Genzyme, though unique, could be a bellwether for US biotech

Is Genzyme, a giant among biotechs, lacking a certain *je ne sais quoi*? Since its launch in 1981, the company has grown from a small, 20-person startup to the biggest biotech corporation in the Boston area, with revenues topping $4 billion annually. But the company has suffered recent setbacks, and last month, as the French drug maker Sanofi-Aventis moved in to take over Genzyme, some analysts saw the possible merger as a sign of how aggressively European pharmaceutical firms are pursuing US biotech companies.

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Viral infection: Genzyme's problem-plagued manufacturing plant in Allston, Massachusetts.

Genzyme has fallen on hard times recently. In June 2009, a virus was discovered to have contaminated bioreactors at two of its manufacturing plants, and the Cambridge, Massachusetts–based company was forced to halt production of Cerezyme and Fabrazyme, top-selling enzyme replacement therapies used to treat Gaucher and Fabry diseases, respectively. The company's stock price took a hit, falling below $50 a share, down from its $83 peak in mid-2008. More than a year and a half later, the company has yet to return to full worldwide production.

News last summer that the French drug maker Sanofi-Aventis had made a $18.5 billion takeover bid for Genzyme—equivalent to $69 per share—put the biotech firm back in the headlines. But Genzyme's board promptly rejected what its members saw as a low offer. In the intervening months, the two companies have gone back and forth on a fair price, and as *Nature Medicine* went to press, a deal looked likely.

Biotech analysts are mixed on whether Genzyme has approached the negotiation table from a position of strength or weakness. "The reason for their loss in value was their manufacturing failures, but we had long been critical of what management was doing there because they had pursued a strategy of diversification," says Geoffrey Porges of Sanford C. Bernstein, a New York–based research firm. "I think this is really a tragedy of the perils of moving away from your areas of expertise."

Over the past 15 years, the company has branched out from its products for rare disease into areas including tissue repair, chronic kidney disease, oncology and surgical products.

Now, however, Genzyme is scaling back. In the wake of its manufacturing woes and spurred on by activist investors, the company recently sold off its genetics and diagnostics units, and Genzyme has announced plans to divest its pharmaceuticals business unit as well. Karen Andersen, an analyst with Morningstar in Chicago, says these moves have strengthened the company by eliminating the least profitable parts of the business. "Over the past year, they've definitely gotten more focused on what they've done best in historically," she says. "We think [Genzyme] has among one of the widest of competitive advantages among biotech companies."

Pitching Campath

One of the largest uncertainties affecting Genzyme is the company's monoclonal antibody–based therapy Campath. Currently approved to treat a form of leukemia in people who do not respond to other medicines, Campath is now also in late-stage clinical development to combat multiple sclerosis—a lucrative market worth around $10 billion worldwide. In a phase 2 clinical trial of more than 300 people with early, relapsing-remitting multiple sclerosis, Campath proved significantly more effective at preventing disease relapse than interferon-beta, a current leading therapy (*N. Engl. J. Med.* **359**, 1786–1801, 2008). But some people taking Campath also had severe autoimmune reactions, and one person on the drug died in the trial.

Genzyme watchers are now waiting with bated breath for the results the company's phase 3 trials, expected later this year. Those data, analysts say, are needed to resolve Campath's true value. (According to media reports, Genzyme is forecasting the drug to generate sales in excess of $3.5 billion per year, whereas Sanofi-Aventis predicts annual sales to peak at only $700 million.) To bridge the valuation divide, Genzyme and Sanofi-Aventis are considering a deal structure known as a 'contingent value right' in which Genzyme shareholders would earn additional payouts if the medicine is approved for multiple sclerosis and then meets certain revenue targets.

Looking beyond Campath, however, Les Funtleyder, a health care strategist at Miller Tabak & Co. in New York, doesn't see many promising new candidates in the works at Genzyme. "Pipeline really drives value in the biopharmaceutical industry, and ex-Campath I don't see a lot in Genzyme," he says.

Phil Nadeau, a research analyst with Cowen & Co. in New York, disagrees. He notes that even though many large pharmaceutical companies, including GlaxoSmithKline, Novartis and Pfizer, among others, have recently launched rare-disease units (*Nat. Med.* **16**, 837, 2010), Genzyme remains the world leader in this sector. "That orphan disorder franchise is a real jewel," he says.

Some see the Genzyme takeover saga as part of a larger trend in which European pharmaceutical firms have snatched up US biotechs, in part because the biologic drugs produced by companies such as Genzyme seem poised to become more important in drugmakers' portfolios. "This is yet another major US biotech company that is being acquired by a European pharmaceutical company," Porges says.

In March 2009, for example, the Swiss pharma giant Roche agreed to a $47 billion merger with the California-based biotechnology leader Genentech. Another Swiss drugmaker, Novartis, acquired another California biotech (Chiron), in 2005. And, in the years between, the British company AstraZeneca acquired the Maryland-based vaccine developer MedImmune, in 2007.

"It's really quite striking how much of the intellectual bedrock of the biopharmaceutical industry is being acquired by foreign companies," Porges notes.

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Correction

In the February 2011 issue, the article entitled "Genzyme, though unique, could be a bellwether for US biotech" (*Nat. Med.* **17**, 145, 2011) incorrectly stated that GlaxoSmithKline had acquired AstraZeneca. Although GlaxoSmithKline has acquired medicines from AstraZeneca in the past, the two companies never merged. The error has been corrected in the HTML and PDF versions of the article.