Uncertain Miracle

A Biotech Drug Extends a Life, But at What Price?

For Ms. Lees, Treatment Bill Now Totals $7 Million; Her Bones Keep Crumbling

Guilt of Another $1,400 Day

By Geeta Anand

For 25 years, Carol Lees thought she would die early.

In the summer after her freshman year in college, she was diagnosed with Gaucher disease, a disorder that swells internal organs and weakens bones. There was no treatment for this disease, so rare it affects fewer than 10,000 people in the world.

THE MOST EXPENSIVE DRUGS

Second in a Series

Then in 1991, at age 44, she received a new drug that had been developed for Gaucher. "This is amazing," she told her husband. "I'm going to be given a second chance."

The drug that gave her hope went on to become one of the biotechnology industry's greatest success stories. Yet today, Ms. Lees still struggles to make sense of the unexpected way her life has been shaped by her disease and the medicine. She is grateful the drug has prolonged her life, but she is in constant pain. And her conscience is ill at ease about the price of keeping her alive—$601,000 a year, or about $7 million so far.

"I often look around and ask myself, 'Is this a $1,400 day?' " says Ms. Lees, who scouted projects for Peter Falk and ran Madonna's production company in the course of a career in the movie business. "Many times, I'm not so sure."

Using incentives passed by Congress to encourage the development of medicine for rare diseases, Genzyme Corp., then a tiny company, brought the drug to market 14 years ago. Genzyme proved it was possible to profit on treatments for very rare conditions. Hundreds of companies have since jumped into the business of developing drugs for "orphan" diseases, defined by Congress as those affecting fewer than 200,000 people.

Genzyme enjoys a gross profit margin of more than 90% on the drug called Cerezyme, similar to many other successful medicines in the industry. Genzyme says the revenue from Cerezyme—$840 million last year—allows the company to conduct research and develop treatments for other diseases. (See related article on page A15.)

Carol Lees

Gaucher disease is caused by a missing or defective enzyme. Without that enzyme, healthy bone cells die and fat cells build up in the liver, spleen and other organs, so they don't function properly. Children with the most severe form of the disease die within a few years; adults become steadily more disabled.

For Ms. Lees, the drug—a synthetic version of the enzyme Gaucher patients lack—has eased some symptoms, given her more time with her husband and allowed her more years at work. But today, at age 58, she constantly questions whether she should continue on the treatment. She lives in a kind of netherworld, kept alive by the medicine but needing pain medication around the clock and a series of surgeries to replace her deteriorating joints.

"It's a half-miracle," Ms. Lees says of the medicine. "The enzyme doesn't stop me from continuing to fall apart."

Ms. Lees was diagnosed with Gaucher when she was a 19-year-old studying music composition at the University of Michigan in Ann Arbor. Doctors told her the genetic disorder killed most patients within a decade.

Ms. Lees went back to college and struggled to find meaning in a life she

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now believed would end prematurely. She began to see a psychologist, Richard Stuart, at the university's department of social work. "The big question in my mind was whether to help her accept the inevitable or defeat the inevitable," Dr. Stuart says. He told her she had the "mind of a survivor," and challenged her to find purpose by focusing on her music.

While playing the electric keyboard in a band at a campus cafe, she met Richard Lees, a young playwright, and fell in love. She introduced him to Dr. Stuart, who was impressed with the young man's intelligence and calm. "Marry him," Dr. Stuart recalls saying. "He will save your life."

The two wed, moved to Los Angeles, and started careers. Ms. Lees defied doctors' predictions, living far longer than expected.

Her husband wrote screenplays, while she wrote the score for a movie. She met actor Peter Falk and got a job reading books that might be made into films for him. That led to other production jobs, including a four-year stint in the 1980s running Madonna's movie company, looking for potential projects.

Throughout, Ms. Lees kept her illness a secret. "I didn't want people to pity me," she says. "The disease had taken over my life at home. I was not going to let the disease take away the purity of my work." In Hollywood, she says, it was easy to hide her symptoms by playing the role of an eccentric: She refused to explain why she wouldn't walk even a block or two. She wore flowing clothes to hide her belly, swollen with an enlarged liver, and scarves to conceal her bulging thyroid gland.

Periodically, symptoms would flare—a sudden fever, accompanied by a severe pain in her stomach that spread to her bones. These "bone crises," caused by the death of bone cells, came on without warning and lasted several days.

Certain she didn't have much time in this world, she and her husband talked about taking their own lives, rather than being separated by her death. That inspired Mr. Lees, who is now a money manager, to write a play called "Right of Way," in which an elderly couple agree to kill themselves after learning of the woman's terminal blood disease. In 1983, it was made into an HBO movie, with Bette Davis and James Stewart.

Ms. Lees found herself thinking short-term in the extreme. She bought travel-size toiletries, didn't plan vacations and resisted buying a house. The couple decided not to have children. "It was always me, Richard and Gaucher disease in our marriage. And the disease came first—you had to watch it, respect it, be kind to it."

Her effort to maintain a productive work life constantly clashed with her disease. Dangerously anemic, she kept a record of her blood counts in her Filofax. She broke a bone in her foot walking to the bathroom. A hug from her husband snapped one of her ribs. "I am an eggshell walking on eggshells," she would say.

In the late 1980s, there was hopeful news emerging from the National Institutes of Health: Researchers had isolated the missing enzyme in Gaucher patients. Ms. Lees traveled to the NIH to provide blood samples for research. "She was already terribly ravaged by the disease," says John Barranger, the former NIH physician who examined her.

Genzyme, then a new biotech company, licensed the enzyme from the NIH and conducted a successful clinical trial among 12 children. In April 1991, the U.S. Food and Drug Administration approved the new treatment for Gaucher disease.

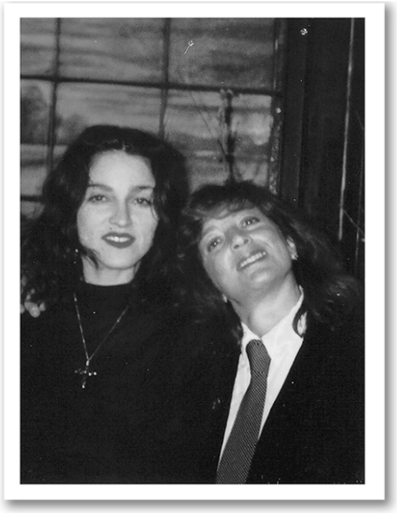
Second Chance

On July 3, her 44th birthday, Ms. Lees received her first intravenous dose at Children's Hospital Los Angeles. On the drive home to their white-washed ranch house in Studio City, she and her husband stopped at a lookout on Mulholland Drive. They stared at the sunset, believing she'd been given a second chance.

The next 2½-hour treatment came two weeks later; others followed at regular two-week intervals. Within a few months, Ms. Lees began to feel more energetic. Her blood counts improved and her liver, once so swollen that she shopped in maternity stores, receded. To celebrate, she bought her first pair of Gap jeans. She could walk unassisted into a restaurant. She planted pansies in the front yard and bougainvillea vines in the back.

But gradually, the medicine's limitations also revealed themselves. Her bones remained painfully fragile. Every month or so, she would curl up in bed on heavy doses of morphine and Vicodin to sweat her way through a bone crisis.

The price of the drug, which is covered by insurance, worried her from the start. "How long are they going to keep paying for this? This is crazy," she recalls telling her husband.



Courtesy Carol Lees

Carol Lees at a **Christmas party with Madonna** *in the '80s, when Ms. Lees ran the star's production company.*

In 1997, the Writer's Guild-Industry Health Fund, through which she and her husband had been covered, wrote with frightening news: The couple owed nearly $550,000 for Ms. Lees's treatment in the early 1990s. The health fund believed Mr. Lees hadn't earned enough as a writer at times to qualify for benefits. Already $100,000 in debt because of Ms. Lees's medical expenses, they took out a second mortgage and hired a lawyer.

The fight made Ms. Lees so anxious she says she needed Valium to get through the days. Eventually, on appeal, the health fund determined Mr. Lees had done sufficient work to qualify for benefits and backed down.

WritersCare, another health-insurance group they had joined, sent a letter saying it was going under because of high costs. Ms. Lees was convinced she had driven the health fund out of business.

"Do I have any right to consume such a large percentage of the health-care dollars in this country?" she asked her husband. "Many people would say I'm being greedy—and they would be right."

"It's not your fault the drug costs so much," Mr. Lees told her.

Relief came when another insurance entity absorbed WritersCare. A few months later, it raised premiums for California members by 22%. Mr. Lees didn't tell his wife about the rate increase. By now, he had stopped showing her any health bills because they made her too upset.

Ms. Lees worked sporadically from her home, helping writers sell screenplays. In 2000, she made a big breakthrough: MGM wanted to make a movie she had been developing for many years. The movie, "Original Sin," starred Angelina Jolie and Antonio Banderas. She got credit as one of the producers and received $240,000, almost enough money to pay off her health and legal debts.

Richard Lees

But sickness still ruled her life. She told the movie cast she was too busy to go to Mexico City for the filming. In reality, she was too afraid to travel away from her doctors. She showed up for a screening in a limousine because she'd just had blood transfusions and wasn't allowed to drive.

In 2003, Ms. Lees's right hip, which had already been replaced once, became so painful she needed to have another operation. Recovery was excruciating because her damaged shoulder joints wouldn't bear her weight when she tried to use a walker. Favoring her hip put pressure on her already damaged vertebrae.

Months later, when she was finally able to walk again, she fell in her closet and shattered a bone in her right arm.

When Ms. Lees came home from arm surgery, she and her husband sat in their kitchen, feeling overwhelmed.

"I don't know if I can keep doing this," she finally said.

"I don't know if I can keep doing this either," he said.

Ms. Lees needed her husband more than ever—to help cook meals, dress her and bathe her. But she found herself saying things to drive him away. "I have to do this. You don't. Why don't you go find someone else healthy?" she said.

Mr. Lees was thankful the drug had given him more years with the woman he loved—but they had been so painful, he sometimes felt resentful as well. "It made me ask, 'What am I here for?' " he says. "What I came back to again and again was that I was put here to take Carol through this world."

Ms. Lees became consumed with whether she was meant to have lived this long: "Did I miss the bus to the next place? Was I supposed to have come back already, as someone else's turtle?"

She remembered Dr. Stuart, the psychologist who had helped her find a reason to live so long ago. They hadn't been in touch in decades. Searching online, she found he was now a professor in the psychiatry department at the University of Washington in Seattle.

"I don't know if you remember me, but I just came across your name on the Internet and thought I'd say hello," she wrote in an email.

Dr. Stuart literally shouted when he saw her note. "Carol—UNBELIEVABLE," he wrote back. He assumed she had died years ago, but still kept a stone she had painted on his desk as a reminder of her. "Your wonderfully surprising message was for me truly a Phoenix risen."

Ms. Lees began to write long emails, some in verse, telling him about the 32 years since they had last talked. She told him of her ambivalence about being saved. "Every day I'm less energetic, less able to pull things together. Little by little it's chopping away at me. I don't like being reduced."

Dr. Stuart told her "an intellectually demanding project is key to your survival—perhaps the equal of the forgotten-to-be-inherited enzyme." He suggested she write about her life, to try to give people insight into the struggle of living after being unexpectedly saved by medicine.

A Reason to Wake Up

Suddenly, Ms. Lees had reason to wake up in the morning. She found herself rushing to her desk, in front of a little "shrine" she had made years earlier with a slide of a Gaucher cell pasted behind a red heart. Before long, a thousand pages, many in verse, had flowed from brain to keyboard to computer to printer.

Hurting, tired, I let the day slip by
Things happened
People came and went
Fed-ex brought my ice cooler of
Enzyme from Memphis
This week's fortune
For tomorrow morning's needle...

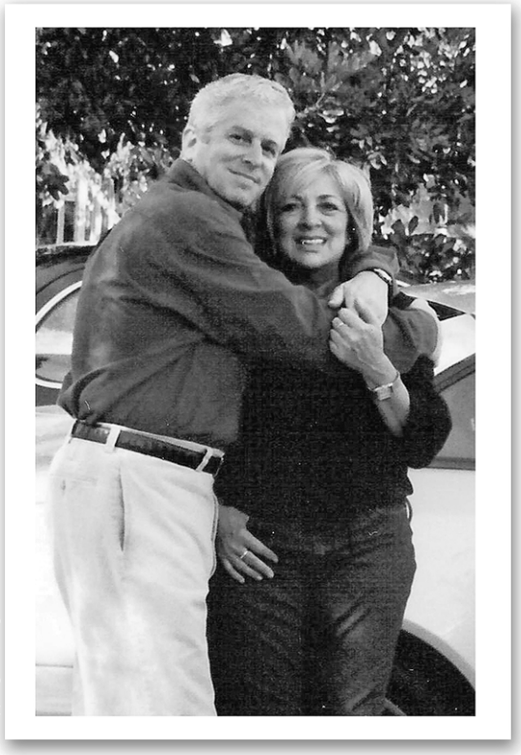
Writing proved cathartic. But it couldn't erase the physical pain of her deteriorating joints.

Maybe, she began to think, the time had come to stop taking her half-miracle drug—and let nature take its course.

Earlier this year, Ms. Lees told her husband she was considering getting off the drug. He fell silent. It wasn't a surprise, he says. It was unbearable for him to imagine life without her, but unbearable to imagine watching her endure another surgery. "Is it the right thing to do, to extend a life?" he asks. "I don't know. We've all implicitly agreed with playing God for profit."

"When do I say enough?" Ms. Lees wrote to Dr. Stuart. "How long can I continue to cling?"

"You're the photo-negative of Terri Schiavo," he responded, referring to the Florida woman whose case recently set off a national debate over end-of-life decisions. "She was a vegetative mind in a healthy body. You have an incredibly vibrant mind in a dead body."



Courtesy Carol Lees

Carol Lees *and her husband, Richard, in front of their house in Studio City, Calif.*

"But I don't want to be someone who's painting with her toes at the end," she said. "That's fine for some people; just not for me."

After months of dwelling on whether to stop taking the Gaucher drug, Ms. Lees began to think about a different route to easing her suffering: taking more of it. Another Gaucher patient, whom she had become friendly with, said she had found relief with an increase over the maximum recommended dose. She had often urged Ms. Lees to consider the idea.

Doubling the Dose

So earlier this year Ms. Lees called her doctor, who runs a treatment center in Beverly Hills for patients with Gaucher disease, to request a doubling of the dose for six months to see if that would restore her energy and reduce her pain.

The doctor, Barry Rosenbloom, had never recommended more than the maximum dose on the drug label for any of his patients. There is no research to prove more enzyme improves a patient's condition, he said. Because of the high price of the drug, he said, it would be challenging to convince an insurer to pay for more. To try to determine if more would help Ms. Lees, he ordered a long list of bone, liver and blood tests.

Ms. Lees hung up the phone and cried. She knew that double the dose would push the price to more than $1 million a year. "I still don't know what makes me so special that I should ask society to spend such an exorbitant amount of money on me," she says.

Still, Ms. Lees went through the tests this summer and fall and now awaits an appointment with Dr. Rosenbloom for his assessment.

Meanwhile, she's had so much joint pain that earlier this month she went back to David Golden, the surgeon at Cedars-Sinai Medical Center in Los Angeles who repaired her broken arm two years ago. He took more X-rays and sat Ms. Lees down to give her the bad news: She would need five joint replacements—on her left hip, both knees and both shoulders.

But because her joints were misshapen by her disease, the surgeries were going to be extremely difficult, he said, "and you really should hold off for as long as you possibly can. You'll know when you can't take it any more."

Last week, when Ms. Lees's left knee hurt so badly she couldn't walk from her bedroom to the kitchen, and neither heat nor cold nor Vicodin would help, she decided the time had come. She would call Dr. Golden the next day.

But in the morning, her knee felt a tiny bit better. "I think I can hold off for one more day," she told her husband. She still doesn't know what she's going to do.

Why Genzyme Can Charge So Much for Cerezyme

Why is the price of Genzyme Corp.'s drug for Gaucher disease $200,000 a year for the average patient?

The reason is simple—Genzyme charges that much today, 14 years after the first version came to market, because it can. There is no competition, patients are desperate and most insurers pay.

Genzyme says it keeps the price high to help it pay for the hunt for other drugs and also to fund programs that allow it to give away a small part of its production.

The company makes a profit of more than 90% on the drug, excluding marketing and corporate costs, but including capital depreciation, according to four current and former employees who were briefed on the numbers.

That means the drug, Cerezyme, costs less than 37 cents to manufacture for each unit sold for $3.70.

Carol Lees's insurer pays $601,000 a year for her treatment, which includes $520,000 for the Cerezyme and about $81,000 for someone to administer it intramates of the current and former employees.

Genzyme is not alone in generating enormous profits on a successful drug. Drug-company analysts say many companies make profits of more than 90% on their biggest-selling medicines. Companies say they use the money to cover the high cost of developing the drug and for research into new medicines.

What makes Genzyme and manufacturers of rare-disease treatments unusual is that their costs—and profits—are spread over a small number of patients. So Ms. Lees and others say they must struggle to keep their insurance coverage, because they can single-handedly drive up the costs of the plans they join to unaffordable levels. Because the drug is a treatment, not a cure, the high costs to insurers continue indefinitely. Genzyme says there are only about 4,500 patients on Cerezyme, the Gaucher medicine.

When Genzyme first brought the drug to market in 1991, it was difficult and expensive to produce, notes Henri Termeer, the search on the drug was done by the National Institutes of Health, and Genzyme spent only about $29.4 million to develop the first version. The company has more than made up this initial expenditure on research and development, reporting $840 million in revenue on the Gaucher drug last year alone.

Mr. Termeer earned a combined salary and bonus of $3 million last year, plus options valued at between $12.6 million and $32 million in 10 years, based on appreciation of the company's stock of between 5% and 10% a year, according to the company's proxy.

Mr. Termeer acknowledges that Genzyme found ways to make the drug more easily and cheaply. In 1994, the company brought to market a new version of the drug that was made in genetically engineered cells. But rather than lower the price, Mr. Termeer said, he has decided to use the extra revenue to give additional Cerezyme away free in countries that can't afford to pay the high price. He said Genzyme gives