Chiron Buys Cetus: A Tale of Two Companies

Chiron rose as Cetus fell. Why? The key lies in different strategies for bringing cutting-edge research to market.

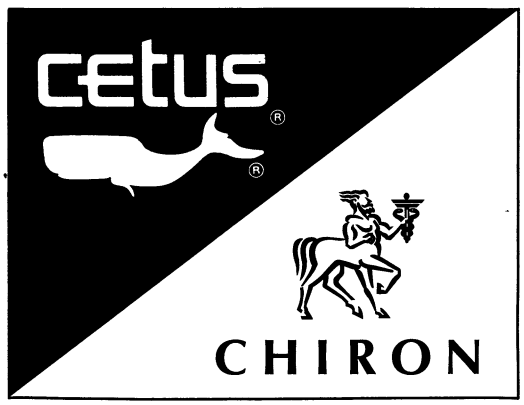
WHEN WILLIAM J. RUTTER RENTED LAB SPACE a decade ago from biotech pioneer Cetus Corp. to start up Chiron, his own small biotech company, he never dreamed that one day he would buy out his landlord. But last week, Rutter announced that his by now moderate-sized firm would buy the large but ailing Cetus in a stock transaction valued at more than $600 million. It was a merger that surprised many industry analysts, reminding one of the "little fish eating the big fish." And the analysts were mixed in their reviews of the merged company. Some thought Chiron might get indigestion from trying to swallow too big a meal; others thought it would do well. But what everyone agreed on was that the story behind the headlines was a fable of two ventures: how a superstar of the early years of biotech went into a tailspin in recent years, while the upstart prospered.

The moral of the tale seems to lie in the strategies each company used to get its research to market. Chiron had a savvy management team with a nose for good science in key areas with commercial potential. They translated that science into a balanced array of key products. Cetus had good science, too, but its officers were unable to capitalize on it. Cetus' big commercial success was the polymerase chain reaction (PCR), introduced in 1985. But long before it was clear how promising PCR would be, Cetus' managers bet the company on interleukin 2 (IL-2), which they hoped would revolutionize the treatment of a deadly liver cancer—and they lost their wager when IL-2 was rejected by the Food and Drug Administration (FDA) last year.

To appreciate how management succeeded at Chiron and failed at Cetus, you have to go back a few years. In 1981, when Cetus completed the largest public offering ever of biotechnology stock, raising $108 million, the future looked rosy. Not only was the company a favorite of Wall Street investors because of its outstanding scientists and wide-ranging research, it had IL-2, considered among the most promising drugs in development at the time, and it would soon have PCR as well. "Cetus was riding high," recalls Steve Burrill, a partner at Ernst & Young who was involved with the merger.

Soon, however, Wall Street started to push for faster returns from biotech, and Cetus was not immune. Management's response was to consolidate projects and focus on one area—developing a few anticancer drugs. As part of that move, in late 1982 the company recruited Robert Fildes as its new chief executive officer. And today it is Fildes, long departed from the company, who correctly or incorrectly takes the heat from the armchair quarterbacks. "You can't separate the Cetus story from Bob Fildes," says Burrill.

On the face of it, Fildes was the perfect choice to lead Cetus into the big leagues. He had an impressive track record in biotech at Biogen and in the drug firms Glaxo Inc. and Bristol-Meyers. Today, Fildes unabashedly admits to pursuing a strategy others denounce: championing IL-2 at the cost, say his critics, of lines of research that might have saved the company. Says Jeffrey Price, former senior vice president of R&D at Cetus, who left last year to start his own neurobiology firm: "Fildes took a chance and moved prematurely (to seek FDA approval for IL-2)."



But at the time, Fildes' game plan looked golden—especially when it landed Cetus on the cover of *Fortune* in 1985 for its planned "Assault on Cancer." Indeed, Cetus was high on IL-2 for substantive reasons: In 1985 early clinical trials showed that the treatment might limit the growth of many cancers. For 8 years, Fildes remained wedded to IL-2—so much so that he was willing to trade away some of the company's options to ensure that IL-2 would be successful. For example, in early 1989, he made a cross-licensing agreement with pharmaceutical giant Hoffmann-La Roche Ltd. of Switzerland that allowed Cetus to continue to pursue IL-2 research without threat of a lawsuit from the larger firm, which also was working on the drug. At the same time, Cetus signed an agreement giving the Swiss company a piece of PCR—exclusive rights to develop in vitro human diagnostic products using the technique.

As if that weren't dangerous enough to future corporate coffers, Cetus management then concentrated on building an expensive manufacturing facility and an international sales force that would be in place to market IL-2 as soon as it won U.S. approval (following its launch in Europe, where it has had respectable sales).

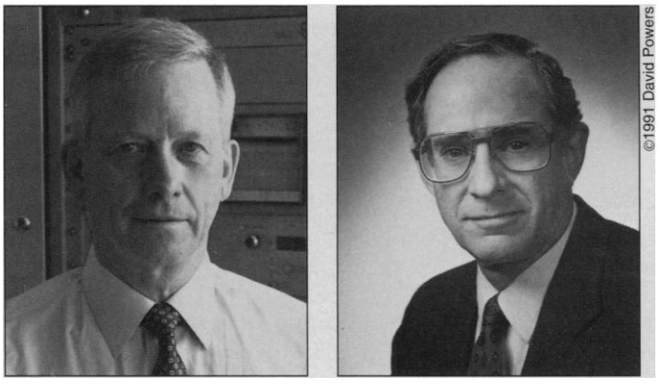
With all of Cetus' eggs neatly gathered in a single basket, the FDA stepped in and pushed the basket off the table. Today, insiders say Fildes should have waited until the clinical data were stronger before he asked the FDA to approve IL-2. True or not, the results were a disaster. "Cetus had a home-run strategy, with everything placed on IL-2 and oncology therapeutics," says Joseph Lacob, a San Francisco venture capitalist who was marketing manager for IL-2 at Cetus until 1987. "When your home run turns out to be a foul ball, you have a problem."

Lacob understates the extent of the problem. Cetus' stock fell from $22 to $6 a share. Fildes left. Cetus co-founder Ron Cape stepped in and took over management of Cetus, overseeing cuts that reduced the staff from a high of 980 to 870. The firm was about $60 million in the red for the fiscal year ending in June 1990, PCR netted only $6 million, and Cape had no hope of raising money from Wall Street. That's when Cape went looking for a partner and found Chiron.

If the stories told about Cetus consist mostly of second-guessing, the ones about Chiron have a different flavor. "What have they done right?" asks Richard Godown, president of the Industrial Biotechnology Association. "It comes down to leadership, science, and luck." Chiron's leadership team includes Rutter, chairman of the department of biochemistry at the University of California at San Francisco for 13 years, and his former postdoc, Edward Penhoet. In the minds of many analysts, they get credit for inspired research: After many other medical research teams failed, Chiron scientists discovered the hepatitis C virus, and developed a diagnostic test that is now used throughout the world to screen blood and diagnose the disease.

But Cetus had excellent research, too, and Chiron's success would seem to hinge even

more on a market focus that included several products from the start: recombinant vaccines and drugs for treating infectious diseases. When Chiron started in 1981, vaccines had fallen out of favor for industry startups. But the Chiron team recognized that recombinant vaccines mimicking the structure of infectious agents had untapped potential. That work has lead to profitable products, including the first recombinant vaccine for hepatitis B, and a recombinant human insulin. It has also prompted a half-dozen joint ventures, including one with CIBA-GEIGY of Switzerland to develop vaccines for herpes, AIDS, hepatitis C, malaria, and cytomegalovirus.



Wins and losses. *Bill Rutter of Chiron* (left); *Ron Cape of Cetus.*

Not that it has all been smooth sailing: Chiron has had its failures, such as a dismal bid to enter a partnership with Connaught BioSciences Ltd., Canada's premier biotech firm, and disappointing clinical trials on super oxide dismutase (to repair free oxygen radical damage after heart attacks) and epidermal growth factor. But the company survived because it had a balanced business strategy—it didn't put so much emphasis on one flagship drug, and it built up a research machine that pumped out a steady stream of potential products. That strategy has paid off handsomely: By last year, Chiron became one of the first biotech firms to turn a profit for its investors—$6.8 million in earnings on revenues of $78.5 million.

So it would seem that the moral of the tale is that balance is better than a tight focus, and Monday-morning quarterbacks fault Cetus for not taking that route. But Robert Fildes is impatient with what he calls "20/20 hindsight." He argues heatedly that when he arrived at Cetus, there was only one product besides IL-2 worth backing (and it was developed in a joint venture). Moreover, Fildes points out that in biotech most winners have succeeded by focusing on one major product and bringing it to market as quickly as possible. In support of his argument, he points to Amgen's big push on EPO, Biogen's on interferon, and Genentech's on TPA.

The difference between Cetus and those winning ventures, he insists, is that "some companies got dealt different cards than others from their research. No one knew in the early '80s what any of these products would do." Furthermore, he argues that if Cetus had ridden out the storm, IL-2 would have paid off. "I personally don't see why they had to turn around and sell the company," says Fildes. "It's like being in a marathon, and throwing it in on the 23rd mile."

Insiders won't give Fildes this way out, though. Even if the IL-2 gambit had succeeded, some say, Cetus would have had problems. Researchers say that in order to feed his pet project—making and selling IL-2—he cut investment on research. In the resulting climate, Cetus hemorrhaged its top scientific staff: Since 1987 the company has lost its directors of research, development, clinical trials, regulatory affairs, and molecular biology.

Meanwhile, Chiron's success allowed it to step forward as Cetus faltered and snap up its larger competitor. What Chiron gets out of the new combination is a manufacturing facility and sales force it lacked, as well as $300 million in cash from the sale of PCR rights for human diagnostics to Hoffmann-La Roche. (The PCR division of Cetus will move to Roche Diagnostics in Alameda, California, where the dissemination of PCR should be similar to what it was in recent years.) Chiron is also acquiring a newly trimmed scientific and development staff from Cetus, whose research into oncology drugs complements Chiron's work to boost the immune system.

While Cetus co-founder Cape says he's saddened to see his firm come to an end, he's pleased about the fact that the new company could become what he calls a "blockbuster" of biotech. Analysts agree. "You put the R&D management of Chiron with the science of Cetus, and all that cash, and it's clear this combined company is going to be a substantial player in the industry," says Lacob. ■ ANN GIBBONS

Kennedy Resigns From Stanford

Concerned at the extent to which he has become a symbol of academic extravagance at taxpayer expense, Stanford University president Donald Kennedy announced last Monday that he will resign next August. "It is very difficult for a person identified with a problem to be the spokesman for its solution," he wrote to the university's board of trustees. Kennedy's departure is steeped in irony: One of his major achievements in his 10-year tenure was in raising private funds, yet he has been brought down by a scandal over the accounting of federal money intended to reimburse the university for the indirect costs of its research.

By announcing his departure a year in advance, Kennedy has given the university time to mount a nationwide search for a successor. In addition, he wrote, the coming year will give him an opportunity to begin "the difficult work of repair" to Stanford's reputation.

That work apparently began last week, when Stanford revealed a series of accounting reforms designed to avoid the kind of embarrassing errors and improper billing that drew the attention of Representative John Dingell (D–MI) and his investigators earlier this year. Although the changes may go some way toward appeasing Stanford's critics on the Hill, a 5-member panel of luminaries established to advise Kennedy on the university's indirect cost mess has argued that they go too far.

The most significant changes will involve a system for setting aside "unallowable" costs as they are incurred, rather than permitting them to flow into accounts charged to the federal government as indirect costs. The university also intends to flag specific departmental accounts with large numbers of unallowable costs for special scrutiny, establish a code of ethics, and write a series of comprehensive manuals to educate its employees. In addition, Stanford has asked Arthur Andersen & Co, the accounting firm that recommended these changes, to conduct an audit of the university's overhead accounts from 1983 to the present—years for which Stanford and the federal government have yet to agree on Stanford's indirect cost charges.

The university's special advisory panel, whose members include Carnegie Institution president Maxine Singer and former Georgetown University president Timothy Healy, was less than enthusiastic about these steps, complaining to the board of trustees that the new system could lead to an "excessive focus" on accounting details and may be "far too expensive for the value sought." Kennedy, meanwhile, wrote the board that he plans to take a sabbatical and then return as a faculty member to pursue environmental studies. ■ DAVID P. HAMILTON