wasn't anything before—that's what really gets me excited."

There was more to Swanson's inspiration. Had he simply wanted to transmute himself from coach to player, he could have done so on any number of fields. Yet he chose biotechnology—untested, untried, unknown. A fascination with science, with *using* science, drove him. Bob Swanson's desire to succeed as a professional gene splicer is representative of his generation's infatuation with technology and with the belief that science and success are synonymous. Swanson, it might be said, is fulfilling his generational destiny. "What got me into science," he says today, sitting in his shockingly tiny corner office at Genentech's South San Francisco complex, "was Sputnik. A lot of people I know fit into that same category. There was a national interest in science and technology and competitiveness that got a lot of young people excited about that field. I think we ought to be able to do the same thing today, get that excitement going." He pauses, and then blurts out, "Because it works! *I'm evidence of the fact that it can work.*"

Swanson's ten-minute audience with Herb Boyer lasted several hours. Until he met him, Swanson didn't realize that Boyer was one of the two people most intimately responsible for making gene splicing a reality. For his part, Boyer found Swanson articulate and able to explain coherently what it was he wanted to do. "Do *you* think," Swanson asked the professor, "this technology can be commercialized?" "Yes," replied Boyer. Swanson was elated. "Oh, God," he thought, "at last a kindred soul! Here's somebody, after all these

people, who agrees with *me*." They fed each other's excitement and repaired to a local saloon. Many beers later each had agreed to put up $500 to form a partnership to exploit recombinant DNA technology.

With Kleiner & Perkins's skeptical blessing (but without any initial financial help), Swanson rented a small office on Sansome Street. Working closely with Herb Boyer, he developed the business plan for the company he hoped to found. The scientist drafted proposals for the technical end of the operation, and the venture capitalist wrote out marketing schemes; they revised and merged their work as they went along. The scheme that resulted was a classic. "You take two naive people and put them in a room," says Boyer, "they just boost each other over the bar."

TAKING HIS "COACH TO player" metaphor to an extreme, Swanson promoted the company's effort to make synthetic human insulin as a competition and called himself the quarterback.

Their strategy violated several implicit rules of high-tech entrepreneurship, as promulgated in Silicon Valley during the 1970s. Instead of raising millions of dollars through an offering to plow into huge expenditures for plant and equipment, and instead of going on a hiring binge, Swanson and Boyer, acting on Tom Perkins's advice, contracted out their early research to university labs. And rather than attempt immediately to bring a product to market (which was, after all, the goal), they opted simply to demonstrate that the technology would actually work—that through genetic engineering a microorganism could be made to produce a substance that it ordinarily does not make. In the original experiments by Boyer and Stanley Cohen, an artificially created gene had simply been replicated—cloned. Now they were trying not only to create and clone a gene in a laboratory, but also to place it inside bacteria and cause the bacteria in turn to manufacture a useful protein. This had never before been accomplished. This certification of the technology, the principals believed, would generate the excitement and money necessary to finance a continuing operation.

In April 1976 Boyer and Swanson dissolved their $1,000 partnership and incorporated their enterprise. What to name it? Swanson claims his suggestion was Her-Bob, which the biologist rejected. Boyer immediately offered an abbreviation for "genetic engineering technology"—Genentech. Without employees of its own, without facilities, without anything but a name and a promising technology, Genentech was going to produce somatostatin.

Somatostatin is a hormone found in the brain. It has no market to speak of, but Genentech chose it as its first product because Boyer felt sure it could be synthesized. Its structure is simple (the somatostatin chain consists of only fourteen amino acids) and well understood; several tests showed its existence in a molecular "soup." The laboratories at City of Hope National Medical Center in Duarte and at Cal Tech, as well as Boyer's own at UCSF, were well equipped to handle the contract work necessary to produce somatostatin. They would synthesize the DNA fragments at City of Hope and ship them up to UCSF, where they would recombine the DNA, insert it inside *Escherichia coli* bacteria (*E. coli* is a fast-reproducing bacterium found in the human intestine), and grow the resulting cells, then send the soup back to City of Hope for the assays to detect the somatostatin. Boyer termed this "the one-two-three approach."

Despite the gravity of the operation, Genentech still had a seat-of-the-pants feel to it. When Tom Kiley, now the company's vice-president for corporate affairs but at the time a partner in one of Los Angeles's most prestigious law firms and Genentech's outside counsel, would journey to San Francisco to discuss company business, he would stay not at a swank hotel but on the couch in Swanson's apartment. For entertainment they would play Ping-Pong on the table Swanson kept in his dining room. (Usually Swanson had his bicycle stashed under the Ping-Pong table.) Swanson also traveled frequently during this period, commuting on a regular basis for six months between the San Francisco and Los Angeles laboratories and, so sure was he that their little demonstration would work, arranging financing for Genentech's postsomatostatin life. Which, on the day they finally hooked up the soup to the scintillation counter to perform the radio-immuno assay, looked like it would be very brief indeed. For instead of finding little molecules of the hormone somatostatin floating around in the vials, Bob Swanson, Herb Boyer, and their contractors found, in the words of one of the scientists, "zip; zero."

"Here I saw my whole career and everything else pass before my eyes," recalls Swanson. "Because here was everything that people said, in theory, should work *years* in the future, okay? We had done it in seven months from start to finish. So the time scale was very compressed. And when we hooked it up the way it was supposed to work, well, it didn't." They had tried to cheat God of his sole command of life and—they thought—lost the match.

"I mean," says Swanson, "I was *worried* then."

Their fear was to be short-lived. Because somatostatin is such a tiny protein, it is vulnerable to attack inside its bacterial host. The scientists theorized that it was being chopped down by another protein harbored by the *E. coli*. They tried to reorder the sequence of amino acids inside the bacteria, essentially inducing the DNA to encase the somatostatin inside a larger polypeptide, one immune to the bacteria's munch mechanism. They performed another assay. "And that was the exciting moment," says Roberto Crea, an Italian chemist who worked on the project at City of Hope, "when we found that by playing this genetic trick of protection, there was really that thing in the soup!"

The business plan, which had remained remarkably stable during this first year, now turned on several factors. If Genentech was to be a successful product-oriented company, it must adopt a focused strategy. Swanson told people he wanted to start the first full-scale, lab-to-market pharmaceutical company in more than twenty years. This meant carefully targeting Genentech's first products.

Early in his partnership with Boyer, Swanson had set down on paper the criteria for the as yet undetermined first marketable product. "A very logical progression," Swanson recalls. "Things like, I felt the first product should have an existing market—as a first product you really couldn't afford to have what they call a 'missionary' marketing effort. And the economics of production would have to compare favorably to the way it is produced currently. It would also have to have a high value for low volume, so that you'd have a lower cost for plant and equipment." The choice was natural; after doing all sorts of calculations, Swanson decided on Genentech's first salable product: genetically engineered, synthetic human insulin. With the decision made, the most crucial task facing him was recruiting—and managing—scientists to carry it out.

RECRUITING MOLECULAR BIOLOGISTS proved to be a special difficulty. Unlike their colleagues in the scientific community, biologists had been left undisturbed by the outside world. "The physicists had been making bombs for the government. The computer scientists were getting money from the computer companies. Chemists had been consulting for pharmaceutical companies since World War II," says Gabriel Schmergel, president of Genetics Institute, a biotech firm in Boston, Massachusetts. "These biologists were sitting in their labs and nobody paid any attention to them."

The view toward industry from inside the university was jaundiced to begin with, to say the least. Not many first-class research papers had emanated from industrial labs. Publishing papers is the single most potent force driving credit-hungry biologists; publishing is the essence of, in their words, doing good science. Because there was so little publishing in industry, it had the reputation of attracting second-rate scientists. Says Herb Boyer: "When you'd attend scientific meetings and there were people from industry here, they weren't always presenting the most exciting research." Adds David Goeddel, now Genentech's chief scientist: "Either all the turkeys went into industry and the good scientists stayed in academics, or industry did not allow publication on something that was likely to be commercial. The effect was the same—to keep good scientists out."

Bob Swanson was not even content with the idea of hiring *good* scientists. He wanted the best. "'Get the best'—his famous words," says Roberto Crea. "'Get the best! We can get the best! And get there before anybody else.'" Swanson's pleasure reading was heavily weighted toward books on dynastic founders; a biography of the Rockefeller family was prominently in his possession at this time. One friend says Swanson was influenced by his reading of Machiavelli and looked upon "the best young scientists" as the latter-day equivalent of the top-notch courtiers a successful prince once needed; in his own mind, Swanson was, of course, the prince. "Surrounding yourself with the best people is critical," he maintains. "The companies that have failed, coming off venture capital, are the companies that didn't have the best people in key areas." Dave Goeddel, who joined Genentech when it had but four employees, recalls Swanson asserting, "We need expertise in *everything*. Molecular biologists first, but we gotta get the protein chemists, we gotta get manufacturing people, fermentation experts ..."

Swanson understood that pharmaceutical companies had hindered their scientists' attempts to write articles for fear that publication would jeopardize patent applications. Genentech would enable its recruits to do good science by adopting

an intensely aggressive patents strategy, filing applications as early as possible and allowing publication immediately thereafter. Other scientists were attracted by Swanson's claims that at Genentech they would have all their scientific needs supplied. "This is a science-driven company," he asserted time and again. "Don't worry about money. Anything you need, you've got."

The management plan matched the promise of the recruitment strategy. Herb Boyer helped to convince Swanson that profit participation, "giving these very creative and essential people a chance to share in the rewards of the risk taking," would be a key to the company's growth. The sense of community was an intoxicant to the scientists, most of whom were accustomed to the rough-hewn, competitive individualism of university labs. Swanson's reason for taking the human-capital approach to management can serve as an apt epigraph for this whole new era of postindustrial economics. "The logic that drives good scientists," he says, "can also drive good business."

There was more to managing good science than merely recruiting good scientists and sharing the impending wealth with them. From the beginning Swanson had to maintain an extremely difficult balance between the science and business sides of his company. Scientists emerge from a tradition where there are few constraints, other than funding, in pursuing their interests. Because biotechnology firms are indeed science-driven, scientific goals naturally tend to overwhelm the business goals. Swanson is credited, by competitors like Genetics Institute's Gabriel Schmergel, with striking "a near-perfect balance" between the two poles of science and business.

To keep morale high during the race to synthesize human insulin, Swanson was forced to act the big brother to many of his scientists. Leaving the university setting was a wrenching experience for many of them. They were vilified as mercenaries and treated as contaminated property. They had stepped off the Olympus of pure science, where people toil only for glory, just to make a buck. Herb Boyer, it's been said, may have jeopardized his chance for a Nobel Prize by going commercial, even though Boyer *rejected* the opportunity to come to Genentech full time, preferring to serve on the board and remain ensconced at UCSF. Venture capitalist Brook Byers terms the reaction toward the scientists who left the university as "analogous to the heat Bob Dylan took when he went electric." It fell to Swanson, who was younger than many of his recruits, to soothe their fears.

Swanson managed to turn the anti-industry sentiment to Genentech's advantage. Taking his "coach-to-player" metaphor to an extreme, he promoted the company's effort to manufacture synthetic human insulin as a competition and called himself the quarterback. There was a university group in Canada, sponsored by Cetus, that had a budget giving it three to five years to synthesize the gene to produce insulin. The task was formidable. The insulin gene was several orders of magnitude more complex than the somatostatin gene. Two DNA chains needed to be created and glued together, a total of twenty-nine building blocks, each DNA fragment itself consisting of twelve to twenty individual units that had to be recombined with enzymes. While proud of their work on somatostatin, the scientists were well aware of the criticism that followed: the "Yeah, so what" attitude, the complaints that any *useful* products of genetic engineering were still years in the future, the assertions that the chemistry was not yet good enough to take on a protein as large as insulin.

Swanson used the naysaying as a recruitment tool. Dave Goeddel signed on with Genentech simply to do insulin. "Clone insulin, and *we got it made*!" Swanson would tell his charges. Night and day they toiled, seven days a week, to design the two chains. Swanson came to the labs every day. "He was more a cheerleader than a mentor," says Robert J. Kunze of Hambrecht & Quist's venture-capital department, who worked closely with Swanson on Genentech's later public offering.

Doing insulin first was also integral to Swanson's business strategy. Immediately after the somatostatin synthesis, Swanson informed Eli Lilly, the $3-billion pharmaceutical giant, of the insulin plan. Lilly had begun marketing insulin in 1923, and by 1979 it held 85 percent of the American insulin market. Swanson had no intention of competing against Lilly; it would have been futile, perhaps suicidal, to challenge its advanced sales and marketing staff.

But Swanson knew that the mere existence of synthetic human insulin would seem a threat to the giant. Would Lilly be interested in purchasing an exclusive *license* to Genentech's forthcoming invention? asked the cocky gene splicer. Perhaps, replied the skeptical but worried drug manufacturer. Lilly signed a letter of intent and began funding the research.

Genentech synthesized the insulin gene's A chain, then the B chain. Throughout, Swanson continued negotiating with Lilly over the eventual disposition of insulin. Then, in the early summer of 1978, the final breakthrough occurred—the recombination of the two chains and the expression of the insulin gene. No announcement was made; Lilly still wanted to haggle. On a Friday in August, fearing he could keep the lid on his excited scientists no longer, Swanson told Lilly that the announcement of the cloning of human insulin would be made the following Monday in Los Angeles. Lilly, Swanson added, had a choice: continue to negotiate or be a part of the announcement. The pressure tactic worked. Lilly's own small corporate jet was already booked. Two senior executives immediately flew the company's large corporate airliner from Indianapolis to L.A. On Monday Genentech announced the cloning of insulin and Eli Lilly's exclusive license to the product.

INSULIN TURNED GENENTECH INTO A company. But for the scientists, it was something of an anticlimax. Once the two DNA chains were synthesized, they had little doubt that the gene could be expressed—that is, that it could be induced to manufacture insulin. For them, as well as for Bob Swanson, the true turning point came a year later, in the form of human growth hormone. That involved the most sophisticated technology of all—making a protein in its native form inside the *E. coli* bacteria without any "protective" protein attached. All future products—interferon being the most prominent and promising—would depend on Genentech's success in cloning human growth hormone. And if all went according to plan, growth hormone, which in its natural state must be procured from human cadavers, would be the first product Genentech would market itself, under its own label. In August, with the insulin announcement, financing was secured and work began in earnest.

As with insulin, the project went smoothly—too smoothly, perhaps, which worried the scientists. They synthesized the gene, placed it inside the *E. coli*, grew the bacteria. The day arrived for the first test. They placed the soup inside the scintillation counter, which measures radioactivity like a Geiger counter. The scientists, who had been working all night to prepare for this first test (it was now close to 10 A.M.), were expectant but not hopeful. "Nothing ever works the first time," says Dave Goeddel. A technician working for Goeddel took the readout sheet off the machine in an adjacent room. As she walked back to the lab she tried to remain calm, but her reserve abandoned her. All the blanks and controls were down low, but there on the graph was one huge spike. The technician broke into a wide grin. "Looks pretty good!" Human growth hormone—on the first try. The lab—Swanson was there, too—erupted into cheers. "It was then the scientists said, 'We can have a successful company,'" says Goeddel. "That's when I was convinced that we could do a lot here, and when the others in the lab realized that we had unlimited potential. Not just potential, but it was really gonna be realized." Swanson left to buy champagne for an afternoon celebration. He returned to find the laboratory empty; his exhausted celebrants had gone home to go to sleep. ●

ROBERT A. SWANSON, CHIEF GENETIC OFFICER

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