

Genzyme's lifelong commitments

The Dutchman Henri Termeer has now held the top job of Genzyme, the world's third-biggest biotech company, for the past twenty years. He has great expectations of gene therapy and the use of stem cells.

By Elske Schouten

Henri Termeer on how biotechnology will change healthcare

[Photo caption: Henri Termeer of biotech giant Genzyme: "Everything we do could potentially lead to safety risks."]

Henri Termeer (58) describes himself as a sidetracked economist. After studying Economics and holding a managerial position at a pharmaceuticals company he became involved in founding the American biotech company in the nineteen-eighties. Genzyme has since grown to be the world's third biggest biotech group. Termeer has now been at the helm as one of the world's most prominent biotech entrepreneurs for twenty years. The fact that he has been living in the US for almost three decades has left its mark: when it comes to talking about work, his preferred language is English.

Wholly at odds with the logic of the pharmaceutical industry, Genzyme concentrates primarily on medicines for diseases that hardly anyone suffers from. The company's most important product is Cerezyme, a remedy for the rare Gaucher's disease. The company is expected to shortly be given approval to sell a remedy for the hereditary Pompe's disease. Babies born with this disease are not expected to live longer than a year without treatment. These days the company is also working on other disorders and genetic diagnostics.

This autumn Genzyme opened four new European establishments in a single week, one of which in Belgium's Geel.

How did Genzyme get started?

"We started out working on a treatment for Gaucher's disease. Our approach at the time was fairly primitive: it involved extracting the enzyme that comprises the medicine from placentas. We needed 22,000 placentas to treat one patient a year. That means that 22,000 babies have to be born, and collecting placentas isn't one of the easiest things to do. We worked together with the Pasteur Mérieux Institute in France, which made the protein albumin from placentas. They used advanced wine presses to extract the liquid from them. We needed the tissue, which they had previously discarded. Against everyone's expectations, we succeeded in isolating the enzyme from it and in 1991, ten years after the company was founded, we gained approval from the FDA (the American Food and Drugs Administration, Ed.).

"To give you an idea of how insane this was: in 1993 we used 70 per cent of all the placentas from the Western world. These days we produce the enzyme in hamster cells. But that initial phase was without a doubt the biggest catalyst that got us so far. Things aren't always as impossible as they first seem."

A lot of biotech companies were established at the beginning of the eighties. How did Genzyme manage to become the world's number three?

"Growth is something you achieve by making products that people are willing to pay a good price for. We worked on medicines that made it possible to keep babies alive, and products like that naturally get a lot of support. Even in the Netherlands, where we are careful with our

money... There is no other explanation for Genzyme's success than the fact that the products worked well and the market was willing to pay for them.

The treatment for Gaucher's disease costs 157,000 euros per patient per year, and the treatment for Pompe's disease will probably cost even more. Why does it have to be so expensive?

"We are still only treating 4,500 patients in the world for Gaucher's disease. Those are all the patients we know exist. We operate the same price in all countries or we provide it free of charge. That's because we treat everyone who has the disease, even in countries such as China, Vietnam and Tanzania. It's like this: if we start to treat a two-week-old baby suffering from Pompe's disease we can never, ever stop providing the treatment. Even if the government says that it isn't concerned about that baby. That means that once we start treating someone, perhaps as part of clinical research or a *compassionate use* programme because we haven't yet got approval for the product, we enter into a lifelong commitment. It could be that we have to build a plant especially for those patients, and that represents a big investment. The plant has to stay there permanently, not just for a year. So the equation isn't as straightforward as with most products, but you can't do it as charity either. It always has to make economic sense, it has to be sustainable. If we go bankrupt, everyone is worse off.

"Our profits aren't as high as those of pharmaceutical companies. But the company is sustainable. We are currently able to invest 20 per cent of our turnover in research. We do not pay out a dividend."

You've had to spend years negotiating with care insurers on what they're willing to pay for your products. Can you put a price on a human life?

"Everyone has their own idea about that. In England there's a large group of economists that puts the maximum at 30,000 pounds (44,000 euros, Ed.) a year. But you can't think in those terms.

"Insurers are no different from us. They've got mothers, children and aunts with illnesses too. They would never refuse to pay for something that works. What they do have a problem with is 'medicine by trial and error'. First we try this, and it doesn't work, so we try that. And it costs 30,000 euros a go. To give an example, there are plenty of cancer treatments that only help 10 per cent of the patients. If it were possible to identify that 10 per cent beforehand so that we could use a different treatment for the other 90 per cent, we'd make strong inroads. We are working on building up a diagnostics branch so that we can set out to do that.

"I hold a lot of talks with health ministers, economics ministers and finance ministers. They are often at loggerheads because the one wants to spend money on health and the other on road building. But if you put them together and ask how much they are willing to spend on being able to predict the course of diseases and knowing in advance which medicine works, all three of them will say 'whatever it takes'.

"We hear a lot of complaints about the costs of healthcare. In England, which spends 6 per cent of its GNP on health, people complain just as much as those in the Netherlands, where the figure is 10 per cent and in the US, where it's 15 per cent. They complain because that's a lot of money, and because there are still a lot of diseases that we can't yet treat properly, such as Alzheimer's. Those people cost us a fortune. They have to go to a nursing home and someone has to look after them, and it takes five or six years before they die. Without any quality of life whatsoever. Cancer is expensive, too, because it strikes people in the prime of

their productive lives. The same goes for strokes and diabetes. That's why we invest in new technologies, to make the course of diseases more predictable and manageable.

But the analogy doesn't hold for diseases like Pompe's and Gaucher's. If they are not treated, the patients die and it costs us nothing

"That's an extremely cynical way of looking at it. No one could go along with that. At the beginning of the nineties I spoke to someone high up in the American government, who said to me, 'We have to introduce price controls to the system, for what will happen if one of you comes up with a treatment for AIDS? He can charge whatever he wants for it.' But the problem there isn't the pricing of a treatment that works, but the fact that there isn't yet a treatment. The simple fact of the matter is that finding new treatments calls for huge investments."

How can biotechnology change healthcare?

"By making medicines more personal through the combination of diagnostics and medication. That will greatly enhance the effectiveness of treatments. That way, we'll be able to take the patient's particulars as a basis for identifying in advance who will benefit from a certain medicine, and who will not. Biotechnology will also have a major impact on combating pandemics, such as the possibility of a human variant of bird flu. Being able to produce vaccines more efficiently, in cultivated cells for instance, will make them available to large groups of people."

What are the most promising technologies?

"Looking ahead twenty years, there are two that I'm very excited about. One of them is gene therapy, which involves having a protein created in the cell, which originally wasn't present or was deformed owing to a genetic defect. The other is the use of stem cells (cells whose function has not yet been established and which can change into all sorts of cells, often originating from embryos, Ed.). This is a huge subject of debate, which gives people the impression that one day it will solve all the world's problems. People underestimate how long that will take. That's how it always goes in biotechnology. We make a new discovery, and then we forget that it takes ten to twenty years before we can use it to treat patients."

What's your viewpoint on the ethical aspects of stem cell technology?

"This is all about revolutionary therapies, and there's no such thing as a quiet revolution. Debate is needed to reach agreement on this. It concerns everyone, so it's very healthy and fitting that governments that represent the people actively discuss it."

President Bush has banned the use of public funding for stem cell research

"Bush has taken an extremely conservative position on stem cells, but there are elections every four years. Decisions like that never give a technology a definitive status, but only a temporary one. I remember that in the early days of biotechnology, the city of Cambridge, which is home to MIT and Harvard University, banned the placing of a gene in another cell. That made it very hard to make progress, even in that progressive environment. But a few years later the city came to its senses and everyone was given support."

Wouldn't biotechnology be easier without rules like this?

"No. It's very important that we can define how we work when it comes to regulation. Consumer confidence in what we do, in the products that we offer and the funds we obtain for it are extremely important to gaining acceptance for these technologies. People have to trust that we know what we're doing and that we can justify it ethically. This field of science would never get anywhere without rules."

The pharmaceuticals industry has been under fire in recent years, not least because of the Vioxx affair. Pharmaceuticals company Merck held back information that showed that this painkiller was unsafe. Thousands of users died of a heart attack.

"Merck operates in a highly competitive market. I think that when doubts began to surface about their product, they wanted more and more proof that there really was something wrong. When it was finally shown by clinical research that there actually were safety issues, they had to take the product off the market. That was a very painful and damaging episode for the company and for the pharmaceutical industry in general.

"This risk of this kind of thing happening is always present if you have conclusive proof of the benefits of a medicine but imperfect data about the risks. In those cases companies try to prove whether or not those risks are present, and that is very difficult to do."

How can that be prevented?

"Everything we do could potentially lead to safety risks. All you can do is increase transparency and make sure that transparency represents an economic interest. That's clearly what is happening now: everyone knows how much this has cost Merck. Everyone will now set out to protect themselves against this, for something like this can destroy a company. There is virtually no conceivable short-term risk that can weigh up against that risk."

Have you got any new plans?

"I'm 58 now, and I think it's too late so start something else. But I do want to find out more about neglected diseases in developing countries. There is much we can do to make sure that more medicines are produced for them. Not that I will be going to them with a sack full of pills, but I could have a role to play in promoting research into it. That would be more a political activity."

[Graph:]

Genzyme spends around 20 per cent of its turnover on research

Research, in millions of dollars

Profit, in millions of dollars

Research spending in millions of dollars