

## CHAPTER TEN

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### *The Crisis*

Standing by the floor-to-ceiling sliding window, arms crossed, Henri Termeer looked out over the Boston skyline from his capacious 12th-floor office. It was a sunny Tuesday afternoon, June 16, 2009. The news had hit the tape, its impact softened by a well-crafted press release that framed the day's news as a "temporary interruption." A viral infection of a bioreactor in its flagship cell culture facility in Allston had forced Genzyme to stop production. The plant needed to be disinfected. The FDA was informed and concurred with the company's decision.

From a distance, the concern seemed minimal. The company's share price hardly budged. Life went on, just another speed bump. Henri shrugged and said to analysts it would all be taken care of in 30 days. It would soon be back to full steam ahead. Disaster airbrushed.

Seasoned Wall Street biotech analysts, however, knew better. One former analyst and investment banker (now Chairman of Biogen), Stelios Papadopoulos, PhD, summarized their reaction, "We looked at each other and said, 'What is he saying? How on Earth can they rectify the problem, pass inspections, and be back up in manufacturing and supplying in 30 days?' It doesn't happen."

And for those down the ranks at Genzyme, they thought they fully well understood what lay ahead, even if Henri Termeer had other ideas. Forever the optimist, Henri had always been able to find a way through these disruptions.

Beyond the potentially troubling strategic and financial implications, the plant's temporary cessation in production was most ominous for the many patients whose lives depended on the medicines made there. This became even clearer on the heels of a company statement on July 22, some 36 days later. The R word—"rationing"—was introduced. Genzyme's medicines were their patient's lifelines, and each patient had come to

rely on the company as a supplier they deeply trusted. Cerezyme, Fabrazyme, and Myozyme were all produced at Allston. And all treated rare diseases. And the two largest, Cerezyme and Fabrazyme, were single-source products.

The big irony of such a disruption at the “Allston Landing” facility, as it was called when it officially opened in 1995, was its proximity to the Harvard Business School, a mere mile up the Charles River. The building was divine, dubbed “the Cathedral on the Charles” by the rowers who passed by each morning. It was designed after a European church and put into service for the expressed purpose of making Cerezyme, a life-saving pharmaceutical. One would have thought Genzyme had long prepared for this scenario—a supply problem or even outage of a critical product. Whatever had happened to the concepts of safety stock and backup site redundancy? Had not some smart MBA sent word downriver?

Some patients were very upset, especially after the July announcement that certain drug supplies would be limited and require allocation. One particularly strident, disgruntled Gaucher patient activist hyperventilated, “People were hysterical at the time... . Everybody was pissed off because once again ... we were the last ones to find out and the first ones to die... . Their medical advisory committee came up with a pecking order of who would live and who would die basically, who got medicine, who didn’t... . Fabry patients, they had no drug. I mean none, like two boxes... . Those people got screwed really badly. And the Fabry patients were even madder than we were. And we get our infusions together, so we knew all of them ... it was a difficult time and people got sick, yeah.”

For Henri Termeer, this was his worst nightmare. Here was a leader whose core principles were individual responsibility, accountability, and placing the interests of patients first. His failure to secure a second source of supply for his patients was a monumental failing he would regret for the rest of his years. Over the ensuing 19 months, he took it hard, and very personally, as the crisis deepened. To his great credit, he never shirked the personal responsibility and accountability for the pain that was to follow. He knew he had let others down and would shoulder the blame. His health suffered, and Termeer’s credibility would take a big hit.

But for now, the show had to go on. The company was facing a ghastly beast. In fact, at first, it was not even sure what beast it faced. But soon it

became clear that the beast was instead a tiny, microscopic bug. The plant's contamination had likely been caused by a latent virus, Vesivirus 2117. It was found in the fetal calf serum Genzyme imported from New Zealand and used in its big tanks to feed the cells that expressed the company's enzymatic products.

After an intense review, it was concluded that a plant shutdown and decontamination was the only way forward. The reality of it all had hit the weekend of June 13. Mark Bamforth, Steve Kennedy, Blair Okita, Sandra Poole, and a coterie of Genzyme's other production leaders dropped everything and came together to create a plan for the site's remediation.

Poole's engagement was representative. She had even been at a Belgian amusement park, outside Brussels, celebrating her son's birthday when she had gotten the call to action. She recalled, "I got the call on Sunday from Steve Kennedy, and Monday morning, I was at the plant. For the next two months, we were in the plant pretty much seven days a week, sleeping barely a couple of hours a day. It was amazing."

They set about, an army of troops with an unlimited budget, to decontaminate the plant. All 180,000 square feet of it had to be dismantled. There was a frantic rush to clean it up. All available employees were deployed; their commitment was of epic proportions. The Doubletree Hotel next door became "home" for many. It was all hands on deck. This was about survival.

Vaporous hydrogen peroxide was used to sterilize the plant's six massive, multi-thousand liter stainless steel production tanks, and the walls in every hallway were bleached. Five miles of insulation, one mile of copper tubing, and 267 HEPA filters were replaced. Chromatography columns were reloaded by the dozens. Everything in the plant was viewed as a risk. Everything in the plant needed to be cleaned, sanitized, or replaced. Everything.

Remarkably, it took only eight weeks before the facility returned to service and the restoration of production capacity began. Termeer checked in with his Allston team each morning. His patients' trust had been rocked, and Genzyme was far from out of the woods.

In late summer, he had more bad news to communicate, but he tried to calm things as the plant reopened. His remarks that morning were directed at Genzyme's inventory supply shortage, "Reaching a decision on the work in process has been difficult for us as we balance the medical

benefit of Cerezyme for patients with minimizing the risk to our newly cleaned Allston plant. In the end, we cannot take the risk of processing material that has any possibility of recontaminating the plant and setting back our ability to supply Cerezyme to patients. Now that we have resumed production, we are focused on the road to recovery.”

The upshot of this decision was the destruction of over half of Genzyme’s inventory, its safety stock, and its work-in-process pipeline. Sandra Poole, by then the newly installed head of the Allston plant, explained, “We lost a significant amount of a year’s supply. We were already running at lower than normal inventory levels.” But the discarded product had been deemed to be at risk. As a result, its Cerezyme and Fabrazyme supplies were nearly depleted. Total write-offs, exceeding \$30 million, were eventually incurred, resulting in yet another hit to Genzyme’s earnings.

Indeed, the usual marketing script had been flipped as Genzyme was forced to resort to “rationing meetings,” a careful, tedious process of making sure none of the lives of its patients were lost. As one executive described the situation, the crisis had “precipitated the company from a honeymoon period into desperation.”

These meetings were regularly attended by numerous Genzyme leaders, but their principles were guided by Termeer. Not only were those who took ownership of delivering the rare disease division’s financial results involved, but also those responsible for the clinical, regulatory, and manufacturing/supply chain organizations. Termeer’s order was to treat all patients equally, irrespective of whether Genzyme received payment for the product delivered or otherwise. The allocations were to be based on medical need, not financial value.

Caren Arnstein, Termeer’s head of corporate communications, described the vibe, “Everyone was devastated. We all knew the instant we heard the news about the Allston plant. Without that plant, we couldn’t supply patients. That is who we were and what we were all about. It was all about getting the patients the drugs they needed and here we were. We were their lifeline. There was this huge sense of ‘oh my god, we’ve let down the patients.’”

Because of national differences in regulatory and other guidelines, different methods were developed by Genzyme for allocation in different territories.

For instance, in the United States, the allocation team would often evaluate individual patient's needs to determine the severity of their condition and the criticality in treating it. In the background, they would rely on a set of decision rules that favored the shipment of Cerezyme to children with more severe disease over older patients with less severe disease. Also, an emergency access program was set up for physicians to receive Cerezyme for patients who were in life-threatening situations. The Genzyme committee would make the final determination as to who would get what, subject to product availability.

In Europe, the regulators took a less forgiving stance. They insisted that its citizens get a full dosage, especially for Fabry patients whose symptoms often included impairment of vital cardiovascular, central nervous system, or renal functions. Dr. John Barranger, a NIH researcher in Roscoe Brady's lab at NIH who helped develop Fabrazyme, commented on the drug's administration, "Adequate dosing matters. If you don't take enough, you get sick."

This, of course, created its own uproar. Allen Black, a personal injury attorney who represented Fabry patients, had this to say in the *Pittsburgh Post Gazette*, "Europeans get a full dosage. Americans don't... . It's absolutely bizarre that Americans should essentially have no choice and be kept on a low dose... ." Black had a point. After all, the NIH had spent \$4.1 million in U.S. federal funds to develop Fabrazyme.

Ed Kaye, Genzyme's Group VP for Clinical Development and a member of the rationing committee, would later explain his perspective on the patient community's reaction, "... people looked at Genzyme as a company with integrity and we were ethical, doing good science, trying to help patients. People remained loyal to Genzyme."

Geoff McDonough, MD, one of the executives responsible for Genzyme's rare disease franchise, tried to reassure the patient community in a prepared statement, "These actions are intended to preserve inventory for the most vulnerable patients and to ensure global equity in this extremely challenging time for patients and physicians."

The company had originally communicated that the supply shortfall would end in October. By August, however, it became clear that this timeline was not going to be met. The company was forced to amend its projection; new product would not be released until later in the year, possibly not until the end of December, adding two more months of uncertainty.

Later, it would come to light that Genzyme had been facing supply pressures for some time. Undetected, the insidious Vesivirus had been attacking Genzyme's cell cultures for months, impairing its cell growth and production yields.

Patients read the news; they were desperate. Jack Johnson, Executive Director of the Fabry Support and Information Group, or FSIG, remembered the situation well, "That was a very difficult time. There were patients suffering a great deal around the country as well as new patients overseas. As a patient advocate, we wanted to know what was going on and receive up-to-date information as soon as we could possibly get it. Unfortunately, what FSIG and others would get was stale, recycled information after the company's investors had been briefed." Johnson conceded it had not been Genzyme's fault. "That's the way the system works," he said. But it stung nonetheless.

As was customary in these situations, regulators had also remained vigilant as Genzyme was rebooting Allston Landing. To monitor its progress, the FDA field office in Stoneham, Massachusetts set up an Allston site inspection, which commenced on October 8. This was part and parcel of the enforcement of the FDA's Good Manufacturing Practices (GMP), its stringent code for ensuring drug safety and quality.

Upon its completion five weeks later, FDA representatives visited Allston to read out their conclusory findings. A Form 483 Report was issued on that dreary, rainy Friday, the 13th of November. They had asked Henri to be present for the meeting. In its 22 pages, there were 49 infractions cited, an extraordinary number. Termeer sat expressionless while Thomas Arista, the lead Field Investigator, read the violations one by one, a recitation that took more than a half hour. As Sandra Poole recounted, "This was a dark, dark moment for Henri." Reality was setting in. A few months later, the FDA notified Genzyme that additional Enforcement Actions would be taken.

A fundamental question that often came up as Genzyme's community of patients and supporters pondered their plight was why the company had not built a backup manufacturing facility. It seemed unfathomable.

One answer was obvious: the cost, a half a billion dollars. But since Allston's opening 14 years prior, Genzyme had been growing exponentially, both organically and inorganically, and its profits were soaring. The company surely had the financial resources to build it.

Since 1995, the company had made numerous updates and improvements to the facility, including the construction of a large new wing to upsize its capacity. Nonetheless, although long planned, the sizable investment in a backup site to produce Cerezyme and Fabrazyme was often bumped from the top of the capital expenditures list.

One prominent reason for deferring the investment was attributable to nine infants and a clutch of genetically modified rabbits, all part of an experimental clinical trial being held in Europe in the early to mid-2000s. The infants had Pompe disease, and the rabbits produced milk that contained a raw enzyme that, once removed from the milk and purified, enabled the babies to be treated. Based on the study results, the enzyme appeared to essentially eliminate their risk of death.

Learning of this potential medical breakthrough, the parents of other Pompe patients came forward, demanding treatment for their children. In some countries, they even went on television and chained themselves to health ministries to publicize their cause. They demanded that the company produce enough enzyme to treat their children and all the others who needed it, not just the first nine.

To address these concerns, a shift in Genzyme's production and supply strategy was made, and the build-out of a backup site in Framingham, Massachusetts was abruptly put on hold. This enabled the reallocation of funds for the construction of Pompe-related production capacity in Geel, Belgium at a site Genzyme had acquired from Pharming Group NV in December 2001. And in the meantime, the rabbits, which were fed and supported at this site, could continue to produce drug product for the nine kids.

Converting this small Belgian plant for the large-scale production of what was to later become Myozyme would take an enormous investment, and Termeer prioritized it because he had seen the drug's dramatic effectiveness in treating Pompe patients. One Genzyme executive later remembered Termeer's assertion that hundreds of babies' lives had been saved as a direct result of establishing this priority.

But in hindsight, this was also a consequential, fateful decision that, although saving many lives, contributed to the inadequate backup of the Allston plant and the company's eventual inability to provide a steady, secure supply of drug product to Gaucher and Fabry patients. Its repercussions would not be fully known for seven years, a stretch of time during

which the question of building an Allston backup site was always in play but never sufficiently addressed.

In looking back, it was obvious that additional backup production capacity—in Framingham or elsewhere—should have been built to ensure the company’s ability to supply Cerezyme and Fabrazyme. The fact that the investment in a backup site was continuously deferred during the 2001–2009 period revealed, at the very least, a level of parsimony gone too far. At worst, it reflected an uncharacteristic blind spot due perhaps to corporate hubris or incomprehension of the disaster that would ensue in the event of a supply outage. Years later, one executive rationalized that it was nothing more than an expression of overconfidence in their capabilities and the fact that “we had never failed before.” Sadly, they now had, and the costs of this mistake were tragic and far-reaching.

In parallel with the Allston production crisis, Termeer began facing a base of restive Genzyme shareholders. Its shares were languishing. Sales and profit targets were being missed because product was not being shipped. Financial guidance was being lowered. How was Genzyme going to make its numbers? It was now a \$4.6 billion corporation and among the Fortune 500, but could this be sustained? In late July 2009, Genzyme adjusted its range of financial guidance for the year ending December 31, 2009. It was revised to \$4.6–5.0 billion, down from \$5.25–5.35 billion. The company ultimately delivered \$4.5 billion for the year. The revenue gap resulted primarily from the triad of products that had been halted at Allston—Cerezyme, Fabrazyme, and Myozyme. Each missed its target.

Looking back, these shortfalls revealed a basic flaw in the strategy that had been foundational to Termeer’s steady, opportunistic acquisition of businesses over his 28 years in leading Genzyme. By the time Genzyme was sold in 2011, the company had done more than 30 acquisitions—far more than any other biotechnology enterprise of its generation—in a wide range of fields including renal, multiple sclerosis, hematology/oncology, biosurgery, pharma intermediates, and genetic testing.

From the beginning, analysts had postulated that Termeer’s true strategy centered not on rare disease, but on diversification. His strategy was to construct a puzzle of disparate pieces that somehow would fit together under the heading of “Patient Care.” These various pieces would insulate



Genzyme from the cyclical vagaries of markets, the disruption of competitive new product launches, patent expiries, and operational hiccups like Allston. One analyst went so far as to posit that Henri was trying to create over decades another J&J—a highly diversified international healthcare products company.

What became evident over the years, however, was that the investments that seemed to be working best, for Genzyme and its shareholders, were those made in treating rare diseases. It is not that the others, especially Renagel, were not able to contribute to the top and bottom line. Many were, just not to the same degree.

So although the nonorphan businesses had provided some ballast as the Allston plant disaster was being stabilized, they were hardly the value-creating engines that Cerezyme, Fabrazyme, and the other rare disease therapies offered.

The analysts and activist investors sharpened their pencils watching the company's fortunes stagger. The company's downward spiral exposed Genzyme's underbelly. There were underperforming units in the portfolio. Before long, the pressure would build to divest them, something Termeer had assiduously resisted over the years as it would impair his bigger dream for Genzyme.

This strategic weakness invited investors' criticism and activism. Ralph Whitworth of Relational Investors was one. Whitworth had come onto the Genzyme scene in 2009 as news hit the papers of not only its Allston troubles, but also as awareness of the underappreciated value of certain of its various business units became recognized. The company's shares were drifting lower that fall as the FDA setbacks and missed financial guidance were closely watched by investors.

For the activists, this had the makings of a breakup candidate. Whitworth had already made a fortune in breaking up companies. He actively sought companies deemed to be underperforming because of poor capital allocation discipline. Boone Pickens had been his mentor. His scalps included the CEOs of Home Depot and IBM who had been forced out at his behest. Although reputed to be a "quieter" activist, Whitworth carried a big stick.

Relational Investors began accumulating Genzyme's shares in late 2008, and by the end of 2009, it owned approximately 4% of the corporation, worth about \$540 million at the time.

Whitworth had been discussing Genzyme's fortunes with Termeer over the course of the previous summer. To say they were "friends" would have been a stretch. "Semi-adversarial" was perhaps a more accurate descriptor, used by one Genzyme insider who had observed their relationship's dynamic. But a dialogue had been established between the two as one would expect of a CEO and a major shareholder.

As the Allston site reopened and the FDA delivered its 483 citations, Whitworth commenced a months-long escalation of pressure that would catalyze far-reaching changes in the composition of Genzyme's board and management team, as well as the company's management practices. Since the mid-1980s, Henri Termeer had had a free rein in leading Genzyme, shaping and guiding its strategic direction, its decision-making apparatus, its human capital practices, and its public persona. That was all nearing an end as external forces began to close in around him.

In many ways, the contest harkened back to the games Termeer had played in the chess halls of Tilburg, those that had honed his ability to look around the corner, strategize, forecast, and prepare. But this time there was a difference as the king on his chess board had landed in a position weaker than any he had encountered since the mid-1980s.

On December 10, 2009, as news on a host of fronts needed updating, Termeer issued a letter to his shareholders, informing them of the many developments at Genzyme. In classic Termeer fashion, it forcefully and optimistically presented his case that Genzyme would "emerge a stronger company that is better prepared to deliver on our commitment to sustainable growth."

The letter replayed the year for its readers, factually stating the conditions that had been successfully navigated. It included not only an update on the Allston plant's turnaround and its outlook, but also the changes in Genzyme's operational leadership, including four new senior managers brought in from outside the company to run various key functions. Termeer also, for the first time, gave readers an insight to his own succession plan: David Meeker, John Butler, and Mark Enyedy, all Genzyme insiders, would share oversight for the company's commercial and manufacturing operations. Of the three, Meeker got the largest share of the responsibility: EVP of Genetic Diseases, Biosurgery, and Corporate Operations, which included Allston.

Tucked into the letter was also the appointment the day before of Robert Bertolini to Genzyme's Board of Directors. Bertolini had been the CFO at Schering-Plough at the time of its \$41 billion sale to Merck & Co. The deal had been a huge success for Schering shareholders, and it had closed just one month earlier. Bob was one of its principal architects, and he was viewed as an investor-friendly director with good judgment. Little fanfare was brought to the appointment, but it was a signal of Termeer's openness to amending his board of directors and providing investors with another independent voice at the table.

Days later, Ralph Whitworth had taken it all in and decided to make his move. On December 15, he rang up Termeer and formally requested a seat on Genzyme's board. It was the holiday season, and the two spent much of it discussing Whitworth's request.

On January 7, the week before the year's most important life sciences investor conference, the 28th Annual J.P. Morgan Healthcare Conference, Genzyme announced that it had entered into a "mutual cooperation agreement" with Relational Investors. Subject to certain conditions, including a standstill provision, Whitworth had agreed to defer his appointment to join the Genzyme Board until later in the year, November. He also agreed to support those who would be nominated by Genzyme to stand for election at the company's upcoming annual stockholders' meeting in June.

On the following Monday, January 11, the opening day of the J.P. Morgan conference, Bob Carpenter was re-elected as Genzyme's Lead Independent Director, a role that had been strengthened and formalized the prior week. The Board had voted to expand Carpenter's role to "include responsibilities that are similar to those typically performed by a chairman who is not a company CEO." It was expected that Carpenter would serve in this role for three years.

The following day at 9 a.m. PST, Termeer presented Genzyme's 2009 performance and its 2010 outlook to a standing-room-only crowd in the Grand Ballroom at the St. Francis Hotel. Summarizing the past year's developments, the challenges ahead, and the shortfalls in Genzyme's financial results could not have been much fun. But Termeer, ever the optimist, found a way through the San Franciscan fog, "In 2009, we continued to successfully execute across our diversified businesses," he said. In the accompanying press release, of the eight annual highlights cited on its first page,

not one spoke to Cerezyme or Fabrazyme. These were buried in the text that followed.

It was not Termeer's best year at J.P. Morgan, but he was by now a member of the royal family—of biotech, that is—and recognized as its longest tenured and one of its most successful CEOs. As a gifted communicator, he pulled off his half-hour presentation with the humor, aplomb, and the charisma all knew of and expected from him.

Meanwhile, Genzyme's shares had closed on January 5, 2010 at \$48.24. By the close of trading on January 12 they were trading at \$52.98, representing a one-week gain of nearly 10%.

Over the next month, things quieted as the company set about closing its year-end books and preparing for the Annual Meeting and Proxy season. Behind the scenes, however, investor activist Carl Icahn had been accumulating Genzyme's stock. He had begun building his sizable position in mid-August 2009. If Ralph Whitworth was the quiet activist, Carl Icahn could be expected to take up the slack and make enough noise for the two of them.

Icahn was not one to disappoint. On the morning of Monday, February 22, Icahn Partners notified Genzyme that it intended to nominate a slate of four individuals for Genzyme's board of directors at the company's 2010 stockholders' meeting, which at this point was scheduled for May 20. Genzyme was already well along in making its preparations. The company's Initial Preliminary Proxy Statement was filed with the SEC on March 11, and it became clear that a proxy fight with Icahn Partners loomed. The annual meeting could turn into something just shy of a riot.

Icahn filed his own proxy statement on March 23, nominating his slate of four Director nominees. It confirmed that Icahn Partners and its affiliates had acquired nearly 4% of Genzyme, worth about \$575 million on the open market. Publicly, Termeer responded by saying about the only thing he could, "... we are open and responsive to shareholder input, and we welcome a constructive dialogue with Mr. Icahn."

Somehow Termeer kept his cool among the constant winds that were buffeting Genzyme. The pressure was intense and building, and it would get worse, but Termeer, being the strong leader and gentleman he was, handled himself and his adversaries with toughness, but also with a measure of equanimity and grace. His team and his board remained firmly

behind him, even if the activists and regulators were launching grenades on a seemingly daily basis.

On Wednesday, March 24, 2010, Genzyme and Termeer would hit their low water mark, perhaps of the entire saga. The FDA had called again, this time with some news.

A Genzyme press release later that day would explain that a Consent Decree of Permanent Injunction, a civil enforcement action resulting from its Allston failures, was being prepared. Termeer and two of his associates would be Named Defendants. The details of the filing in the District Court of Massachusetts were due to be released in several weeks.