Chapter 4

Traditional Theories of Property and Profit

Case Study

New Protocol: How Drug's Rebirth as Treatment for Cancer Fueled Price Rises

GEETA ANAND

WARREN, N.J. — When Celgene Corp. got its first drug approved, it priced a 50-milligram capsule at $6. Today, it sells the same white capsule for nearly five times the original price, or $29.

Little has changed to affect the cost of making the drug since it was first sold in 1998 as a treatment for leprosy and severe weight loss, or wasting, caused by AIDS. But today, it is primarily prescribed for **cancer,** a disease whose patients and advocacy groups have shown little interest in fighting for lower U.S. prices.

"When we launched it, it was going to be an AIDS-wasting drug," says Celgene's chief executive, John Jackson. "We couldn't charge more or there would have been demonstrations outside the company."

Celgene's drug is thalidomide, which earned world-wide notoriety in the 1960s for causing birth defects. The story of its reincarnation as an AIDS and cancer treatment shows how the political environment and drug companies' perception of what the market will bear drive decisions on drug prices in the U.S. For some serious diseases such as cancer, the sky is virtually the limit — although it may not stay that way.

The ability to price medicines ever higher has helped fund the pharmaceutical industry's research and development programs, which bring new medicines to patients. It also fills the coffers of some companies and their executives. Meanwhile employers, insurers, and sometimes patients must pay the tab.

"New Protocol: How Drug's Rebirth as Treatment for Cancer Fueled Price Rises" by Geeta Anand, *The Wall Street Journal*, Eastern Edition, November 15, 2004, p. *A1* (Copyright (c) 2004, Dow Jones & Company, Inc.). Reprinted with permission of Dow Jones & Company, Inc. in the format textbook via Copyright Clearance Center.

"For patients, the side effect of taking this drug is penury," says Raymond Comenzo, a hematologist at Memorial Sloan-Kettering Cancer Center in New York City.

Thalidomide is inexpensive to make. Fundacao Ezequiel Dias, a government laboratory in Brazil, sells 100-milligram capsules to the Brazilian government health system for seven cents. The pills are given to leprosy and cancer patients free of charge. A Netherlands pharmacy sells the same dose for about $2.60.

Celgene began as the biotechnology department inside a big chemical firm, Celanese Corp., in the late 1970s. In 1987, after Celanese merged with another company, it decided to spin off the biotechnology division. The new company, named Celgene, at first focused on using biological processes to make industrial chemicals. But in the early 1990s it decided to move into pharmaceuticals because the old focus was "a lousy business," says Sol J. Barer, a founder of Celgene who is now chief operating officer. "Chemicals are priced on the cost of ingredients," he says, while pharmaceuticals are "priced on value."

In the 1990s, Dr. Barer, a chemist, was wandering the halls of Rockefeller University in Manhattan in search of products when he bumped into a scientist who was studying why thalidomide helped treat leprosy. She theorized that the drug acted to inhibit a protein associated with inflammatory diseases from asthma to rheumatoid arthritis.

Dr. Barer grew excited about thalidomide's potential but was wary of its history. In the early 1960s, the drug was found to cause horrific birth defects in the babies of mothers who had taken the drug for morning sickness. Most of the babies were born in Europe because the drug was never approved by the U.S. Food and Drug Administration. Some babies had no arms or legs, while others had deformed limbs.

Thalidomide was still being used in poorer countries because it was cheap and effective in treating leprosy and wasting in tuberculosis patients. U.S. AIDS patients were importing thalidomide illegally to treat wasting. Dr. Barer concluded that Celgene could get the FDA to approve thalidomide, despite its notoriety, if the company sought to sell the drug for AIDS.

Celgene began clinical trials to show thalidomide could reduce wasting in AIDS patients but unexpectedly found the amount of AIDS virus in patients' blood seemed to rise temporarily on thalidomide. That meant more testing would be needed. Dr. Barer says he decided on a quicker route: getting the drug approved for treating leprosy, for which substantial data existed in public health databases around the world. Once the drug was on the market for leprosy, doctors could prescribe it for AIDS or any other disease, a practice known as "off label" prescribing.

The company devised a system for dispensing the drug that requires, among other things, regular pregnancy tests for patients of childbearing age. Since thalidomide had been around for decades and the composition couldn't be patented, Celgene would eventually patent this system of controlling distribution.

The FDA faced pressure from AIDS activists who wanted access to thalidomide. In July 1998, the FDA granted Celgene approval to market thalidomide for leprosy under the brand name Thalomid, giving the green light to those who wanted to prescribe the drug off-label for AIDS wasting.

The next challenge was setting the price. Mr. Jackson, a lanky former Marine who had held executive positions at Merck & Co. and American Cyanamid, took over as Celgene's chief executive in 1996. Mr. Jackson and Dr. Barer wanted to avoid antagonizing AIDS activists. "Our pricing people said if you charge more than $3,000 [per year], they'll show up at the door," Mr. Jackson says.

Only after the price had been set at $6 for each 50-milligram capsule did the two men fully realize thalidomide's potential to treat cancer. In 1997, Bart Barlogie, a cancer specialist in Little Rock, Ark., tried thalidomide on an elderly man with multiple myeloma, a cancer of the plasma cells in bone marrow that afflicts 50,000 Americans. Dr. Barlogie was acting on the suggestion of Judah Folkman, a researcher at Children's Hospital Boston who studied substances that can deprive cancer cells of new blood vessels for growth. Dr. Barlogie's patient had a nearly complete remission.

On Dec. 6, 1999, Dr. Barlogie reported the results of a clinical trial: About 30% of 169 patients who had relapsed after other treatments saw levels of a protein associated with myeloma decrease by 50% or more after taking thalidomide.

Thalidomide was reborn as a cancer medicine just as the drug was eclipsed by new AIDS medicines that made wasting virtually a thing of the past in the U.S. Again it was being prescribed off-label since Celgene hadn't received FDA approval to sell the drug for cancer.

Celgene, like many small biotech companies, had lost money every year since its founding. In 1998, it reported a loss of $32 million on revenue of $3.8 million. Now it could begin to tackle those losses. Mr. Jackson says he knew he could charge a lot more for thalidomide as a cancer drug. The question, he says, was whether to double or triple the price immediately or make more gradual increases. He decided on the latter. In 1999, he raised the price by 21% to $7.23 from $6 for the 50-milligram thalidomide capsule. The cost for consumers at pharmacies is typically between 20% and 25% higher than what Celgene charges to drug distributors.

Celgene's revenue soared to $38 million in 1999 and $85 million in 2000. It became a star on the stock market, even though it continued to post losses. In February 2000, Mr. Jackson did a secondary offering, raising $298 million at $101 a share. Mr. Jackson and Dr. Barer, who had dreamed of turning Celgene into a major pharmaceutical company, acquired a San Diego cancer research firm in June 2000 for $200 million in stock.

As the use of thalidomide spread, some cancer doctors noticed that they could get the same results with a lower dose. That was significant because thalidomide can cause a nerve disorder and sleepiness, especially at higher doses. At the end of 2000, the company says it found the average daily dose per patient had fallen by about 25% to 225 milligrams, from 300 milligrams a day per patient at the start of the year. That meant the average patient was spending less per day on thalidomide — $35.70 compared with $43.38 at the start of 1999. Mr. Jackson believed Celgene could raise the price.

Over 2001 and 2002, he did so several times. The medicine remained cheaper than many cancer drugs and Mr. Jackson says he received few, if any, complaints. By the end of 2002, Celgene was selling the 50-milligram capsule for $11.03. "By bringing it up every year, it was heading toward where it should be as a cancer drug," says Mr. Jackson.

It was a time in which "companies just raised the price and somebody paid the bill and nobody objected," says Margaret Tempero, a cancer specialist who is the immediate past president of the American Society of Clinical Oncology.

In December 2002, Mr. Jackson made another acquisition, a New Jersey company that harvested stem cells from human placentas after pregnancy, for $45 million in stock. At the end of 2002, Celgene reported a loss of $100 million on revenue of $136 million, as it continued to significantly boost its research and development spending.

The next year brought another reason for raising the price. A biotechnology firm in Cambridge, Mass., Millennium Pharmaceuticals Inc., brought the drug Velcade to market in May 2003 for multiple myeloma, priced about twice as high as thalidomide. Velcade, delivered in an infusion in the hospital, cost about $4,400 per month for the average patient, compared with around $1,800 per month for a typical thalidomide user.

In June, one month after Velcade came to market, Mr. Jackson raised thalidomide's price by 10% to $15.76 from $14.33. "We felt certainly from a competitive perspective that would be justifiable," he says. By the end of 2003, the 50-milligram capsule of thalidomide cost $22.32. In 2003, thalidomide sales nearly doubled to $244 million. Celgene declared its first profit, of $13.5 million.

Mr. Jackson says the price increase wasn't as rapid as it seems because in 2003 Celgene also introduced 100-milligram and 200-milligram doses of thalidomide and didn't raise the prices of those higher doses as frequently. More than 60% of patients take 200 milligrams per day or more of the drug, according to Celgene. Previously they had to take four 50-milligram pills; now they could take a single 200-milligram pill and save some money.

Each year, as thalidomide revenue grew, Mr. Jackson plowed more money into research and development of new medicines. By 2003, the R&D budget at Celgene had reached $123 million, which amounted to nearly half of the company's revenue of $271 million. Part of the research budget funded three clinical trials of Revlimid, a drug the company believes could be more effective than thalidomide in certain cancers without the potential to cause birth defects.

As revenue grew, the company raised pay for top officers. In 2003, Mr. Jackson earned $1.8 million in salary and bonus, compared with $365,000 in 1998. He says he took a pay cut to take the job in 1996 because of the potential upside, particularly the stock options. By the end of 2003, he held 1.5 million stock options valued at $31 million, according to the company's proxy statement. Other senior executives also received big increases in their salaries, bonuses and options.

Also last year, Celgene raised $400 million in a convertible debt offering. The money helped it buy a Welsh manufacturer of thalidomide for $110 million this year. The company still sits on about $800 million in cash and marketable securities. Celgene's shares, which have split twice since 2000, stood at $30.41 in 4 p.m. Nasdaq Stock Market trading Friday, giving the company a market capitalization of about $5 billion.

In theory a generic-drug company could sell thalidomide in the U.S., since the patent on the drug's composition expired long ago. However, it would need to get the FDA's approval for a distribution system to keep the drug out of the hands of pregnant women. Such a system would be difficult

to devise without violating Celgene's five patents on its own system. And the FDA might hesitate to approve an alternative system because Celgene's system has worked well to prevent birth defects from thalidomide. Celgene says no other company has attempted to bring thalidomide to market in the U.S.

Celgene is seeking FDA approval to market thalidomide for multiple myeloma; currently, since the drug is only approved for leprosy, Celgene sales representatives aren't allowed to directly promote it for other uses.

This year, Mr. Jackson has raised the price of the 50-milligram capsule twice, by a total of 32%, to take it to $29.44 from $22.32. The current price of the 200-milligram capsule is $75.60, or about 36% cheaper than the 50-milligram capsule on a per-milligram basis. Patients who take 200 milligrams a day are now paying about three times as much as they did in 1998, while those with a 50-milligram daily dose are paying nearly five times as much.

Still, Mr. Jackson says a month of thalidomide for a typical patient costs only about 60% as much as a month of Velcade, meaning there's room for more price increases. He says if he brought his drug to market today he'd sell it for the same price as Velcade. In fact, he told investors during a recent presentation at an industry conference to expect Celgene's next product, Revlimid, to be priced at twice the cost of thalidomide "unless the political environment changes."

Some on Wall Street believe such a change is looming. Oncologists have begun to complain that prices are out of hand. And the Centers for Medicare and Medicaid Services, the federal agency that covers health-care costs for seniors and the indigent, has proposed cutting federal reimbursements for the infused biotechnology medicines covered at present. Analyst Eric Schmidt at SG Cowen & Co. says he expects the federal agency to exert more pressure on drug prices when it begins covering most prescription medicines for seniors in January 2006.

Mr. Jackson argues the high prices don't hurt patients. "Either people are wealthy enough to pay or health insurance pays or our company gives the medicine away for free," he says. Don Baylor, the New York Mets' hitting coach last season, takes thalidomide to treat his multiple myeloma and says in an interview the cost of the drug is covered under Major League Baseball's health-insurance plan.

But other patients bear much of the cost themselves. Mary Lou Wright, a retired insurance agent in Harrisonburg, Va., says she has paid a portion of the cost of thalidomide under her insurance plan, although she has enough income to make the expense manageable. Until Ms. Wright went off the drug recently, she paid $289 a month for her prescription of 50 milligrams a day. "The price of the drug is outrageous," says Dr. Comenzo, the Sloan-Kettering oncologist who treats Ms. Wright and Mr. Baylor.

Celgene's free drug program, generous by industry standards, helps patients who earn less than $38,000 a year and also have assets of less than $10,000. It doesn't apply to people whose insurance is paying part of the bill. Dr. Comenzo's nurse, Alice Ford, says she sees many patients who struggle to pay for thalidomide and don't qualify for Celgene's free drug program. For that reason, she says, "I discourage the doctor from putting people on it." Velcade, though more expensive, has been covered by Medicare.

The two biggest advocacy groups for multiple myeloma haven't made lower drug prices a priority. "I try to focus on the positive rather than

coming after them on price," says Kathy Giusti, president of the Multiple Myeloma Research Foundation.

Susie Novis, president of the International Myeloma Foundation, says taking on drug companies over pricing is a losing battle. "They won't even discuss it. They say, 'It is what it is,'" she says.

Dr. Comenzo, while praising the advocacy groups' work, accuses them of shying away from the pricing issue because they receive substantial donations from Celgene and Millennium, among other drug companies. Ms. Giusti says drug-company donations don't influence her views on pricing. Ms. Novis says she surveyed her group and found only a minority of U.S. members worried about price. But she may take up the price issue in Europe, where patient groups and doctors have raised an outcry.

Celgene licensed the right to market thalidomide in Europe to Pharmion Corp. of Boulder, Colo. Pharmion sells the drug under a program for making lifesaving medicines available before they've been officially approved by regulators. A patient in Europe on a daily dose of 100 milligrams would pay about $30 a day to get thalidomide from Pharmion.

Pieter Sonneveld, a hematologist at the University of Rotterdam in the Netherlands, says his patients complained so much about Pharmion's price that he helped set up a pharmacy to make thalidomide and sell it at cost in the Netherlands through hospital pharmacies. It costs about $2.60 for 100 milligrams, he says. However, if Pharmion gets marketing approval from European regulators it would have exclusive rights to sell the drug for multiple myeloma, making it more difficult for low-cost alternatives such as Dr. Sonneveld's to survive.

Case Study

Plasma International

T. W. ZIMMERER • P. L. PRESTON

The Sunday headline in the Tampa, Florida, newspaper read:

Blood Sales Result in Exorbitant Profits for Local Firm

The story went on to relate how the Plasma International Company, headquartered in Tampa, Florida, purchased blood in underdeveloped countries for as little a 90 cents a pint and resold the blood to hospitals in the United States and South America. A recent disaster in Nicaragua produced

"Plasma International," case prepared by T. W. Zimmerer and P. L. Preston, reprinted from *Business and Society: Cases and Text*, ed. by Robert D. Hay, Edmund R. Gray, and James E. Gates (Cincinnati: South-Western Publishing Co., 1976). Reprinted with permission of the authors.