

# novo nordisk history

1970



1990



1980

2000

changing diabetes



## Preface

Behind the Novo Nordisk we know today lies an exciting story that goes back more than 85 years. It began with two small Danish firms established in Copenhagen in the 1920s – Nordisk Insulinlaboratorium and Novo Terapeutisk Laboratorium\* – who under modest circumstances began manufacturing a revolutionary new medicine, insulin, that had just been discovered by two Canadian scientists.

Competing intensely with one another, the companies developed into two of the best in their field. When at last they decided to merge in 1989, they created one of the world's largest biotechnology groups – a group that has been expanding rapidly ever since.

This booklet tells in words and pictures of the many events that are the story of Novo Nordisk – a fascinating tale of one pioneering product after another, developed through the inspired thinking of talented and ambitious people.

We hope you will enjoy the story!

\* Both Nordisk Insulinlaboratorium and Novo Terapeutisk Laboratorium changed their names several times over the years. To make things easier for our readers, we refer to the two companies as Nordisk and Novo respectively.

*Novo Nordisk is a global healthcare company with more than 85 years of innovation and leadership in diabetes care. The company also has leading positions within haemophilia care, growth hormone therapy and hormone replacement therapy. Headquartered in Denmark, Novo Nordisk employs more than 30,000 employees in 76 countries, and markets its products in 179 countries. Novo Nordisk's B shares are listed on NASDAQ OMX Copenhagen (Novo-B). Its ADRs are listed on the New York Stock Exchange (NVO). For more information, visit [novonordisk.com](http://novonordisk.com).*

## Nordisk Insulinlaboratorium is founded



1 In 1921, two Canadians, Charles Best (left) and Frederick Banting (right), became the first researchers in the world to produce an insulin extract from pancreases and treat a diabetic dog with it.

2 The University of Toronto.

3 August and Marie Krogh (1874–1949) (1874–1943). The photo was taken during their trip to the US and Canada in 1922.

4 Excerpt from Marie Krogh's letter to Hans Christian Hagedorn about the revolutionary discovery of insulin for the treatment of diabetes.

The story of Nordisk Insulinlaboratorium began on an autumn day in 1922, when August and Marie Krogh arrived in the United States by sea. August Krogh was a professor at the University of Copenhagen and had received the Nobel Prize in physiology in 1920. The couple had been invited to the US by researchers at Yale University, who had asked August Krogh to lecture throughout the country on his medical research.

### Marie Krogh's illness

On their tour of the US, the couple heard daily reports of people with diabetes being treated with insulin – a hormone discovered in 1921 by two Canadian researchers, Banting and Best.

Marie Krogh was particularly interested in the treatment. Herself a doctor, she had in 1914 also become the fourth Danish woman to earn a doctorate in medicine. She was a researcher with her own medical practice and had several patients with type 1 diabetes. Marie Krogh herself had type 2 diabetes.

### The meeting in Toronto

During their stay in the US, August Krogh wrote to Professor Macleod, head of the institute in Toronto where the first insulin extract had been produced. Meanwhile, Marie Krogh wrote to her colleague in Copenhagen, Dr Hans Christian Hagedorn,

who together with the pharmacist Norman Jensen had developed a very precise method of measuring blood sugar:

“Since I believe that you... will be interested in this preparation, I have persuaded my husband to write Dr Macleod in Toronto and ask him if it would be possible to obtain its method of manufacture, making it possible for you to perform experiments with it in Denmark.”

Both letters were well received, and after the meeting in Toronto, the couple returned to Copenhagen in December 1922 with permission to manufacture and sell the vital insulin in Scandinavia.

### Back in Denmark

The day after the couple's return to Copenhagen, Krogh and Hagedorn decided that some intensive research was required. Before they could begin, however, they had a problem to solve: research costs money. Krogh and Hagedorn sought help from the Danish pharmacist August Kongsted, who owned the pharmaceutical company Løvens kemiske Fabrik (Leo Pharmaceutical Products). Kongsted offered to pay for the research and help start production, on condition that Krogh and Hagedorn called their first insulin product 'Leo' – the Latin word for lion.



Da jeg tænker mig, at de haardt  
fra et teoretisk og et praktisk  
Skadepunkt vil være interesse.  
ret i dette Prop., har jeg  
faaet mine Mand til at skrive  
til Dr. Mc. Glod i Toronto og  
spørge ham, om det var  
muligt at faa Bemøstelligs-  
mødet, saaledes at det  
kunne blive muligt for Dem  
at gøre Forsøg med Prop. i  
Danmark.



1 Hans Christian Hagedorn (1888–1971).

2 In 1923, Nordisk produced Insulin Leo, the first insulin product in Scandinavia.

3 In 1927, Nordisk established its first factory buildings in Gentofte.

4 Labelling of insulin vials.

### The first insulin

The first experiments took place at Hagedorn's house and at Krogh's institute, the Laboratory of Zoophysiology, and shortly afterwards – on 21 December 1922 – the two men succeeded in extracting a small quantity of insulin from a bovine pancreas. Krogh and Hagedorn were thrilled – Krogh was, in fact, so excited that he said during a lecture on 2 January 1923: "I feel that it is right to set aside my own work, at least for a time, and concentrate all my efforts on this matter..."

### The first patients treated

In March 1923, the first patients were treated with insulin manufactured by Krogh and Hagedorn. The treatment was not always successful, but Hagedorn wrote the following about a nine-year-old girl: "... this child, who was previously very quiet, has become lively and alert, almost uncontrollable." In the spring of 1923, Krogh and Hagedorn moved to new and larger premises. Hagedorn

stopped practising medicine to become the head of the laboratory, which was given the name Nordisk Insulinlaboratorium. At the same time, they began marketing Insulin Leo, which was the first Scandinavian insulin product.

The company Nordisk Insulinlaboratorium was thus a reality, and 1923 is today considered the year in which Novo Nordisk was established.

### An independent institution

In February 1924, Nordisk became an independent institution under the management of Krogh, Hagedorn and Kongsted. The three men decided that any profits should be used for scientific and humanitarian purposes. Insulin production in Denmark was in full swing.





## Novo Terapeutisk Laboratorium is founded



1 Harald Pedersen (1878–1966).

2 Thorvald Pedersen (1887–1961).

3 Insulin Novo and the Novo Syringe, marketed in 1925.

4 The Apis bull became Novo's logo in 1926. The Apis bull was one of the ancient Egyptians' sacred animals and was worshipped as the incarnation of the god Ptah.

When Krogh and Hagedorn began to manufacture insulin at Nordisk in 1923, they agreed that Harald Pedersen was the right man to build the machines they needed for insulin production. Harald Pedersen was an unusually talented inventor who had worked for Krogh for a number of years as manager of the mechanical workshop at the Zoophysiology Laboratory. Harald's brother, Thorvald Pedersen, was a pharmacist who was later hired by Nordisk to analyse the chemical processes involved in insulin production.

### Cooperation problems

The two brothers' work for Nordisk did not last very long, however. Thorvald Pedersen did not get on with Hagedorn, and in April 1924 things came to a head and Hagedorn fired him. Out of loyalty to his brother, Harald Pedersen decided to hand in his notice to Krogh, even though he enjoyed working for him.

### The brothers set up on their own

The two brothers decided to try to manufacture insulin themselves. The brothers made a good team, and in the

spring of 1924 they succeeded in producing a stable liquid insulin product which they called Insulin Novo. At the same time, Harald Pedersen designed a special syringe – the Novo Syringe – that ensured that patients could comfortably inject themselves with correctly dosed insulin. The brothers were ready to place their products on the market, but doubted whether they could cope with the marketing themselves. Therefore they contacted Nordisk to offer some form of cooperation. Krogh and Hagedorn turned the offer down, however, and the brothers decided to go it alone.









1 The villa 'Rolighed', where the Petersen brothers developed Novo's first insulin.

2 The letter to Danish pharmacists dated 16 February 1925 is Novo's birth certificate.

3 Device used in Novo's test production for the comminution of glands.

4 Working with the filling and sealing machine constructed by Harald Pedersen.

5 In 1932, Novo moved to new premises, and two years later a new factory plant was built on the neighbouring property. It was designed by the architect Arne Jacobsen.

#### The firm is named

The brothers named their firm Novo Terapeutisk Laboratorium, and on 16 February 1925 they sent a letter of introduction to Danish pharmacists, informing them that Insulin Novo and the Novo Syringe were now on sale. That date is regarded as the date on which Novo was founded.

#### A family firm

Right from the beginning, Novo was a family firm. The two brothers received financial assistance from their sister, Thora Pedersen, and from Harald Pedersen's wife, Mine Pedersen. Thora Pedersen was a teacher and women's rights activist who lent her brothers a monetary gift she had received as thanks for her efforts to secure equal pay for teachers of both sexes. Mine Pedersen's inheritance and savings were used to purchase the house called 'Rolighed', where there was room for the family and manufacturing insulin.

#### The Novo spirit

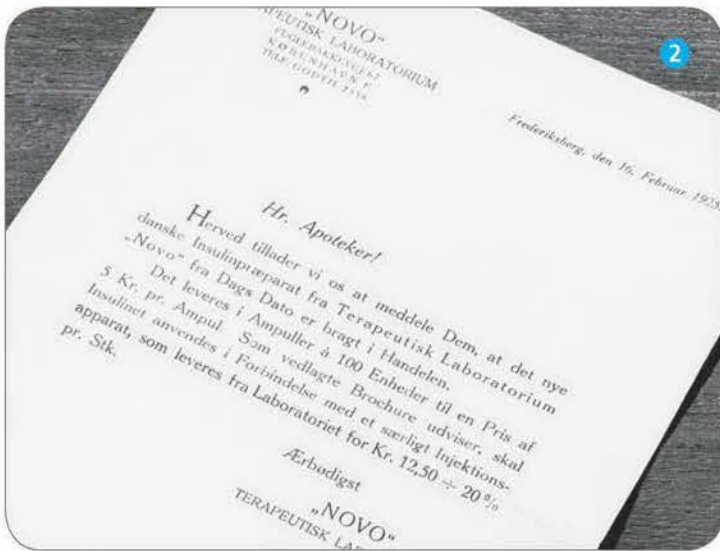
The entire family took an active part in the manufacture of Novo's products. Soon they began to hire other employees, but the sense of family and community at Novo remained. Having grown up with very modest means, the brothers found it important that conditions for Novo's employees were as

good as possible. In his New Year's speech to his staff, Thorvald Pedersen said for many years: "If Novo does well, we all do well." Novo's employees had good working conditions compared to other workplaces at the time. Even in the first decades, benefits included a salary increment for employees with dependents, a modern, well-appointed factory with an excellent staff canteen and a yearly company picnic for all employees.

Harald Pedersen, the other co-founder of Novo, has been quoted as having a favourite saying of the company's daily work: "We must be able to do better". By the same token, employees strove to improve both research and production, benefiting the company's products and turnover. The sense of community within the company developed over time into a mutual loyalty – a loyalty that came to be known as the Novo spirit.

#### Two companies

Nordisk's earlier start had enabled it to get established before Novo in the Scandinavian countries, so Novo sought growth in other markets. But both companies grew rapidly. By 1936, Novo had 56 employees, and 90% of its production was exported. Denmark now had two companies that in the years to come would develop into the world's leading manufacturers of insulin.



## New insulin products

At the beginning of the 1930s, insulin researchers recognised that the effect of the existing insulin products was too short – a serious disadvantage because patients had to inject themselves with insulin several times a day. Therefore, Nordisk and Novo turned their attention to developing a longer-acting type of insulin.

In 1935, Thorvald and Harald Pedersen marketed an insulin with adrenaline – a substance which had been shown to prolong the effect of insulin. However, it soon disappeared from the market because it turned out not to have the desired effect. Attention was instead focused on a sensational discovery made at Nordisk.

### “The most important advance”

In 1936, Hagedorn and his colleague Norman Jensen discovered that the effect of insulin could be prolonged by adding to it a protein called protamine, developed from the milt of river trout. The discovery was hailed worldwide as a breakthrough, and in 1937, the American nestor of diabetology, E P Joslin, wrote: “Protamine is the most important advance in the treatment of diabetes since the discovery of insulin in 1921.” In 1936, on the basis of Hagedorn and Norman Jensen’s scientific work, Nordisk was able to introduce a completely

new, long-acting insulin product. This was of great benefit to patients, who now needed fewer daily injections.

### News from Canada

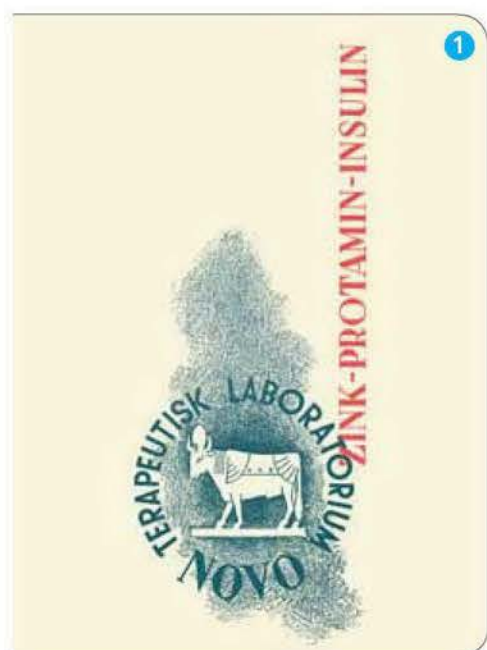
The new product had a disadvantage, however: patients had to add a neutralising liquid before use. So it was good news later that year when two Canadian researchers, D A Scott and A M Fisher, developed a long-acting product – zinc-protamine-insulin (ZPI) – that only had to be shaken before injection. Novo marketed the new product in 1938, and this triggered a lawsuit that attracted a great deal of media attention in Denmark.

### In court

Hagedorn claimed that Novo was making ZPI insulin using a method patented by Nordisk. Harald and Thorvald Pedersen denied the allegation and the case ended up in court. The brothers won the first round, but Hagedorn appealed to the Supreme Court and won his case by a majority of one. The ruling meant that Nordisk was entitled to a share of the money earned by Novo from sales of ZPI.

### Two hospitals

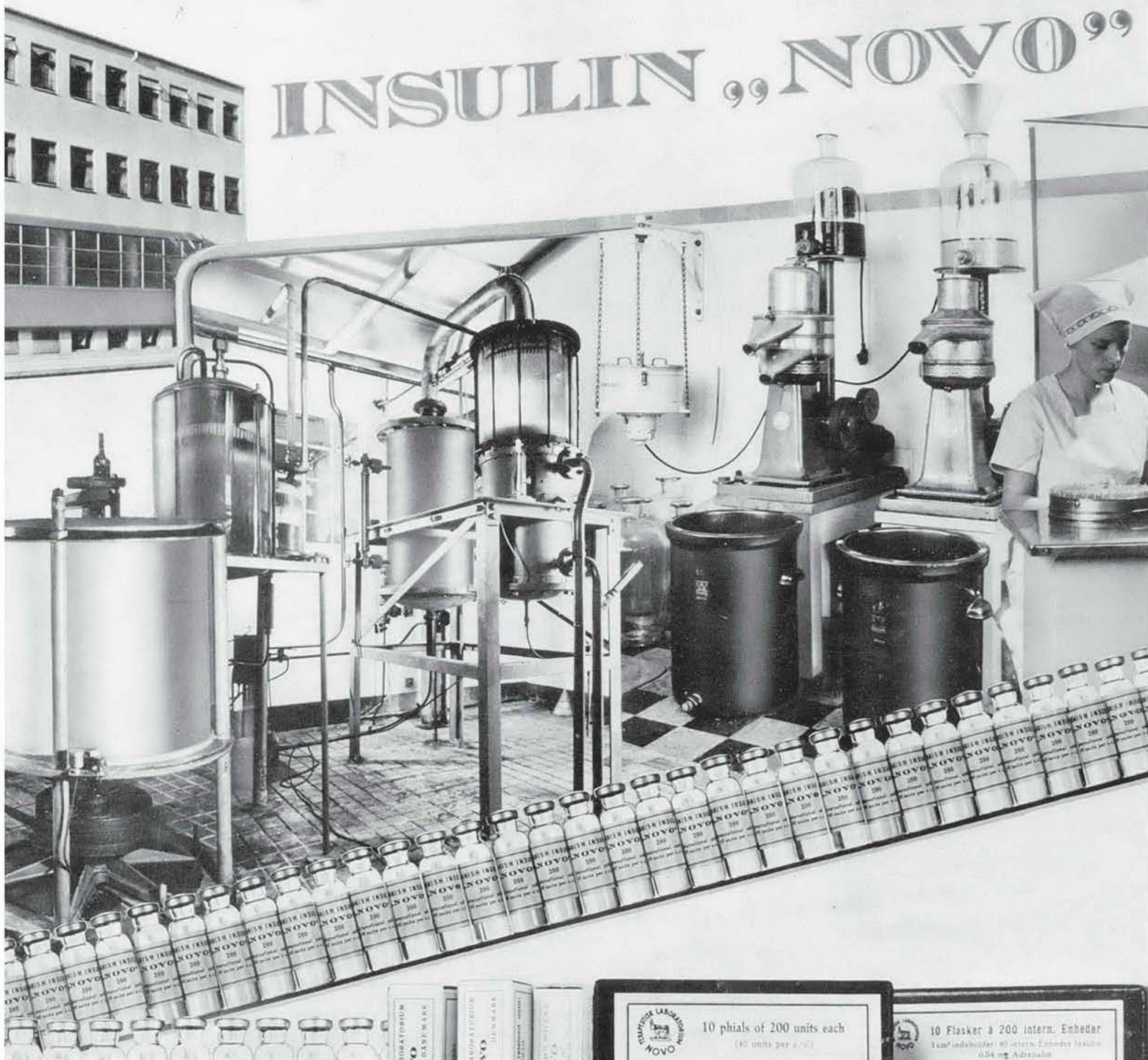
In 1932, Nordisk inaugurated Steno Memorial Hospital. Hagedorn and Krogh chose this name in honour of one of





1 Long-acting zink-protamine-insulin, marketed by Novo in 1938.

2 Photo collage illustrating the manufacture of insulin at Novo in the 1930s.

# INSULIN „NOVO“




 10 phials of 200 units each  
 (40 units per c.c.)


 10 Flasker à 200 intern. Enheder  
 (40 indholdeder à 40 intern. Enheder Insulin  
 0.54 mg Adrenalin

1



1 NPH insulin (Neutral Protamine Hagedorn).

2 Steno Memorial Hospital, which Nordisk opened in 1932. The hospital was designed by the architect Ivar Bentsen.

3 The beautiful Hvidøre Palace, inaugurated by Novo in 1938 as the Hvidøre Diabetes Sanatorium.

4 Knud Hallas-Møller (1914–1984) working in the laboratory in the late 1930s.

Denmark's pioneers in the field of science, Niels Steensen, who lived in the 17th century. This luxuriously equipped hospital treated diabetes patients and conducted research into the causes and development of diabetes. The results of the research were so good that Steno Memorial Hospital became the largest and most important diabetes centre in Scandinavia. In 1957, a research laboratory was attached to the hospital, and in 1978 it was named the Hagedorn Research Laboratory. Its purpose was basic research. In 1938, Novo founded Hvidøre Diabetes Sanatorium, the name of which was changed to Hvidøre Hospital in 1949. At Hvidøre, the treatment received by patients at public hospitals was checked and adjusted. For many people with diabetes, a stay at Hvidøre enabled them to live an almost normal life when they returned home. Hvidøre also became a centre for research and clinical testing of Novo's new insulin products. In 1992, Steno Memorial Hospital and Hvidøre Hospital merged to form the Steno Diabetes Center.

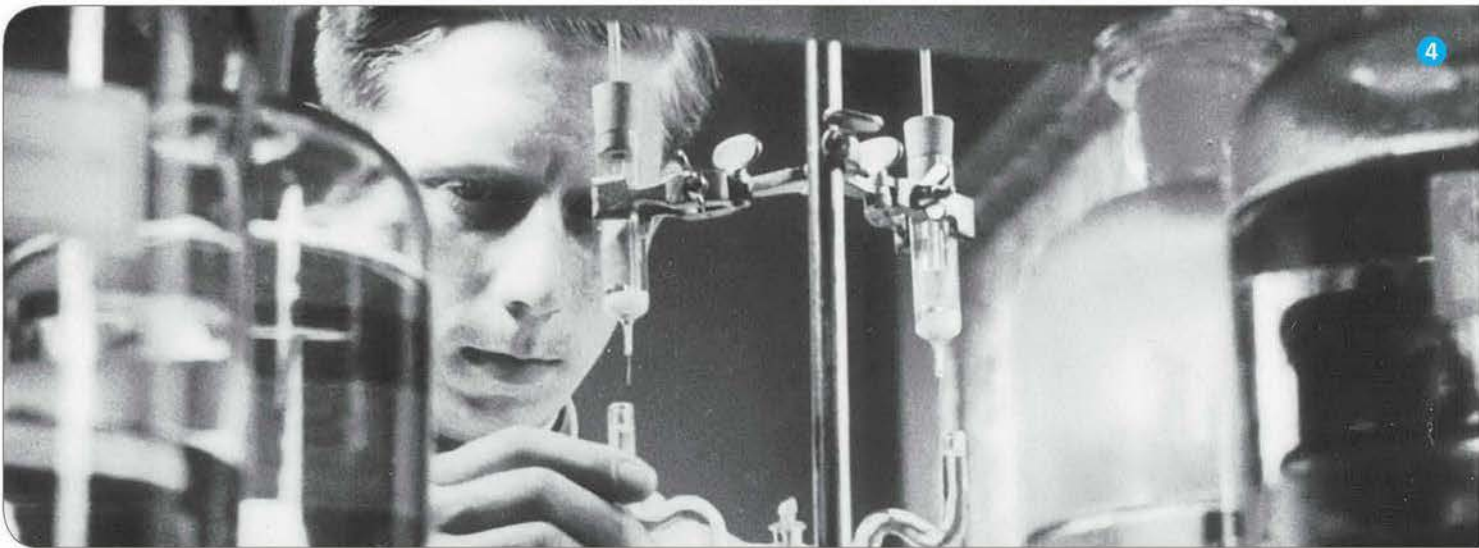
#### New man at Novo

In 1937, a pharmacist, Knud Hallas-Møller, joined Novo. He had an extraordinary talent for research and management, and over the next decades he became a central figure in the firm. His first task at Novo

was to find an alternative to ZPI, the action profile of which was not optimal. In 1944 he developed a number of insulin products with both rapid and slow action. While these products were widely used in many countries, ZPI remained popular among patients and continued to account for a substantial part of Novo's insulin sales.

#### News from Nordisk

The main event in diabetes treatment in the 1940s took place at Nordisk. In 1946, two of its researchers, C Krayenbühl and Th Rosenberg, succeeded in producing crystalline protamine insulin. The crystalline form meant that it was now possible to mix protamine insulin with rapid-acting insulin without any loss or change of effect in either product. This unique product was launched on the US market in 1950 under the name NPH – short for Neutral Protamine Hagedorn. NPH was a great success and soon accounted for a large part of the western world's consumption of longer-acting insulin.



## The search for purer insulin

Following the introduction of the successful NPH insulin by Nordisk, a research team was gathered together at Novo with the aim of developing an insulin product that would be just as good as NPH insulin or perhaps even better.

The research team achieved its aim. In 1953, Novo was able to present the Lente® products, which for several years covered nearly a third of the world's insulin consumption. The Lente® series consisted of three medications, each with its own degree of prolonged action, achieved through a chemical combination of insulin and zinc. This enabled doctors to prescribe a dosage regimen suited to the needs of the individual. At the same time, the prolonged action was achieved without use of non-insulin-related agents. For patients, this had the added benefit of fewer allergic reactions.

### Insulin and antibodies

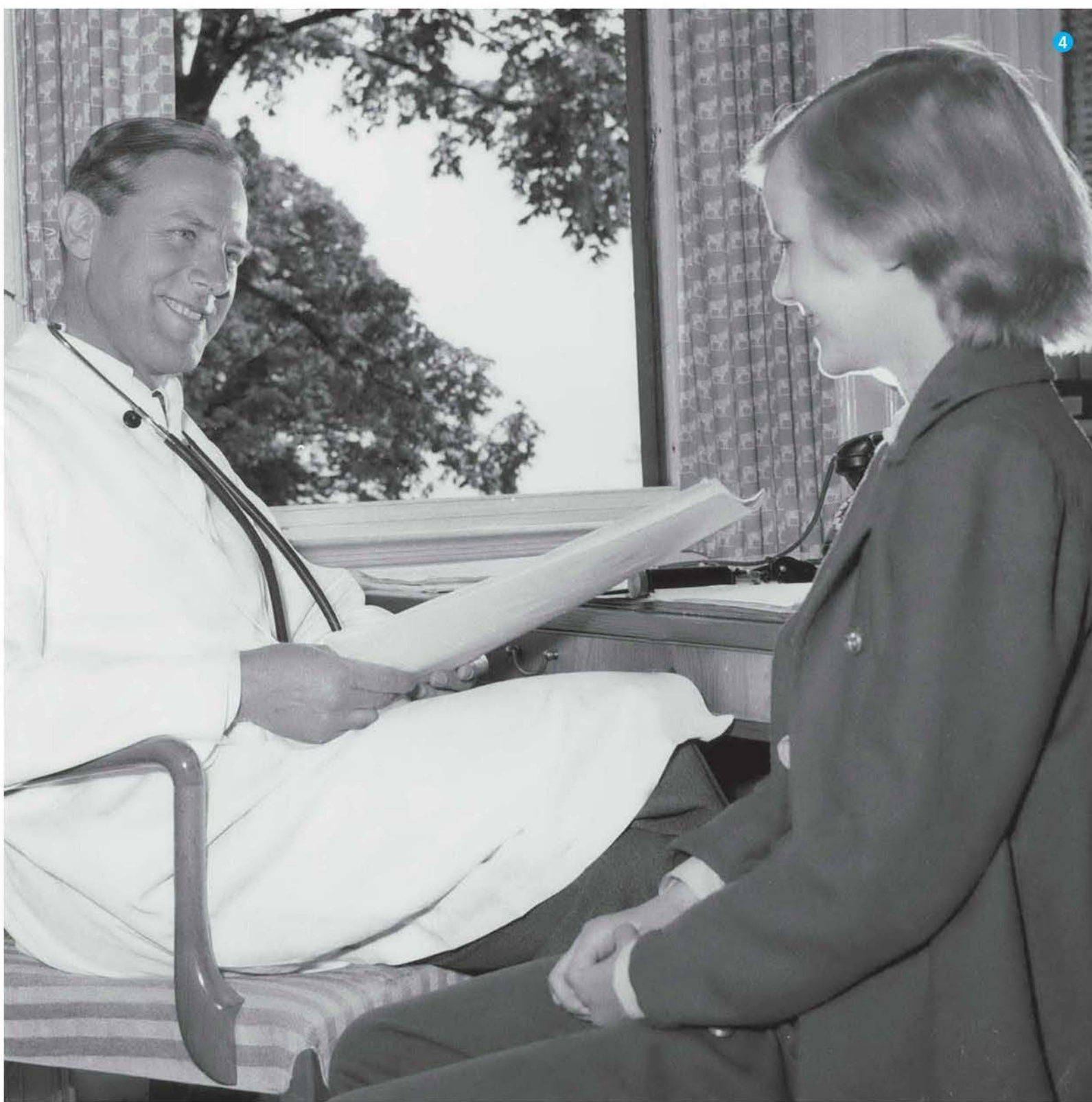
Although insulin products had become much purer than in the 1920s, there were still many problems to be solved. In 1960, US studies showed that all people with diabetes formed antibodies against insulin. This meant that the effect of the insulin was somewhat weakened and that patients would need

larger and larger doses to keep their disease under control. There were also still cases of patients becoming allergic to insulin.

To find the reason for these effects, insulin was studied with the help of new and very sensitive methods. This revealed 'impurities', ie small quantities of substances originating in the basic material for insulin production. Researchers at both Novo and Nordisk now concentrated on purifying the insulin products to reduce or perhaps even avoid 'impurities' and the development of antibodies.



- 1 The three inventors of the Lente® products, (from left) Knud Hallas-Møller, Jørgen Schlichtkrull and Karl Pedersen.
- 2 In 1952, the first 200 Arne Jacobsen 'Ant' chairs were produced for Novo's new canteen.
- 3 For a time, the Lente® products covered up to a third of the world's insulin consumption.
- 4 A consultation at Hvidøre Hospital in the 1950s, when Novo launched the Lente® products.







### New, highly purified products

In 1973, the research on antibody reactions led to the introduction by Novo of Monocomponent insulin (MC insulin). The name refers to the product's unusual purity, in that it consisted largely of just one component: the insulin itself. In 1977, Novo was able to market a complete range of insulin products of MC standard.



Nordisk also developed improved purification methods, and in 1974 it launched a highly purified porcine insulin. Nordisk made only porcine insulin after 1967, when US studies revealed that bovine insulin produced more antibody reactions than porcine insulin.

Clinical tests showed that people with diabetes formed far fewer antibodies when treated with highly purified insulin from Novo and Nordisk. Doctors therefore felt safe in prescribing the new products for patients who had previously developed insulin allergies.

It was also found that with highly purified insulin, the dosage needed to control the disease could be reduced.

1 By 1977, Novo's entire portfolio of insulins was of Monocomponent quality.

2 In 1974, Novo's kindergarten opened in Bagsværd. It was one of the first company childcare facilities in Denmark.

3 Highly purified insulin from Nordisk.



## International growth



1 Knud Hallas-Møller, Novo's CEO from 1961 to 1981, and Mads Øvlisen, CEO at Novo from 1981 to 1989 and Novo Nordisk CEO from 1989 to 2000.

2 A 1935 export advertisement for Insulin Novo.

3 In 1958, Novo established its first subsidiary in Mainz, Germany. The building was constructed a decade later.

4 In the 1960s, Novo moved to a 122,000 square metre site in Bagsværd, north of Copenhagen.

At the beginning of the 1970s, Novo and Nordisk could look back on 50 years in which they both had developed insulin products that had improved the quality of life of people with diabetes. Novo was the larger company, having gained an impressive worldwide market share. The Pedersen brothers began exporting to the rest of Scandinavia and Germany as early as 1926, later expanding into other European markets, the Middle East and Latin America. By 1936 Novo was supplying insulin to no less than 40 countries.

### New markets

The Lente® insulins made Novo one of the world's leading insulin manufacturers. In 1959, Novo built its first laboratories in Bagsværd, and in the 1960s, this city became the headquarters of the company's activities. Subsidiaries had been established a few years earlier in Germany, France and South Africa, and by 1975 Novo had 14 subsidiaries.

### Continuity and innovation

Knud Hallas-Møller played a crucial role in the development of Novo, first as a scientist and later as CEO from 1961 to 1981. To cope with the growing sales, Hallas-Møller restructured the company at the beginning

of the 1960s, creating a dynamic, product-oriented organisation that generated further growth for Novo in the ensuing decades. In 1974, this continuous growth culminated in the introduction of Novo's B shares on the Copenhagen Stock Exchange.

Two years earlier, in 1972, a young lawyer was hired for a one-year project aimed primarily at introducing the company on the stock exchange. The lawyer's name was Mads Øvlisen, and he had just returned to Denmark with an MBA from Stanford University in California. As secretary to the Board of Directors, it was his job to facilitate the public offering by going through the company structure.

What began as a temporary assignment turned into more than three decades of service to the company, during which he as CEO from 1981 to 2000 exerted a decisive influence on some of the most important events in the history of the company. With his special talent for commitment, Mads Øvlisen also brought an exceptional quality to Novo Nordisk. Based on ideas that reach back to the founders of the company, he developed, defined and implemented the fundamental values that still characterise the Novo Nordisk of today.





1 In July 1981, Novo became the first Scandinavian company to introduce its shares on the New York Stock Exchange.

2 A restructuring in 1980 created Nordisk Gentofté. The company's shares were listed on the Copenhagen Stock Exchange in 1986.

3 Novo's B shares were quoted on the Copenhagen Stock Exchange for the first time on 17 May 1974.

### Sales in the US

In 1979, Novo's subsidiary in the US began marketing the company's MC insulins. This was difficult initially, because Novo was not allowed to mention the advantages of the new products until American clinical studies had confirmed the results of the European tests.

However, by collaborating with the US pharmaceutical company Squibb, which had an extensive sales organisation and a nationwide distribution system, the US became in 1982 Novo's largest market for insulin and other pharmaceutical products.

In 1980, Novo established its own sales organisation in Japan. This resulted in explosive sales growth, and Japan quickly became Novo's largest pharmaceutical market, closely followed by the US.

### Problems at Nordisk

At the beginning of the 1970s, the situation at Nordisk was critical. The company had almost no exports. The reason for this was

that the management, led by Hagedorn, did not want increased marketing of the company's products. What mattered most, the management felt, was research and the treatment of diabetes.

### Changing times

During the 1970s, however, the new management pursued an intensive marketing policy which resulted in Nordisk gaining a share of export markets including the US, particularly with its highly purified porcine insulin. The management restructured the company in 1980, spinning off production, sales and applied research into a separate unit under the name of Nordisk Gentofté. In 1984, Nordisk Gentofté was transformed into a public limited company, and in 1986 its shares were listed on the Copenhagen Stock Exchange. With this, the company – like Novo – had a corporate structure that was well prepared for continued international growth.



## Human insulin



Following the introduction of highly purified insulin in the 1970s, both companies set their sights on a new goal: to produce human insulin – insulin that was exactly like the insulin produced by the human body.

Many difficulties had to be overcome, but in 1982 Novo succeeded in its endeavours, becoming the first company in the world to convert porcine insulin into human insulin by replacing a single amino acid in the porcine insulin molecule. This produced an insulin with the same molecular structure and properties as the insulin produced by the human body. Nordisk took up the gauntlet, and was able to introduce human insulin just two years later.

Tests showed that patients developed even fewer antibodies when treated with human insulin, and that those who suffered allergic reactions to highly purified porcine insulin could benefit from the new human insulin.

### Genetic engineering

In 1987, Novo began industrial production of human insulin on the basis of genetically engineered yeast cells. This meant that Novo was no longer dependent on animal pancreases and could therefore produce almost unlimited quantities of insulin. Nordisk also developed a method of making human insulin by means of genetic engineering, but did not manage to get the product to market before the merger in 1989.

1 Jan Markussen was a research chemist at Novo. In 1979, he suggested a method of converting porcine insulin into human insulin.

2 Human insulin from Novo.

3 Novo's presentation of the world's first human insulin in 1982 was a big event.

4 Human insulin from Nordisk.









1

**Nordisk Infuser and NovoPen®**

In the 1980s, doctors became aware that long-term diabetic complications such as kidney failure and blindness could be delayed or avoided with better control of patients' blood sugar. In 1983, Nordisk therefore marketed an insulin pump called Nordisk Infuser. Just like the pancreas of healthy people, this pump constantly released small quantities of insulin to the body, giving the patient an almost normal blood sugar level.

delighted with the convenient NovoPen® device, and before long it was selling all over the world.

Nordisk decided to develop an insulin pen as well, and in 1986 it introduced its Insuject® device to the market. Three years later, Novo presented the world's first disposable insulin syringe, NovoLet®. Because it was prefilled with insulin, it was the simplest way of taking an insulin injection – NovoLet® was always at hand, easy to operate and offered high dosage accuracy. With their highly purified insulin products, human insulin, elegant pen devices and mastery of the new genetic engineering techniques, the two Danish companies were now in a strong position as international competition increased. Before long, however, they had to admit that they could achieve even better results by combining their efforts.



2

Novo chose a different solution, introducing in 1985 the elegant NovoPen® device. The pen gave people with diabetes a simple means of injecting themselves with precisely the right dose of insulin several times a day. This meant better control of their blood sugar level and a reduced risk of developing the unpleasant long-term diabetic complications. Patients were

1 Nordisk Infuser.

2 The first NovoPen® device.

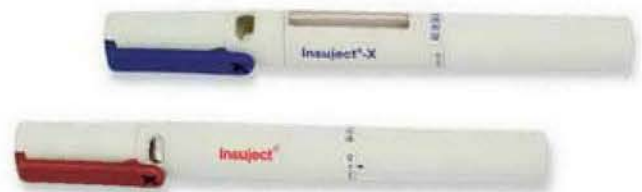
3 Insuject®.

4 Patient injecting himself using a NovoLet® device.

5 NovoLet® – the world's first disposable insulin syringe.

6 Training in the kitchen at Steno Memorial Hospital, ca. 1990.

3





## More than insulin



1 Alexander Fleming, the discoverer of penicillin, in his laboratory.

2 Novo's first fermentation tank for the production of penicillin.

3 Novo's range of penicillin products in the 1950s.

4 Drums and sacks of amylase, which was used in the textile industry.

During World War II, rumours of the incredible properties of penicillin reached Denmark. The Pedersen brothers and Hallas-Møller immediately realised the potential of this new drug, and in 1943 they started a series of experiments with fermentation of penicillin. The experiments presented many problems, but in 1947 Novo was able to introduce Penicillin Novo, the company's first product to be made by fermentation.

The next few years brought rapidly rising sales of penicillin and other antibiotics, and Novo had to increase its fermentation capacity. However, at the end of the 1960s, competition on the international market was so tough that Novo decided to reduce its range of products to just a few types of penicillin.

Nevertheless, penicillin continued to account for a substantial part of the company's turnover. In 1994, Novo Nordisk decided to divest its penicillin business because the management wanted to concentrate on the group's core businesses.

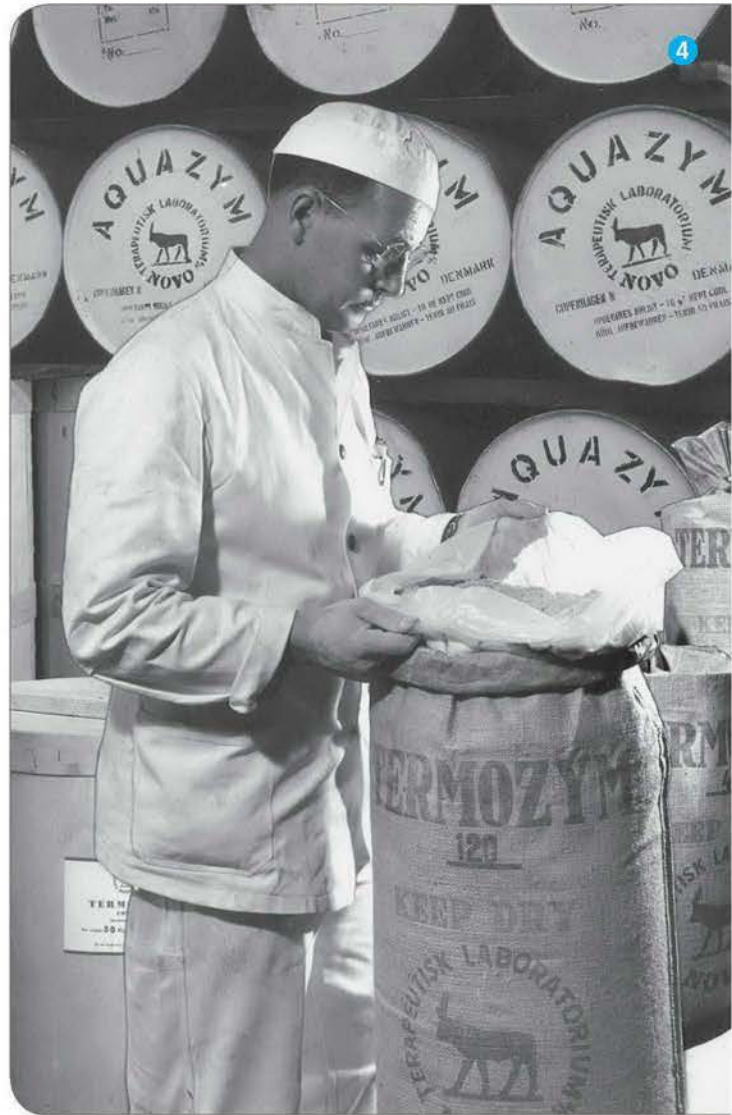
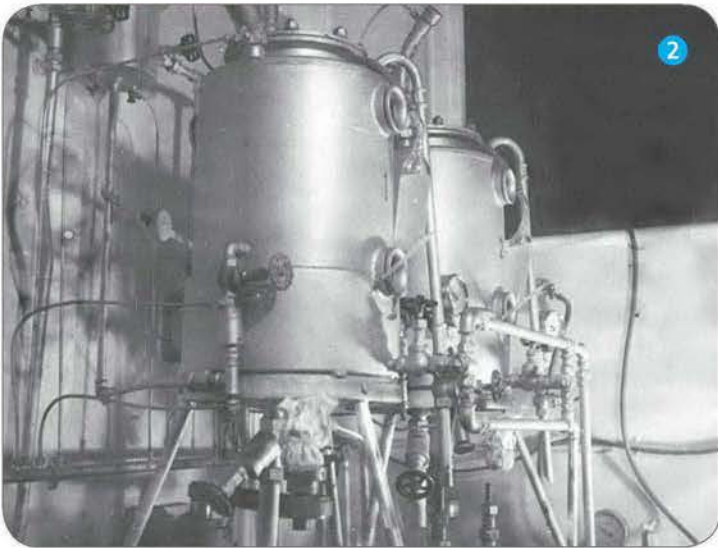
### Trypsin

Thorvald and Harald Pedersen were already aware in 1925 that the pancreas also contains trypsin, an enzyme used in the

tanning industry to soften leather. They assumed, however, that the process of extracting insulin destroyed the trypsin. But during World War II there was such a shortage of pancreases that Novo decided to look for a method of extracting insulin and enzymes from the same gland. The effort succeeded, and in 1941 Novo was able to introduce its first enzyme product for industrial use.

### An employee gets a bright idea

Trypsin sold brilliantly in the 1940s, and therefore, Novo decided to market yet another enzyme extracted from the pancreas. This was amylase, which is used in the textile industry for desizing. Just as production was about to begin, the Novo fermentation chemist Bruno Steinhardt had an unusually good idea. He suggested making amylase by fermentation – that is, by finding a bacterial strain that could produce the enzyme in a fermentation process. The idea was an obvious one, since Novo was already using fermentation technology to produce penicillin. Novo's management was not entirely convinced that the idea would work, but gave permission – somewhat reluctantly – for a series of tests. The management's misgivings quickly proved groundless. After a short time, company researchers succeeded in getting bacteria to





1 Dust-free Alcalase®.

2 Newspaper articles announcing that detergent enzymes present no danger to consumers.

3 Detergents containing Alcalase®.

produce amylase. That event heralded Novo's immense success with the fermentation of enzymes.

#### A true detergent enzyme success story

In 1960, Novo's researchers accidentally found themselves in possession of a remarkable enzyme. To their astonishment, they found that it had all the properties detergent manufacturers were looking for. It could remove obstinate blood and sweat stains and interact easily with other substances in the detergent. The new enzyme product was named Alcalase® and became Novo's first detergent enzyme produced by fermentation.

In 1963, a Dutch firm launched the detergent Bio-tex, which contained Alcalase®. Bio-tex became a huge success, and before long detergents containing Alcalase® had conquered the world market.

#### Problems in the US

In 1969, an article that created serious problems for Novo's enzyme production appeared in a medical journal. According to the article, some workers at a British detergent factory had developed an allergy after inhaling concentrated enzyme dust. The article attracted massive media attention in the US due to fears that consumers might

also develop allergies. Then the American consumer activist Ralph Nader launched a campaign against enzymes in detergents. For the first time, Novo experienced the great influence an NGO campaign could have on public opinion and, consequently, on company sales. From 1969 to 1971, Novo's yearly turnover plummeted from over 500 million to 250 million Danish kroner. This in turn made it necessary to dismiss 400 Danish employees, reducing the total company workforce from 2,100 to 1,700.

#### All's well that ends well

To reduce the risk of allergies, Novo developed dust-free enzyme products, and in November 1971, the US Food and Drug Administration concluded that detergent enzymes presented no risk to consumers. Everyone at Novo was relieved, and over the next couple of years, sales figures and the number of employees began once again to grow.

However, the confrontation with activists such as Ralph Nader laid the groundwork for a focus on exchanging views with external stakeholders to find common solutions. This focus grew along with an increasing interest in sustainable development, and today Novo Nordisk works with a great many NGO partners.

**ENZYMIER  
TILVASK...**





1

1 In Japan, about half of the detergent market in the 1980s consisted of detergents with enzymes. Novo was the sole enzyme supplier.

2 Enzyme production in 1969 at Novo's new enzyme factory in Kalundborg.

3 In 1979, Novo built an enzyme plant in North Carolina, US.

4 The number of Novo employees tripled during the 1960s.

5 The world's most modern enzyme factory was built in 1986 at Ishikari Bay, Japan.

### Enzymes for the starch industry

In the years that followed, Novo launched a number of new and improved enzyme products, not just for detergents, but for many other industrial applications. The starch industry in particular became a big customer, using enzymes to convert starch into sugar. In 1974, Novo marketed the enzyme product Sweetzyme®, which breaks starch down into high-fructose syrup – a mixture of fructose and glucose with the same sweetening capacity as sugar. The syrup is used as a sweetener in many food products, including soft drinks, ice cream and confectionery. Sweetzyme® was the first immobilised enzyme made in large quantities for the starch industry. The word 'immobilised' means that the enzymes can be used continuously for several months. The US became by far the largest market for Sweetzyme®, but countries like Japan and South Korea also became major customers.

### New plants

To keep up with the growing demand for industrial enzymes, Novo's management decided on a substantial increase in fermentation capacity. The first step was a new enzyme plant at Kalundborg, Denmark, inaugurated in 1969. In 1979, Novo celebrated the opening of a plant in

the US city of Franklinton, North Carolina. In 1986, the company built a plant in Japan – one of the world's largest markets for industrial enzymes – and in 1989, Novo Nordisk opened an enzyme plant at Curitiba, Brazil.

### The world's first fat-splitting enzyme

Although Novo had developed a wide range of efficient detergent enzymes, company researchers still needed to solve a major problem. They had not yet found an enzyme that could dissolve greasy stains. The breakthrough came in the autumn of 1987. Novo's researchers became the first in the world to develop a bacterial strain that could produce large quantities of a fat-splitting enzyme. The enzyme was given the name Lipolase®. This was Novo's first genetically engineered enzyme product, and it reached the market just four months after the enzyme researchers' triumph in the laboratory. Novo had once again managed to develop an enzyme with desirable properties, and before long Lipolase® was being used in a wide range of detergents all over the world.







### Other pharmaceutical products

Enzymes and insulin were not Novo's only successful products. In 1951, the company launched Heparin Novo, which was used to prevent blood clots. Novo sold the product to hospitals and dialysis centres and exported it to Japan and other countries. At the end of the 1980s, Novo began clinical testing of Logiparin® – a low-molecular heparin with considerably better properties than traditional heparin. This product was launched by Novo Nordisk in 1991, but in 1994 the company decided to divest it because of unsatisfactory sales.

In 1964–65, Novo introduced a number of hormone products, including oral contraceptives. However in the mid-1970s, tests showed that these medications contained a steroid which, when given in large doses, was harmful to dogs. The researchers did not know whether the steroid was also harmful to women, but, preferring to be on the safe side, Novo immediately withdrew its oral contraceptives from the market. However, Novo continued its gynaecological research, introducing Trisequens® in 1977 and Kliogest® in 1984. Both were hormone replacement therapy (HRT) products used to treat menopausal problems and to prevent osteoporosis.

Novo now also turned its attention to developing pharmaceuticals to treat diseases of the central nervous system (CNS). This field of research was strengthened in 1986, when Novo took over the Danish pharmaceutical company Ferrosan A/S, whose staff included internationally recognised CNS researchers. In 1992, this research enabled Novo to launch Seroxat®, a medication for the treatment of depression. In 1995, Novo Nordisk decided to divest Ferrosan as a result of a new corporate strategy to focus on the company's core businesses.

1 Trisequens® and other HRT products in tablet dispensers.

2 Filling machine constructed at Novo for tablet dispensers with HRT products.

3 Novo marketed its oral contraceptives with photographs of the 'mother and child' sculptures by the Danish artist Kai Nielsen.



**Delpregnin<sup>®</sup>**

3

**Familieplanlægning med Delpregnin  
– det orale antikonceptionsmiddel**

Sanofi Exhibit 2137.034  
Mylan v. Sanofi  
IPR2018-01676

## News from Nordisk



At the beginning of the 1960s, Hagedorn received a visit from a specialist in children's diseases, Professor Henning Andersen. In his work, Professor Andersen had seen the unhappy consequences of growth disturbances in children. He therefore asked Hagedorn to begin manufacturing human growth hormone, which was used for treating short stature due to growth hormone insufficiency. It was a good suggestion, because Nordisk's experience in purifying insulin could also be used to extract and purify growth hormone.

### Production begins

Growth hormone was extracted from the human pituitary, a pea-sized gland at the base of the brain. Following a strict procedure, Hagedorn and his employees began collecting pituitary glands from the pathology departments of several hospitals. The glands were frozen and taken to Nordisk for extraction of the hormone. In 1966, Professor Andersen treated the first patients with the growth hormone Nanormon®, which was made by Nordisk. The results were good, and in 1973, Nanormon® was approved by the health authorities in Denmark.

### Rising sales

Sales of Nanormon® rose rapidly through the 1970s and 1980s. Most of the output was exported, and Nordisk became one of the world's largest manufacturers and exporters of human growth hormone. One reason for this success was that Nordisk had developed new methods of purification which improved the purity of the growth hormone.

Together with doctors at the Steno Memorial Hospital, Nordisk also investigated how often patients should take the growth hormone. Normally, patients were given a specific dose of growth hormone every other day, but the company's researchers discovered that growth was far better when the growth hormone was taken every day.

1 Nanormon® was Nordisk's first human growth hormone.

2 Norditropin®.

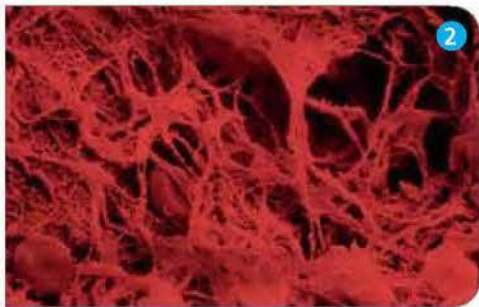
3 Norditropin® is made by fermenting genetically engineered microorganisms.



Sanofi Exhibit 2137.036  
Mylan v. Sanofi  
IPR2018-01676



1 A few of Nordisk's laboratory and production buildings in Gentofte, circa 1987.



2 Blood products were manufactured from plasma of human blood.

3 Optimising the fermentation process during the manufacture of growth hormone.

4 Nordiject® enabled patients to inject themselves easily and almost painlessly with growth hormone.

5 A nurse explains how to use Nordiject®.

### Genetic engineering

When children of short stature due to growth hormone insufficiency were treated with Nanormon®, they achieved normal or almost normal height. However, difficulties in obtaining sufficient human pituitary glands made it impossible to treat all the children needing the growth hormone.

Therefore, in 1982, Nordisk began manufacturing human growth hormone by means of genetically engineered microorganisms. This meant that enough growth hormone could now be produced to treat all children suffering from growth hormone insufficiency. The first treatments with Nordisk's new, genetically engineered growth hormone, which was given the name Norditropin®, took place in 1985, and by 1988 the product had been approved in most European countries and in Japan.

At the end of the 1980s, researchers at Nordisk began to study whether Norditropin® could be used to treat other diseases, including Turner syndrome, stunted growth in children due to chronic renal insufficiency, and growth hormone deficiency in adults.

In 1990, Norditropin® was approved for the treatment of Turner syndrome, and in 1995 it was marketed for the treatment of children of short stature due to chronic renal insufficiency. In 1989, the company launched Nordiject®, a pen device with which patients could inject themselves with growth hormone.

### Plasma products

In the 1970s, at the request of the Danish health authorities, Nordisk launched a number of products made from plasma of human blood. The reason for the authorities' request was that the World Health Organization (WHO) had asked all countries to become self-sufficient with regard to blood products.





1 Blood plasma products from Nordisk.

2 Fermentation tank for the production of growth hormone.

3 Blood plasma production.

### Albumin and haemophilia medications

The first plasma product introduced by Nordisk was albumin. It was used to treat patients who had suffered loss of fluid in connection with, for example, a traffic accident or an operation. The company also began production of the haemophilia medications factor VIII and factor IX. The blood of people with haemophilia lacks the ability to coagulate, but when treated with the factor products, coagulation is almost normal. During the 1980s, Nordisk supplied blood products to a large part of the Danish market.

### New products developed

Nordisk followed up with a number of new and improved blood products. In 1988, the company developed Nordimmun®, which was given to people with a reduced capacity for producing antibodies; in 1991, it was launched in Denmark by Novo Nordisk, and within two years it had conquered half the Danish market. Before long, the product was also marketed in other parts of Europe. In 1988, Nordisk began developing Nordiate®, a new, double virus-inactivated factor VIII product which was almost 10 times purer than earlier factor VIII products. It was marketed in Denmark by Novo Nordisk in 1995.

### The haemophilia lawsuit

Like a number of other countries in Europe and elsewhere, Denmark has had its 'haemophilia lawsuit': in 1987, the Danish Haemophilia Society brought a civil action against the Ministry of the Interior, the National Board of Health and Nordisk. The Haemophilia Society alleged that a number of Danes with haemophilia had been infected with the HIV virus after using haemophilia medicine from Nordisk. The High Court ruled in 1995 that it had not been proven that haemophilia patients had been infected by blood products from Novo Nordisk. Therefore, it gave judgment in favour of the defendant.





## A dynamic merger

A lot had happened since that modest start in the 1920s. By the end of the 1980s, Nordisk had become the world's third-largest insulin manufacturer and one of the world's largest manufacturers and exporters of human growth hormone.

Novo had become the world's second-largest manufacturer of insulin and the world's largest manufacturer of industrial enzymes. Both companies exported more than 90% of their production and both had subsidiaries and information offices in many countries around the world.

### Novo Nordisk A/S

In January 1989 came the news that Nordisk Gentofte A/S and Novo Industri A/S\* were joining forces under the name

of Novo Nordisk A/S, giving Denmark the honour of having the world's leading manufacturer of insulin. The decision to merge was made because cooperation between the two companies' strong research units would increase the possibility of developing new products within diabetes treatment and allow intensified research in other areas. Moreover, the two together would have the size and strength to improve their competitiveness on international markets. Having competed with each other for more than 60 years, the two companies could now concentrate their combined forces on conquering the world markets.



1 Novo Nordisk's logo, as it looked after the merger in 1989.

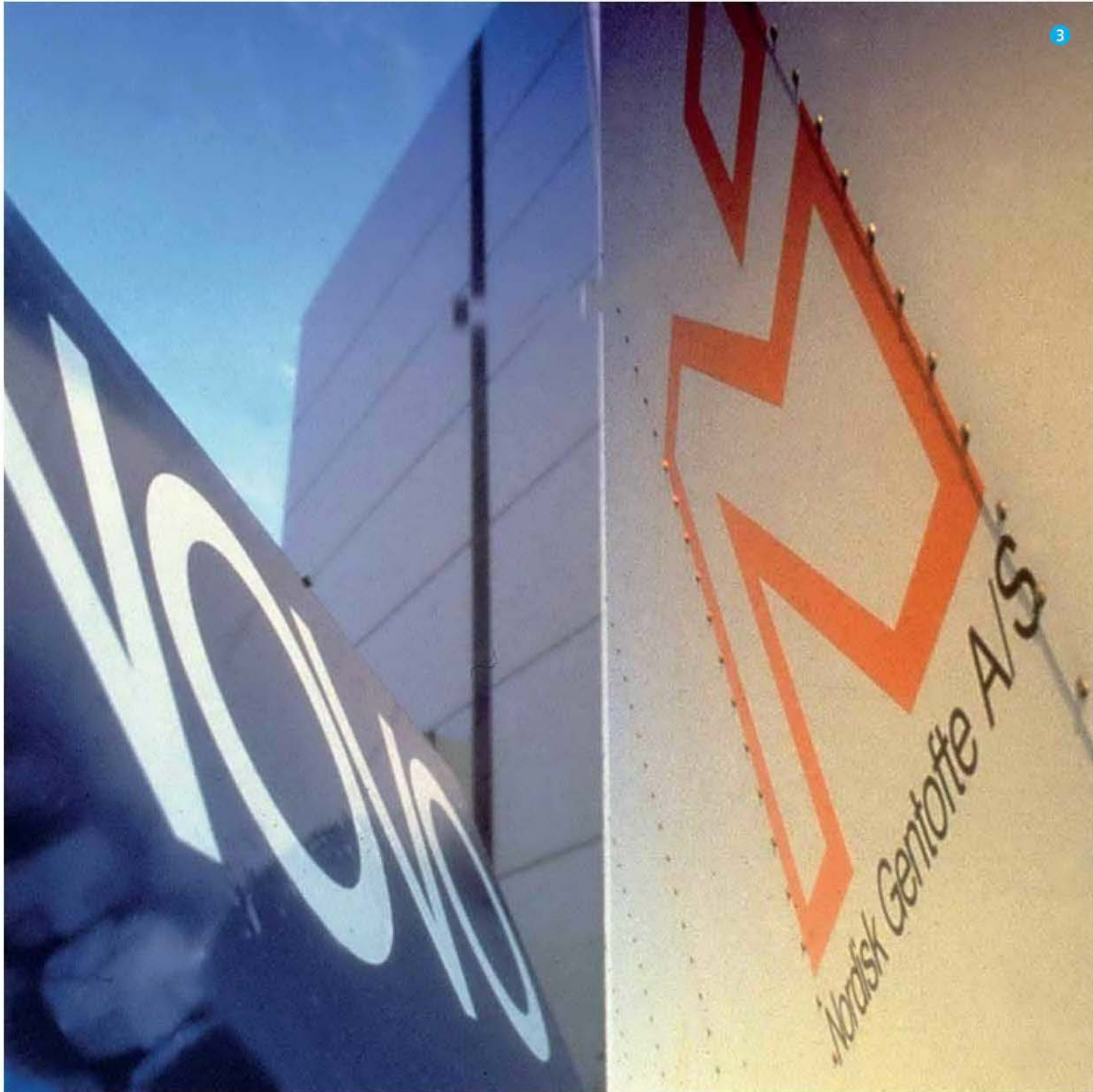
2 The two chief executives in Novo Nordisk: Henry Brennum (left) from Nordisk and Mads Øvlisen from Novo. In 1990, Henry Brennum died and Mads Øvlisen became president and CEO.

3 The merger made the two companies considerably more competitive.

2



\*With effect from January 1976, the parent company Novo Terapeutisk Laboratorium A/S was amalgamated with its subsidiary under the name of Novo Industri A/S.



## The Novo Nordisk Foundation



1 The Novo Nordisk Foundation's flagship is the Novo Nordisk Prize. Professor Jan Fahrenkrug (left), DMSc, chairman of the Novo Nordisk Foundation's Prize Committee, presents the Novo Nordisk Prize 2009 to Professor Søren Nielsen, MD, CEO.

2 Nordisk Insulin Foundation was established in 1926.

3 The Novo Foundation was established in 1951.

4 The Novo Nordisk Foundation was established in 1989 by a merger of Nordisk Insulin Foundation and the Novo Foundation.

The merger in 1989 also brought the establishment of the Novo Nordisk Foundation – an independent institution whose objectives were to create a solid basis for the operation of Novo Nordisk and to support scientific, humanitarian and social causes.

The Foundation owns all Novo Nordisk's A shares and thus has the majority vote at general meetings. This ensures that Novo Nordisk will remain an independent company in Danish hands.

The funds distributed by the Foundation come from interest, capital gains and dividends on the Foundation's shares in Novo Nordisk. The Foundation is headed by a board of directors which is not involved in the day-to-day management of the company.

### Nordisk Insulin Foundation

The Novo Nordisk Foundation was not the first foundation in Novo Nordisk's history, however. In 1926, Krogh and Hagedorn established Nordisk Insulin Foundation to provide financial support for scientific purposes. The foundation's funds consisted of a portion of Nordisk Insulinlaboratorium's profits plus the return on the foundation's equity capital.

Until the merger, the board of the Nordisk Insulin Foundation consisted of 12 scientists from the Scandinavian countries, and August Krogh was its first chairman.

### The Novo Foundation

In 1951, Harald and Thorvald Pedersen established the Novo Foundation. At the time, Novo was enjoying a period of rapid growth, and the foundation was meant to ensure Novo's future as an independent Danish company. The Pedersen brothers also decided that the foundation should provide financial support for scientific, humanitarian and social causes. Over the years, medical research in Denmark has benefited greatly from the Novo Foundation, the Nordisk Insulin Foundation and their present-day successor – the Novo Nordisk Foundation.

2

**NORDISK INSULINFOND**

3

**NOVO'S FOND**  
OPRETTET 1951

**NOVO NORDISK FONDEN**



## A global challenge



1 Aleksey Evstratov lives in Russia and has type 1 diabetes.

2 A diabetes clinic in Tanzania.

3 In 2001, Novo Nordisk established the World Diabetes Foundation with the aim of supporting projects to improve diabetes care in developing countries.

4 In 2005, the Novo Nordisk Haemophilia Foundation was established with the purpose of supporting projects which contribute to improving haemophilia care in developing countries.

5 Lu Zhongqian from China, pictured here with his parents, is one of the people with haemophilia to benefit from the first successfully completed project in China supported by the Novo Nordisk Haemophilia Foundation.

According to an estimate by the International Diabetes Federation (IDF), there were approximately 285 million adults with diabetes in the world in 2009. IDF further estimates that the number will increase to 435 million worldwide before the year 2030. Thus, as one of the most costly diseases in human as well as economic terms, diabetes is growing into one of the world's biggest health problems. Especially in the developing world, where the rise in the number of people with type 2 diabetes has reached epidemic proportions, there is a need for concerted action to defeat diabetes. That is why Novo Nordisk in 2001 launched a number of initiatives that aim to improve diabetes care in developing countries. These initiatives, known as LEAD (Leadership in Education and Access to Diabetes care), are based on cooperation with international NGOs (nongovernmental organisations), local authorities and diabetes associations.

### World Diabetes Foundation

The most prominent of the LEAD initiatives is the World Diabetes Foundation, an independent foundation whose purpose is to support projects to improve diabetes care in developing countries. The foundation was established by Novo Nordisk, and the company committed itself to a donation of

500 million Danish kroner over the following 10 years. The World Diabetes Foundation is a modern continuation of the Novo Nordisk Foundation's tradition for supporting humanitarian and scientific work.

### Haemophilia

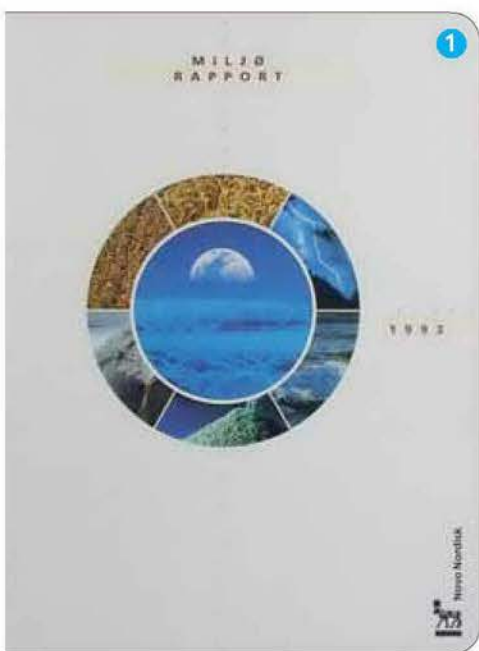
Access to care and treatment is also a problem for people with haemophilia in the developing world, where 75% of the global haemophilia community resides. Many lack diagnosis and adequate care, as haemophilia is not a healthcare priority in these countries.

### Novo Nordisk Haemophilia Foundation

To address this need and move haemophilia higher up on the global agenda, Novo Nordisk launched a new initiative in 2005 called the Novo Nordisk Haemophilia Foundation (NNHF). The NNHF works with the haemophilia community, authorities and other relevant partners and funds development programmes that include patient education and training of healthcare professionals as well as diagnostic facilities and registries. Funding consists of donations from the Novo Nordisk Haemophilia Foundation.



## Sustainable development



1 In 1994, Novo Nordisk published its first environmental report; in 1995, the company received an award for best green accounting in Europe.

2 The principle of the Triple Bottom Line.

3 Since 2007, the company's energy savings have been earmarked to buy electricity from DONG Energy's offshore wind farm in the North Sea.

4 Organic waste is reused as fertiliser.

5 Novo Nordisk works continuously to improve conditions for experimental animals.

In 1974, the first environmental protection act was passed in Denmark, and in 1975, Novo established an independent environmental unit whose tasks included measuring waste water, noise and smell from production. In 1992, the UN held an environmental conference in Rio de Janeiro. For Novo Nordisk, this conference was an inspiration that further strengthened the company's direction towards sustainable development.

### Environmental reporting

In 1993, Novo Nordisk was the first company in Denmark, and one of the first in the world, to prepare an environmental report describing its resource consumption, emissions and use of experimental animals. The report was published in 1994. Since then, Novo Nordisk has set new targets every year for its environmental performance. Targets include more efficient use of resources and minimising the use of animals for research. Environmental reporting helps maintain a focus on continuous improvement and creates transparency about impacts and goals.

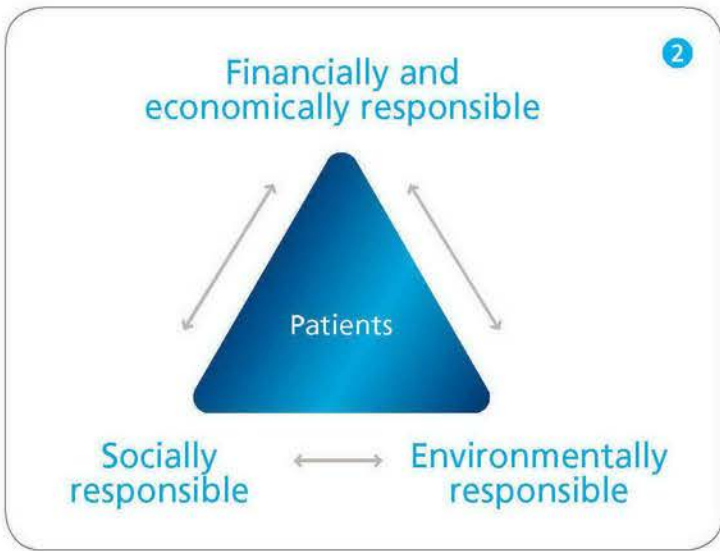
### Social reporting

In 1999, Novo Nordisk published its first report on social responsibility, covering activities in 1998. The report set targets

and followed up on the company's efforts to live up to its social responsibility towards employees, patients, communities and other stakeholders. In 2002, Novo Nordisk signed the United Nations Global Compact, promoting good corporate principles within human rights, labour, environment and anti-corruption. In 2006, Novo Nordisk joined the WWF's Climate Savers initiative, committing itself to reducing CO<sub>2</sub> emissions by 10% by 2014 compared to 2004, despite significant projected growth in production.

### The Triple Bottom Line

In 2004, Novo Nordisk's Articles of Association were amended to specify that the company will "strive to conduct its activities in a financially, environmentally and socially responsible way". This reinforced the company's commitment to the principles of the so-called Triple Bottom Line. Since then, environmental and social performance has been presented in the annual report alongside financial results.





## Business strategy



1 In 1997, a new plant in Koriyama, Japan, was inaugurated.

2 In 2000, Novo Nordisk inaugurated a 16,000 m<sup>2</sup> facility in Hillerød, Denmark, for the production of the NovoLet® prefilled insulin pen. Two years later, the foundation stone was laid for a new NovoSeven® factory.

3 In 2007, Novo Nordisk's insulin production plant in Montes Claros, Brazil, was expanded, and production at the site increased fivefold.

4 The groundbreaking ceremony for Novo Nordisk's new plant in Tianjin, China, took place on 7 November 2008.

In 1994, Novo Nordisk implemented a new business strategy to ensure progress in a rapidly changing and ever more competitive world. Focus was on the two core business areas, Health Care and Enzyme Business, while other areas such as Ferrosan (dietary supplements and other over-the-counter products) and Plant Protection (biological plant protection) were divested.

The plan for Health Care was to develop the diabetes care business to encompass a broader portfolio of products and services that offer patients and healthcare professionals better treatment solutions. At the same time, efforts were made to reinforce growth hormone therapy and hormone replacement therapy (HRT) with new indications and introduction into new markets.

### The best in its markets

In 1996, this focused business strategy was followed up by a reorganisation of the staff and service functions, and the management strategy was adapted a year later. Procedures and activities that did not add substantial value to Novo Nordisk were dropped, and the resources thus liberated were used for development and marketing. This change process produced results and helped fuel Novo Nordisk's significantly

increased performance in turnover and market share in the years approaching the new millennium. By 2001, sales in the five-year period up to that year had doubled.

Markets grew in Europe, the US and Japan. The same trends held in other, less well-developed markets in Eastern Europe, Asia and Latin America. As turnover increased, the company needed increasingly larger and more modern production facilities, as well as more employees. Thus Novo Nordisk embarked in 2001 on the biggest investment programme in the history of the company.

### Increased globalisation

The company became increasingly globalised in the following years. In the first decade of the new millennium, Novo Nordisk invested in large new production plants in Brazil and China and a sizeable expansion of the organisation outside Denmark. In 2007, for the first time, more than half of Novo Nordisk's workforce was employed outside Danish borders. Strong focus on the company's core competences combined with willingness to invest in markets with long-term growth potential are cornerstones of Novo Nordisk's future business strategy.



## A unique product



In 1996, after more than a decade of development, Novo Nordisk marketed NovoSeven® – a unique product to help people with haemophilia who are not responsive to traditional medications. NovoSeven® is a recombinant coagulation factor (rFVIIa) that promotes safe and effective blood coagulation in patients with inhibitors to factors VIII or IX. The use of NovoSeven® increased significantly following introduction in the US in 1999.

In 2004, NovoSeven® was approved for treatment of congenital factor VII deficiency and Glanzmann's thrombasthenia. In the US, approval was also granted in 2005 for use in surgery on people with haemophilia, and in 2006 for treatment of acquired haemophilia. Meanwhile, Novo Nordisk also began to develop improved treatment options for general haemophilia and new versions of the NovoSeven® molecule.

### Other new products

Novo Nordisk also introduced new products within the company's other focus areas – growth hormone and HRT – around the turn of the millennium.

### Growth hormone therapy

Novo Nordisk is a leading manufacturer in the field of human growth hormone. In 1999, the company marketed Norditropin® SimpleXx®, the world's first liquid growth hormone. This user-friendly profile was further simplified in 2003, when the product was launched in the prefilled NordiFlex® pen. Norditropin® is approved for treatment of growth hormone deficiency in children and adults, Turner syndrome, SGA (Small for Gestational Age), chronic renal disease, Noonan syndrome and skeletal dysplasia.

### Hormone replacement therapy (HRT)

Novo Nordisk is also one of the world's largest manufacturers of hormone replacement therapy (HRT) products and offers a range of low- and ultra-low-dose medicines to treat menopausal symptoms. The low-dose combination HRT products Activelle® and Novofem® were introduced in 1998 and 2000, respectively, followed by ultra-low-dose Eviana® in 2007. Most recently, ultra-low-dose Vagifem® 10 mcg was introduced in 2010 for the local treatment of vaginal atrophy.

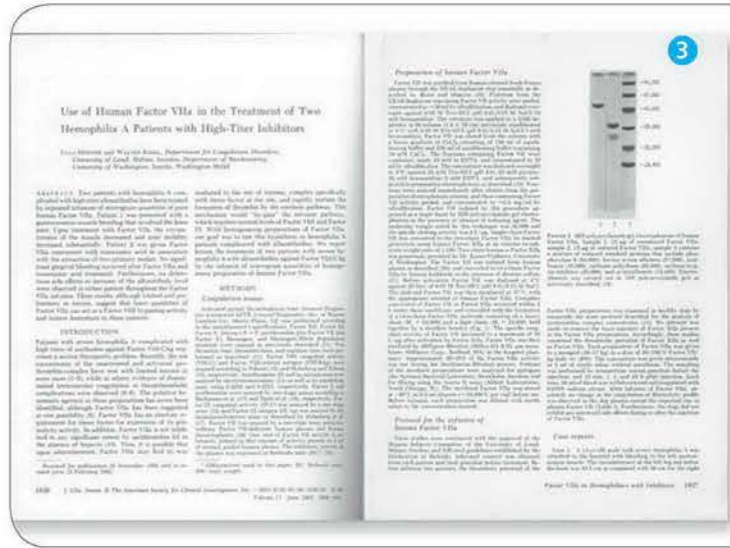
1 NovoSeven® means increased life expectancy and improved quality of life for people with haemophilia.

2 Ulla Hedner, researcher at Novo Nordisk and professor at the University of Lund in Sweden, conceived the idea that led to the development of NovoSeven®.

3 In 1983, Ulla Hedner and Walter Kisiel published their first findings on the treatment of haemophilia patients with factor VIIa in *Journal of Clinical Investigation*.

4 Six-year-old Patrick Moll from Germany has growth hormone deficiency.

5 Norditropin NordiFlex®.



## A broad selection of products for the effective treatment of diabetes

In 1998, the results of what was then the world's largest diabetes study, the United Kingdom Prospective Diabetes Study (UKPDS), were published. The study confirmed the need for improved blood glucose control – in line with Novo Nordisk's strategy within diabetes care.

### Modern insulins

With the so-called modern insulins (insulin analogues), a new milestone in insulin therapy was reached. Modern insulins are a tailored form of human insulin in which the insulin molecule has been altered at specific sites so as to alter the onset and duration of action of the insulin. The rapid-acting modern insulin NovoRapid® was marketed in Europe in 1999 and in the US and Japan two years later. NovoRapid® provides better control of mealtime blood glucose levels as well as the opportunity for a more flexible lifestyle, because injections can be taken immediately before or after a meal. On the basis of NovoRapid®, Novo Nordisk developed an insulin product with both a rapid-acting and a long-acting component, also known as a dual-release modern insulin. The first dual-release product, NovoMix® 30, was launched in 2002. Two years later, the long-acting, once-daily modern insulin Levemir® was launched. Levemir® covers the need for basal insulin of most people with

diabetes – without the weight gain often associated with insulin treatment. With these new products, Novo Nordisk became the first company in the world with a full portfolio of modern insulins.

### Delivery systems

Several advanced delivery systems were launched along with the new insulin products. In 2001, for example, InnoLet® was launched for insulin users with poor eyesight or reduced manual dexterity. The same year, Novo Nordisk introduced FlexPen®, a new prefilled pen.

### A new kind of treatment

With the introduction in 2009 of Victoza® on the European market, Novo Nordisk moved into a new kind of treatment of type 2 diabetes. Victoza® is a once-daily dosed human Glucagon-Like Peptide-1 (GLP-1) analogue developed for the treatment of adults with type 2 diabetes. Victoza® works by stimulating insulin secretion only when blood sugar levels are too high. Victoza® provides improved blood sugar control and other benefits, including weight loss, blood pressure reduction and improvement of beta-cell function. Impairment in beta-cell function is an important indicator of disease progression.



1

1 InnoLet®.

2 Zouheira Harrabi of Tunisia has type 1 diabetes.

3 Levemir® FlexPen®, NovoRapid® FlexPen® and NovoMix® 30 FlexPen®.

4 Victoza® pen.



## Engagement and values

As Novo grew and expanded, the need arose at the beginning of the 1970s for a more specific statement of the ideals that had characterised the company since its beginnings. The purpose of this was to engage employees and managers in the common cause of making Novo a global leader while still upholding its historical ideals.

### Mission statement and vision

Novo's first mission statement was unveiled in 1974, the same year the company's B shares were listed on the Copenhagen Stock Exchange. The mission it expressed was to be an independent company working to meet society's need for medicine and industrial processes. In addition, Novo aspired to base its activities on a high, ethical foundation in an open and communicative environment.

The mission statement was regularly updated and revised, but the basic ideals remained the same.

The company's first vision, Novo Nordisk Vision 21, was launched in 1994 as a further development of the mission statement. It was worded in a way

that linked specific goals to long-range strategies for Novo Nordisk's global development. In this vision, Novo Nordisk declared its intention of being the best in its business areas while at the same time being a challenging workplace with four values: ambitious, responsible, honest and open. In their daily work, every Novo Nordisk employee was to strive towards the realisation of both the vision and the values.

### Employee shares

In the decades after the release of the mission statement and later of Vision 21, a number of supporting activities were developed to motivate and train employees.

For example, in 1974 – the same year Novo was publicly listed and presented its mission statement – employees were given the chance to become part-owners of their company by purchasing employee shares at a favourable price. The following year, Novo celebrated its 50th anniversary with a gift of employee shares to everyone. In so doing, Novo wanted to thank employees for their efforts and strengthen their interest in the company. Every few years since then, employee shares have been offered for sale on attractive terms.



1 Employee shares were offered by Novo as early as 1974.

2 Novo Nordisk's Vision 21 was presented to employees in a colourful paperboard form that could be folded into a stand-up figure and placed on a desk or table. The figure became affectionately known as 'the milk carton'.

**Purpose**  
 It is Novo Nordisk's business to develop and market products which satisfy real needs - improving the way people live and work.  
 Novo Nordisk wishes to grow as an independent company making all important business, people, and policy decisions.  
 We must be:  
**Ambitious**  
 We must set our ambitions high, work towards the highest standards, reach challenging goals, and enjoy our achievements as an inspiration on our way towards new goals.  
**Accountable**  
 Each of us shall be accountable - to our colleagues, our colleagues, and ourselves - for the quality of our efforts, the achievement of our goals and the ongoing development of our culture and the values we share:  
 • Respect for the tasks we handle  
 • The desire to deliver products and services of real value  
 • Our belief in the individual and in the benefits and excitement of teamwork  
 • Mutual trust  
 • Respect for our natural environment and its resources  
 • The obligation we feel also to serve society in our work  
**Participative**  
 Each of us must contribute to a working climate of initiative, participation, creativity and open communication. Power, which stimulates achievement, self-renewal, willingness to change, and job satisfaction.  
**Open and honest**  
 We must be forthright, whole fair and uncompromising.  
 Our business practices shall be open and honest to protect the integrity of the company and each individual employee.  
 100 years\*

**Mission**  
 Best in our businesses and a challenging place to work.  
 Novo Nordisk shall be recognised as one of the world's significant companies.  
 It is our business to find new and better ways to eliminate the stress and burden of disease and to bring sustainable progress to industry and agriculture.  
 We will:  
 • Be the preferred partner in business and science  
 • Be the leader in all our markets  
 • Be the company where highly talented people seek an opportunity to work  
 • Work to earn the highest level of public trust and confidence  
 To achieve this we must:  
 • Work with a fundamental understanding of our customers so that we truly satisfy their needs better than anybody else  
 • Set and reach stretching goals for everything we do  
 • Have the right people in the right positions  
 • Focus on activities which are essential to our continued growth  
 • Build on world class discovery and product development activities to turn advances in the sciences into market-driving products and technologies faster than any competitor  
 • Energise our company through the removal of organisational barriers and of every unnecessary procedure which does not give customers added value  
 • Achieve a sustainable competitive financial performance  
 ~ 10 years/SPP

**Objectives**  
 Growth and expansion  
**Market leadership**  
 • We shall offer the best combination of the highest product quality, service, reliability, certainty of renewal, and cost to satisfy each customer's particular needs better than any competitor.  
**New products**  
 • A strong portfolio of product candidates to be built before the end of 1996 in order to bring new, significant products to the market in a larger number and faster than forecast in SPP93.  
**People and organization**  
 • All business practices and processes must over the next five years be reviewed and wherever possible redesigned to ensure quality, minimize waste of time and resources and to achieve constant productivity improvements.  
 • Build throughout Novo Nordisk an awareness of the rules and regulations which govern our activities in order to achieve across-the-board compliance and to be able to respond to changing demands.  
 • Year by year we shall acquire a broader business experience base to improve our capacity for renewal and to expand our managerial reserves.  
**Financial performance**  
 • Novo Nordisk shall, as a corporation, operate with:  
 - a growth in net profit of at least 5% p.a.  
 - a return (before tax) on non-financial assets of at least 20%, and  
 - a positive Net Cash Flow  
 to generate the resources necessary to grow existing businesses, to expand into new ones, and to maintain the financial strength and flexibility required to pursue new ideas without delay.  
 3-0 years/MTP - AB

**Focus areas**  
 • Quality  
 • Productivity  
 • Accountability  
 • New Product Development  
 Now

Novo Nordisk





1 Participants in the Lighthouse leadership programme gain new insights at the Great Wall of China in 2006.

2 Novo Nordisk recruits and trains gifted students from around the world through its Graduate Programme.

3 The Novo Nordisk facilitator team in 2007.

4 In May 2011, the Novo Nordisk Centre of Learning opened at the historic Favrholm Manor near Hillerød, Denmark.

### Education and training

To help employees live up to the requirements that came with the company's growth and development, Novo placed an increasing focus on education during the 1970s. A great many courses were held on such topics as language, financial management, leadership, teamwork, safety and technical subjects. In 1982, a new training centre opened in Bagsværd, and by the mid-1980s some 3,000 employees a year were participating in coursework at the centre.

After the merger with Nordisk in 1989, employee training became an important means to integrate the two company cultures and ensure that everyone worked according to the same basic mindset. By now, Novo Nordisk could offer a portfolio of qualifying courses that grew proportionately with the company's expansion both in and outside of Denmark. Individual units and affiliates were free to develop training according to their own needs; headquarters supported these efforts, ensured a common set of values and created a common approach to the development of talented leaders.

Today, employee development grounded in the values of the company is still highly valued as a way of retaining talented, engaged people.

In 1985, the company introduced the Novo Interview programme. All salaried personnel participated in the programme, in which employees met with their managers once a year to discuss job-related efforts, plans and wishes. After the merger with Nordisk and up to the present day, conversations of this type remain a regular part of the professional life of many employees.

### Facilitators

In 1997, Novo Nordisk established a corps of internal consultants called facilitators. The job of these very experienced managers was to evaluate the extent to which the company operated in accordance with its values. By gathering data and through interviews, especially with employees, facilitators determined whether company values and management philosophies were fully observed in daily work, or whether improvement was needed.

Today, facilitators run audits against the code of conduct called the Novo Nordisk Way (formerly the Novo Nordisk Way of Management). Through this unique approach, facilitators help maintain the company's strong culture and approach to responsible business.



## The Novo Group – one company becomes many

Novo Nordisk celebrated a new chapter in its history on 13 November 2000. At an extraordinary general meeting, the company's two core businesses, Health Care and Enzyme Business, became independent legal entities.

The name Novo Nordisk A/S was carried on by the former Health Care, while Enzyme Business took the name Novozymes A/S. The holding company Novo A/S was established at the same time to manage the funds of the Novo Nordisk Foundation – including all A shares of the two companies. The objective of the new structure was to give each company a well-defined area of focus and thus greater operational freedom to create a clear profile on their markets. The three new companies are today part of the Novo Group, a family of independent companies with a set of shared core values as defined in the Group's charter.

### Corporate values

Following the demerger, Novo Nordisk became a focused healthcare company, but its corporate values remain the same as always. The Novo Nordisk Way of Management, announced along with the new organisation, sets out the vision, charter and policies in force for the company's employees worldwide.

Along with the establishment of the new companies, Novo Nordisk's president and CEO for 19 years, Mads Øvlisen, retired from the top management post and was replaced by Lars Rebien Sørensen, who had joined Novo in 1982. He had been a member of management since 1994, and in 2000 he assumed leadership of the new Novo Nordisk.



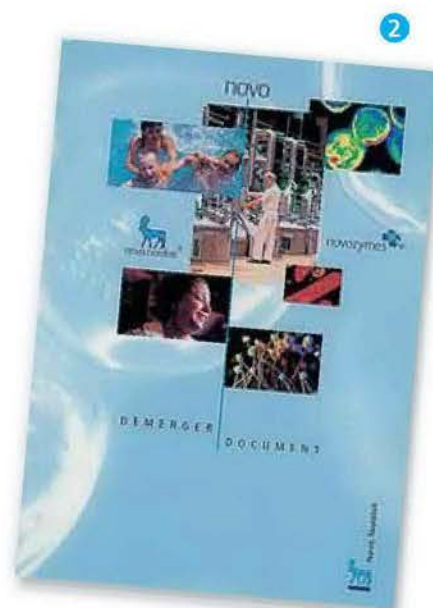
1 The former and the current president and CEO of Novo Nordisk: Mads Øvlisen and Lars Rebien Sørensen.

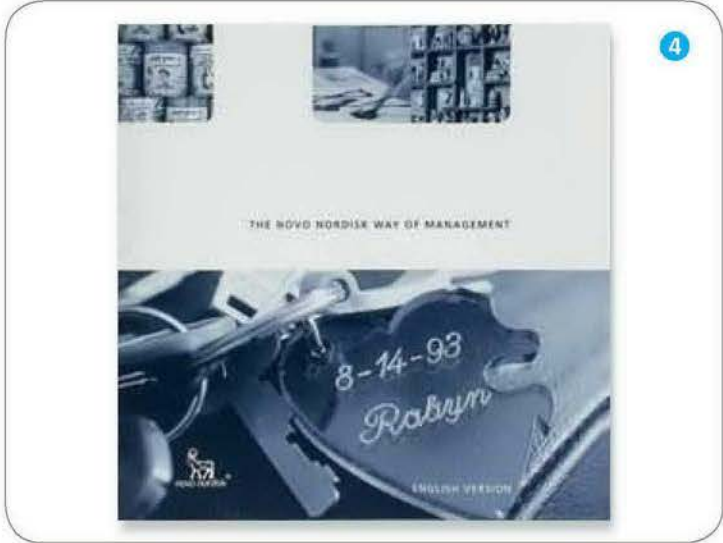
2 The demerger document was published prior to the extraordinary general meeting on 13 November 2000.

3 Novo Nordisk's logo, the Apis bull, was redesigned in connection with the launch of the new Novo Nordisk.

4 The Novo Nordisk Way of Management contains the company's vision, values and policies.

5 Karin Sørensen, Novo Nordisk employee in Denmark.





## Novo Nordisk is its employees

Novo Nordisk entered the 21st century with a new management, a focused business strategy and the recognition that the success of the company depends on the skill and enthusiasm of its employees. In addition to its educational and facilitation efforts, new initiatives were now launched to strengthen employee engagement.

### A focus on patients

In 2000, to show how employees help change lives, Novo Nordisk initiated a series of 'Meet the Customer' meetings in which people with diabetes and other diseases within the company's therapy areas spoke about their daily needs and challenges. These meetings were later integrated into the mandatory introduction training for new employees at Novo Nordisk in Denmark, while company affiliates held similar events on a voluntary basis.

### Pride

Strong employee engagement is at the heart of the TakeAction programme launched in 2003. The programme offers employees the chance to participate in voluntary projects that are based on the principle of the Triple Bottom Line. Projects cover everything from diabetes awareness to disaster assistance, and participant feedback shows that the

programme has created pride in being a Novo Nordisk employee.

In 2008, 'Life-Changing Careers' was launched as a global employer brand showing what Novo Nordisk offers current and potential employees. The brand highlights the possibility of changing one's own and others' lives in the course of a career at Novo Nordisk and shows how the company differentiates itself from other employers on the global job market.

### A new Way

Ten years after the launch of the Novo Nordisk Way of Management, the document was updated. Executive Management obtained input from almost 1,000 internal and external stakeholders to ensure that the new version would reflect a global company that had doubled its employee count and tripled its turnover since 2000. The new 'Novo Nordisk Way' was launched on 2 February 2011.

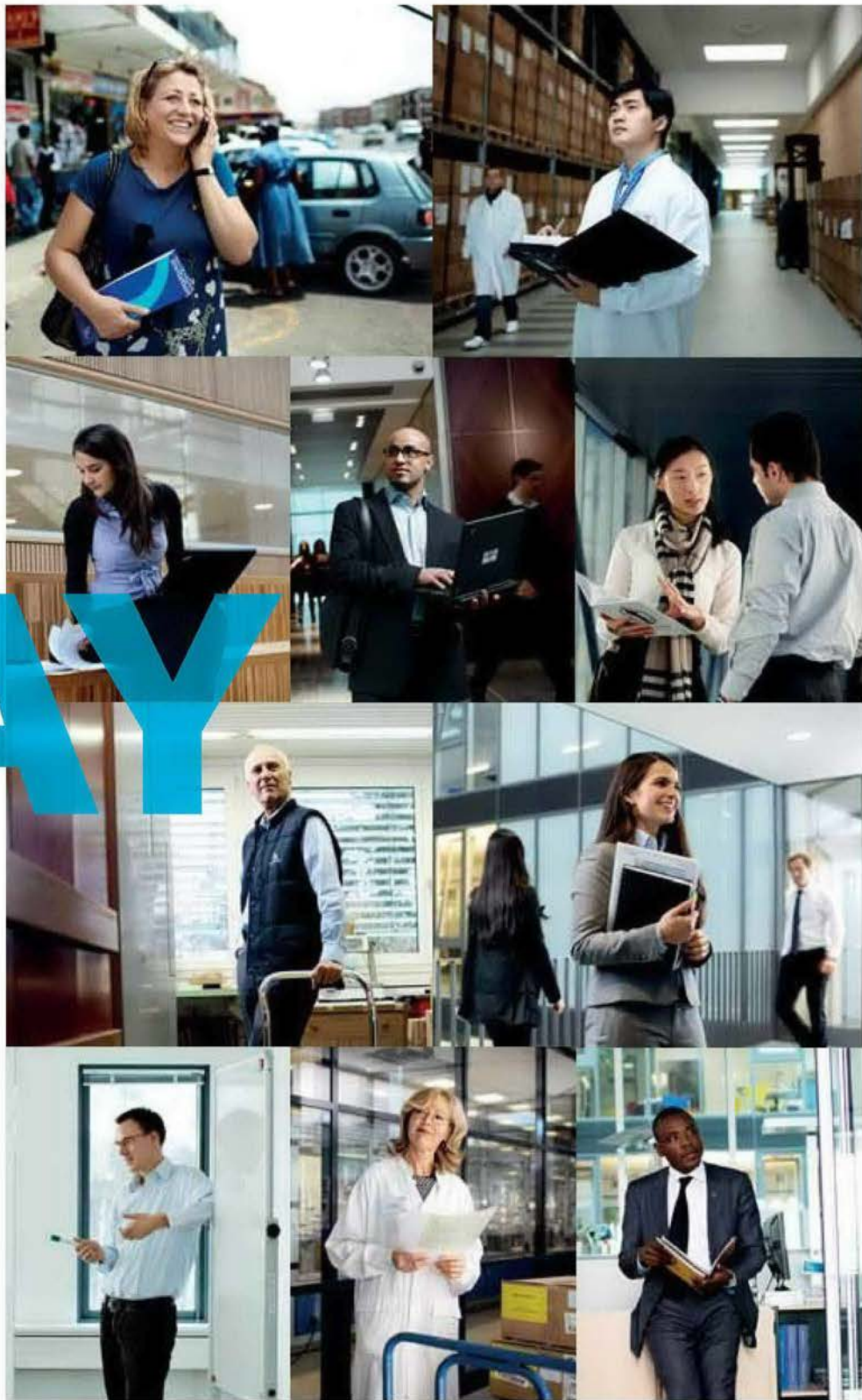
Its basic values were the same as before, but the document was much shorter and in a simpler form. At the same time, the stage was set for an engaging and global employee discussion of specific means by which the Novo Nordisk Way can be lived out in the various countries.



1 The brand concept of 'Being there', introduced in 2000, focused on real patients expressing their wishes and needs. The illustration shows a young Indian girl, Shanthala Shamarao, who has type 1 diabetes.

2 The new Novo Nordisk Way provides the company's many employees with a guide placing great emphasis on Novo Nordisk's history and values. It also includes an even stronger patient focus and a specific reference to haemophilia as a therapy area.

2



NOVO NORDISK

WAY

**changing  
diabetes®**

1

- 1 Novo Nordisk's corporate brand concept, Changing Diabetes®, is a concerted effort to create positive changes in the lives of people with diabetes around the world.
- 2 In 2006, the Novo Nordisk Changing Diabetes® Bus embarked on a world tour with information about diabetes and its prevention.
- 3 Punithevel Thankikachalam lives in India and has type 2 diabetes.
- 4 Novo Nordisk participated in the Unite for Diabetes campaign, which in 2006 succeeded in making World Diabetes Day a UN-recognised day.
- 5 Zandile Signoria Mzayifani from South Africa with the words she expressed about living with type 2 diabetes.

## Novo Nordisk today and tomorrow

In 2005, Novo Nordisk launched the corporate brand concept Changing Diabetes®. With this promise of change Novo Nordisk recognises that as a world leader in diabetes care, the company has the responsibility to make a difference by both offering innovative treatments and driving initiatives to create real change in the lives of people with diabetes and at risk of diabetes. These initiatives target a wide variety of stakeholders including patients, healthcare professionals and policy-makers.

Among these initiatives is DAWN™ (Diabetes Attitudes, Wishes and Needs), launched by Novo Nordisk in 2001 to discover the psychosocial needs of people with diabetes. DAWN™ was established prior to the concept of Changing Diabetes® but has since been refined.

In 2006, a worldwide campaign was initiated by the International Diabetes Federation to gain UN recognition of World Diabetes Day 14 November. That inspired Novo Nordisk to create the Changing Diabetes® Bus, a mobile awareness-raising and diabetes-screening unit. It embarked on its worldwide journey in 2006 and was prominent in the IDF campaign, which was a success. In December 2006, the Changing Diabetes® Bus rolled into New York to

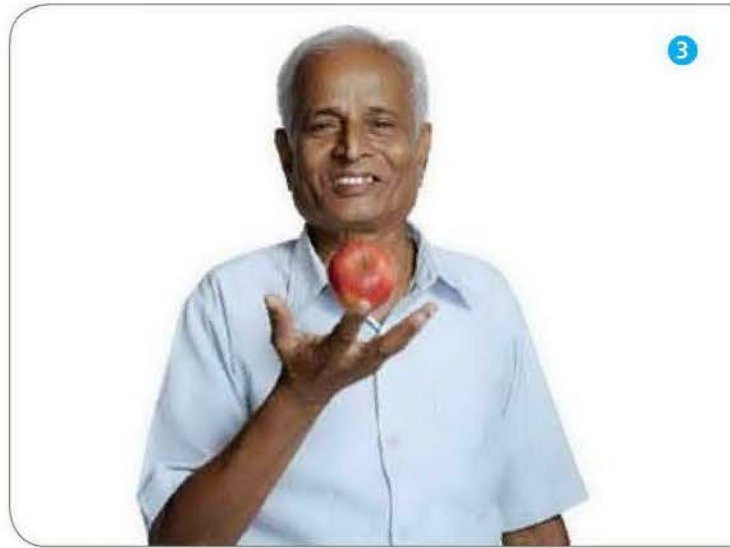
celebrate the UN adoption of a Resolution on diabetes making World Diabetes Day an official UN day.

A further change initiative is the series of Changing Diabetes® Leadership Forums where experts aim to get diabetes on the global political agenda. The first forum was held in 2007; at this gathering, the development of a Changing Diabetes® Barometer to measure the progress of diabetes care around the world was announced. The Changing Diabetes® Barometer website was launched in 2009.

With the arrival of the new Novo Nordisk Way in 2011, the Changing Diabetes® concept was strengthened to deeper reflect the company's commitment to patients.

### Building on the past – looking to the future

Novo Nordisk will continue to develop treatments and initiatives to benefit people with diabetes. In this way, the company will continue to build on the legacy left by the founders of Novo Nordisk and do whatever it takes to change diabetes. Our history tells us it can be done.





## Milestones in Novo Nordisk's history

Novo Nordisk was created in 1989 through a merger between two Danish companies – Novo Industri A/S and Nordisk Gentofte A/S.

- |      |   |      |   |
|------|---|------|---|
| 1923 | Nordisk Insulinlaboratorium founded.  | 1985 | NovoPen® is launched – an injection system similar in appearance to a fountain pen, with replaceable insulin cartridges.  |
| 1925 | Novo Terapeutisk Laboratorium founded.  | 1987 | Novo starts production of human insulin with the help of genetically engineered yeast cells.  |
| 1926 | Nordisk establishes the Nordisk Insulin Foundation with the object of supporting physiological and endocrinological research and people with diabetes in Scandinavia.                   | 1988 | Novo markets Vagifem® – the first vaginal tablet for atrophic vaginitis.  |
| 1932 | Nordisk founds the Steno Memorial Hospital.   | 1988 | Nordisk markets Norditropin® genetically engineered human growth hormone.   |
| 1938 | Novo founds Hvidøre Diabetes Sanatorium.  | 1989 | Nordisk Insulinlaboratorium, the Nordisk Insulin Foundation and the Novo Foundation merge to become the Novo Nordisk Foundation. The objects are to provide a stable basis for the Novo Group companies' operations and to support scientific causes. |
| 1946 | Nordisk develops isophane insulin (NPH), a neutral insulin with prolonged action.   | 1989 | Novo Industri A/S and Nordisk Gentofte A/S merge to become Novo Nordisk A/S – the world's leading producer of insulin.  |
| 1947 | Penicillin Novo is launched – Novo's first product to be manufactured through fermentation.   | 1989 | NovoLet® is marketed – the world's first prefilled insulin syringe.   |
| 1951 | Novo establishes the Novo Foundation with the object of supporting scientific, social and humanitarian causes and to provide the best possible protection for the company.              | 1991 | Novo Nordisk joins the environmental charter of the International Chamber of Commerce (ICC).  |
| 1953 | Novo launches Lente® – a long-acting insulin–zinc suspension.   | 1992 | The Steno Memorial Hospital and Hvidøre Hospital merge to form the Steno Diabetes Center.   |
| 1973 | Nordisk markets Nanormon® growth hormone for the treatment of growth hormone insufficiency. The growth hormone is extracted from human pituitary glands.                                | 1994 | Novo Nordisk is the first company in Denmark – and one of the first in the world – to publish an environmental report.  |
| 1973 | Novo introduces Monocomponent (MC) insulin – the purest insulin available.  | 1996 | NovoSeven® is launched – for the treatment of haemophilia patients with inhibitor reaction.   |
| 1974 | Novo's B shares are quoted on the Copenhagen Stock Exchange.  | 1998 | NovoNorm® (Prandin® in the US) – a new oral treatment for type 2 diabetes – is launched in the US and a number of European countries.   |
| 1981 | Novo becomes the first company in Scandinavia to be quoted on the New York Stock Exchange.  | 1998 | Activelle® (Activella® in the US) is introduced – the first low-dose continuous combined oral HRT for postmenopausal women.   |
| 1982 | Human Monocomponent insulin is launched – the world's first insulin preparation identical to human insulin. It is extracted from the pancreases of pigs and converted to human insulin. | 1999 | Novo Nordisk publishes its first social report.   |

- |      |   |      |  |
|------|---|------|--|
| 1999 | NovoRapid® (NovoLog® in the US) – the company’s first modern insulin, a rapid-acting insulin analogue – is marketed. Modern insulins are designed to better mimic the normal insulin response to changes in blood sugar levels. | 2006 | Novo Nordisk signs an agreement with WWF that commits the company to reduce its carbon emissions by 10% by 2014 compared with 2004. Novo Nordisk is the 10th company in the world to join the WWF Climate Savers initiative. |
| 1999 | Norditropin® SimpleXx® is launched – the world’s first liquid growth hormone in a dedicated pen system.   | 2007 | Activella® 0.5 mg/0.1 mg is launched in the US – the first ultra-low-dose oral HRT for women with menopausal symptoms.   |
| 2000 | Novo Nordisk is split into three separate companies operating under the umbrella of the Novo Group: Novo Nordisk A/S, Novozymes A/S and Novo A/S.   | 2007 | In Montes Claros, Brazil, Novo Nordisk inaugurates its largest insulin production facility outside of Denmark.   |
| 2001 | InnoLet® is launched – the first insulin delivery system specially designed to suit the needs of insulin users with poor eyesight and reduced dexterity.  | 2009 | Victoza® – human Glucagon-Like Peptide-1 (GLP-1) analogue for once-daily treatment of adults with type 2 diabetes – is launched in Europe.   |
| 2001 | Novo Nordisk establishes the World Diabetes Foundation with the purpose of improving diabetes care in developing countries.   | 2010 | Vagifem® 10 mcg is launched in the US and Europe. The medication provides the lowest dose of vaginal oestrogen commercially available for women with vaginal atrophy.  |
| 2001 | NovoRapid® FlexPen® is marketed. FlexPen® is a new prefilled pen, designed for easy and discreet use.   | 2010 | Novo Nordisk launches NovoPen Echo®, a new insulin pen developed especially for children. Initially launched in Denmark, the pen includes a memory function and half-unit dosing increments.                                 |
| 2002 | Novo Nordisk signs the United Nations Global Compact, a platform for promoting good corporate principles and learning experiences in the areas of human rights, labour, environment and anti-corruption.                        |      |  |
| 2002 | NovoMix® 30 is introduced – a dual-release modern insulin.  |      |  |
| 2003 | Norditropin NordiFlex® is launched – the world’s first prefilled growth hormone pen.  |      |  |
| 2004 | Levemir® is launched – a long-acting modern insulin.  |      |  |
| 2004 | Novo Nordisk’s Articles of Association are amended to specify that the company will “strive to conduct its activities in a financially, environmentally and socially responsible way”.  |      |  |
| 2005 | The Novo Nordisk Haemophilia Foundation is set up in response to the significant need to improve haemophilia treatment in the developing world, underlining the company’s social responsibility within haemophilia care.        |      |  |

Not all products have been introduced worldwide. Trade names may vary from country to country.

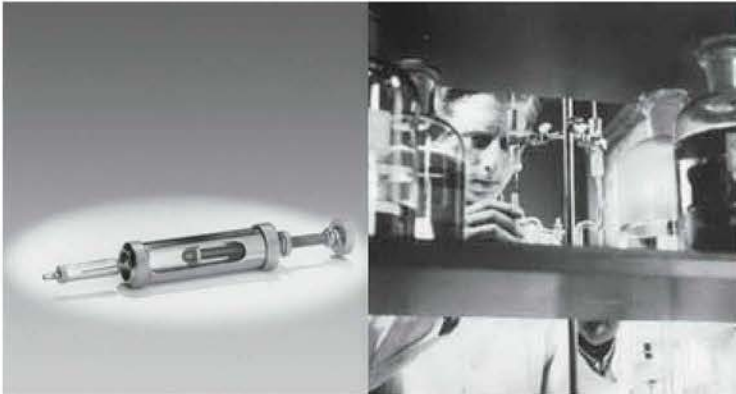
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**Sanofi Exhibit 2137.067**  
**Mylan v. Sanofi**  
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1930



1950



1940

1960

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