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# Novo A/S

Novo A/S is a Danish private limited liability company fully owned by the Novo Nordisk Foundation. It is the holding company of the Novo Group and the controlling shareholder in the publicly listed companies, Novo Nordisk A/S and Novozymes A/S, and together with Novo Nordisk in NNIT A/S.

Novo A/S was established in 1999 prior to the demerger of Novo Nordisk, where Novozymes was established as a stand-alone, publicly listed company.

Novo A/S' objectives are to meet the Novo Nordisk Foundation's strategic and commercial goals. We do so by being a strong owner of the companies in the Novo Group, and by:

- complying with the rules and principles that are set out in the statutes of the Novo Nordisk Foundation regarding exercise of the voting rights of A and B shares in Novo Nordisk and Novozymes, respectively;
- always maintaining a material influence on Novo Nordisk and Novozymes; and
- maintaining a liquid buffer to support any investment needs in the Novo Group.

By investing in the life science sector, Novo A/S can meet the commercial objectives of the Novo Nordisk Foundation and ensure value creation because the Novo Group has a unique heritage and purpose within life science.

Novo A/S' capabilities as investor include life science investment competences, a strong industry network, financial strength, and a long-term investment horizon.

Novo A/S' investment objectives are to:

- generate competitive financial returns;
- be a responsible investor;
- help to address unmet medical needs; and
- generate broader support for the life science industry.

The common denominator for all Novo A/S' investments is that they must comply with – or at least not act against – the values and commitments defined in the Charter for Companies in the Novo Group and Novo A/S' governance framework.

# 2016 in brief

#### **THE NOVO GROUP**

Novo A/S is the controlling shareholder in Novo Nordisk A/S and Novozymes A/S. Both companies increased profit and dividend pay-outs during 2016, in addition to continuing their share buy-back programmes. Furthermore, NNIT continued to develop its business with increased profits and dividend pay-outs.

All three companies faced challenging business environments in 2016, resulting in share price declines for both Novo Nordisk, which decreased by 36%, and Novozymes, which decreased 26%. Nevertheless, income from the Novo Group increased to DKK 7.1 billion in 2016, representing an increase of 67% compared to 2015.

In 2016, Novo Nordisk paid its annual dividend in connection with the Annual General Meeting (AGM) in March 2016. Moreover, in 2016 Novo Nordisk decided to introduce an interim dividend pay-out and consequently paid this in August 2016. Due to Novo Nordisk's introduction of interim dividends in 2016, Novo experienced an increase in dividends received. Going forward, Novo Nordisk will pay dividends twice annually: an interim dividend in connection with the first half-year report in August, and a final dividend in connection with the AGM in March.

### LIFE SCIENCE INVESTMENTS

It is Novo's vision to be recognised as a world-leading life science investor with a focus on creating long-term value. Novo divides its Life Science Investments into three distinct areas: Large Investments focuses on established companies; Novo Ventures focuses on venture investments primarily in the US and Europe; and Novo Seeds focuses on early start ups primarily in the Nordic region. By the end of 2016, Novo had DKK 37.7 billion allocated to life science investments.

#### Large investments

In 2016, Large Investments added SYNLAB and ERT to its portfolio. Both investments were carried out in partnership with private equity firms, SYNLAB with Cinven and ERT with Nordic Capital.

The portfolio value in 2016 was adversely impacted by the unfavourable development in the share prices of Chr. Hansen Holding A/S and Ophthotech Corp. At the end of 2016, our Large Investments portfolio comprised 10 companies, of which eight are located in Europe and two in the US. The portfolio consists of majority positions in Sonion and Xellia, both headquartered in Europe, and minority positions in Chr. Hansen, Symphogen, SYNLAB, Orexo, Veloxis, BTG (all European) and ERT and Inogen (both in the US). By end of the year the Large Investments portfolio was valued at DKK 31.5 billion.

#### Venture investments

As in previous years, Novo worked to further consolidate its position as a major international investor within life science ventures.

In 2016, Novo invested in 14 new companies, made followon investments in 29 of our existing portfolio companies, and successfully exited six companies. Our investments this year totalled DKK 2,091 million, exit proceeds amounted to DKK 759 million, and the value of IPOed companies came to DKK 2,001 million. By the end of the year, the value of our venture portfolio reached DKK 5.9 billion.

#### Seed investments

To enable early investments in the life science area, Novo runs a seed programme. In 2016, we invested DKK 149 million in 19 early-stage life science companies and the value of the portfolio by the end of 2016 was DKK 291 million.

Novo assists the Novo Nordisk Foundation in a pre-seed programme that aims to identify and support academic research with commercial potential. In 2016, eight projects received grants from the pre-seed programme.

### FINANCIAL INVESTMENTS

In 2016, we continued the strategy of a broad diversification with a focus on equities. By year end, the portfolio reached an accumulated value of DKK 38.7 billion.

#### **NOVO'S ORGANISATION**

In 2016, a new executive management team took the helm at Novo. Kasim Kutay was appointed CEO and Peter Haahr was appointed CFO.

Kasim Kutay joins Novo from a position as Co-head of Europe at the investment banking firm, Moelis & Company. Prior to that, he spent 18 years at Morgan Stanley advising mainly healthcare companies. Kasim Kutay has previously advised Novo on both acquisitions and disposals and has a close relationship to Novo Nordisk.

Peter Haahr joins from a position as Head of Strategy & Business Development in Novo Nordisk A/S. Peter Haahr started his career as an equity analyst and joined Novo Nordisk from the capital markets in 2000 as Head of Investor Relations. Since then, he has held various positions in Novo Nordisk, including seven years in operations outside Denmark.

In 2016, Novo welcomed 24 new colleagues incl. four Student Assistants. The organisation is expected to expand in the coming years as we seek to effectively execute on our strategic goals.



# Letter from the CEO

# 2016 SETS THE TREND FOR THE EXPANSION OF NOVO A/S' HIGH RETURN LIFE SCIENCE PORTFOLIO

During 2016, Novo A/S invested a record DKK 8.7 billion in life sciences companies, representing close to a 200% increase over 2015. This was primarily driven by the allocation of funds to larger equity stakes in private companies by the Large Investments team, as well as increased investments in the US by the Ventures investment team. At year end, we partly or fully owned more than 80 portfolio companies in the life sciences, and our objective is to continue to grow our investments in this sector in the years to come.

While the return on Life Science Investments was down by 4% for the year, mainly due to drops in the share prices of Chr. Hansen Holding A/S and Ophthotech Corp, the longterm IRR (Internal Rate of Return) of the portfolio remains at a highly attractive 21% on a five-year basis and 16% on a ten-year basis.

We also took part in the successful public listings of eight portfolio companies in the US market in 2016, highlighting our position as one of the most active global investors in life sciences today.

## **RECORD DIVIDEND FROM THE NOVO GROUP**

The growth rates of Novo Nordisk A/S and Novozymes A/S slowed during 2016. Nevertheless, both companies increased their profit and dividend pay-outs to new record levels. Income from the Novo Group in 2016 amounted to DKK 7.1 billion, corresponding to a significant increase of 67% compared to 2015, and I am confident in the future prospects of both companies.

#### **INVESTING IN THE FUTURE OF LIFE SCIENCE**

Novo A/S spans the entire range of life science investments: from early-stage ideas that need financial and commercial nurturing, to well-established biomedical and bioindustrial companies that require significant capital and a long-term investor to accelerate growth. We are able to provide the managerial, financial and strategic support that companies need to develop to the next stage, and we have the financial strength to stay the course.

Following an extensive strategic review in 2016, Novo A/S plans to significantly grow its large investments and venture portfolio in the years to come. Although healthcare reforms are adding pricing and other pressures on the life science sector, we believe that the underlying long-term industry trends are attractive, and that Novo A/S will be able to continue to leverage its significant experience and expertise in the sector to generate an attractive IRR.

Our Seeds investment team are supporting early-stage life science companies at a record pace. This is in line with a strategic decision we made several years ago to contribute to the strengthening of the biotechnology sector in the Nordic countries. In the coming years, we will build on the successes of our seed investment portfolio in the Nordic countries and expand internationally. As we broaden our international seed investing network, we believe we can also attract international investors to the Nordic region.

#### ADDING VALUE TO SOCIETY

Novo A/S will remain a strong owner of the companies in the Novo Group. In accordance with the Articles of Association of the Novo Nordisk Foundation, Novo A/S has a permanent commitment to remain the controlling shareholder in Novo Nordisk and Novozymes. On the investment front, Novo A/S will deploy its capital in the life science sector to generate attractive returns that will enable the Foundation to continue to increase its grants for scientific, humanitarian and social purposes. ■

It gives me great pleasure to be writing this Letter from the CEO.

I moved from London to Copenhagen in August 2016, and I have very much enjoyed settling in this wonderful city. I would like to take this opportunity to thank my colleagues at Novo A/S, the Foundation and the rest of the Novo family for their very warm welcome.

As you will read in this letter and elsewhere in this report, 2016 has been a very busy year for Novo A/S. We are executing on a number of new operational and strategic initiatives, to build on and enhance our position as a global leader in life science investing.

The basis for attaining any such vision is people, and I am very proud to be part of such a talented group with an outstanding investment track record.

> *Kasim Kutay* Chief Executive Officer

# MANAGEMENT REPORT 2016

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# Management report 2016

or the Annual Accounts and Review of 2016 and going forward, Novo A/S has made a number of adjustments to improve the quality of its financial reporting. Novo A/S will now present the components of its holding and investment results in three categories: the Novo Group (Novo Nordisk, Novozymes and NNIT), Life Science Investments and Financial Investments. This adjustment will enhance the visibility of the performance of each individual area.

Furthermore, while the Annual Accounts and the Review present the income statement and assets for the single year 2016, they are less representative of Novo A/S' long-term investment performance. The main reason for this is that Novo A/S is a holding and investment company, as opposed to an operating company. Novo A/S makes investments with a view to long-term returns, and we use Internal Rate of Return (IRR) as our return measure for Life Science Investments and Time-Weighted Rate of Return (TWR) as our return measure for Financial Investments. We have added a short section to the Management Report that provides an insight into Novo A/S' long-term value creation and investment performance.

#### LONG-TERM VALUE CREATION AND PERFORMANCE

Given the inherent long-term nature of Novo A/S' equity stakes in the Novo Group companies, we measure the performance of the Novo Group in terms of dividends received and proceeds from the sale of any shares into the companies' share buy-back programmes.

Novo A/S' Life Science Investments and Financial Investments (together the 'Investment Portfolio') are largely held on a longterm or evergreen basis, and the returns over an extended period are what drives our investment decision process. Therefore, the performance of the Investment Portfolio is assessed on the basis of its ongoing return. We consider the IRR and TWR as the appropriate measures for the performance of the Investment Portfolio, as they compare the value of investments to the entry price (plus any cash in- or out-flow associated with the investments).

The performance analyses are updated internally on a quarterly basis and will be presented externally on an annual basis, as illustrated below as of year-end 2016. For the sake of completion and comparison, the results for 2016 and 2015 are also included in the chart below.

	2016	2015	Last 5 years	Last 10 years
Income from Novo Group (Bn DKK)	7.1	4.3	-	-
Return on Life Science Investments – IRR (%)	-4%	35%	21%	16%
Return on Financial Investments – TWR (%)	8%	11%	11%	8%

Note: All returns are in DKK and reflect total returns, excluding internal cost. Return on Financial Investments pertain to the liquid assets in the portfolio.

As a leading global life science investor, Novo A/S aims to deliver long-term competitive returns and compares its performance to relevant benchmarks, as for example the MSCI World, MSCI Health Care and other relevant indices.

# 2016 RESULTS DRIVEN BY RETURNS FROM THE NOVO GROUP

The income and investment return for 2016 amounted to DKK 8.4 billion, versus a record DKK 15.8 billion in 2015. This development is largely attributed to the negative return for Life Science Investments. In contrast, income from the Novo Group increased to the highest level ever in 2016, and Financial Investments yielded a similar return as in 2015.

All Novo Group companies continued to increase profits and dividend pay-outs, resulting in an increase of the total contribution from the Novo Group to DKK 7.1 billion, versus DKK 4.3 billion in 2015, corresponding to an increase of 67%. In 2016, Novo Nordisk paid its annual dividend in connection with the Annual General Meeting (AGM) in March 2016. Moreover, in 2016 Novo Nordisk decided to introduce an interim dividend pay-out which was paid in August 2016. Due to Novo Nordisk's introduction of an interim dividend in 2016, Novo benefited from an increase in dividends received. Going forward, Novo Nordisk will pay dividends twice annually: an interim dividend in connection with the first half-year report in August, and a final dividend in connection with the AGM in March.

In 2016, return from Life Science Investments was adversely affected by the decrease in the values of Chr. Hansen Holding A/S and Ophthotech Corp., as well as the overall drop in share prices in the life science sector, as illustrated by the MSCI World Pharmaceuticals Biotechnology & Life Sciences Index, which recorded a decrease of around 7%

for the year. Therefore, a negative return of DKK -1.5 billion was realized in 2016 versus a return of DKK 8.6 billion in 2015. However, and more importantly, the returns from this business area remain strong, with the five and 10 year IRR standing at a highly attractive 21% and 16%, respectively. Despite recent volatility, today's market value of investments such as Chr. Hansen is substantially higher than Novo A/S' entry cost, resulting in this strong IRR performance.

Financial Investments contributed with a very satisfactory result of DKK 2.8 billion in 2016, thereby delivering a return in line with the average returns for the past five and 10 years of 11% and 8%, respectively. The favourable development in the shareholding in FLSmidth A/S contributed to the good performance in 2016.

DKK billion	2016	2015
Income from the Novo Group	7.1	4.3
Return from Life Science Investments	-1.5	8.6
Return from Financial Investments	2.8	2.9
Income and Investment Return	8.4	15.8

Note: Income from the Novo Group include dividend and income related to sales of shares in Novo Group companies, whereas the returns from Life Science Investments and Financial Investments represent realised and unrealised gains and losses during 2016.

# A 27% DECREASE IN TOTAL ASSETS BUT THE HIGHEST CASH INFLOW EVER

At the end of the year, Novo A/S' assets totalled DKK 275.7 billion, of which investments outside the Novo Group companies amounted to DKK 76.5 billion.

2016	2015
199.2	308.0
37.7	31.9
38.8	37.9
275.7	377.8
	199.2 37.7 38.8

Note: Shares in Novo Nordisk and Novozymes in this table reflect the value of all A and B shares based on the market value per B share at closing on 31 December 2016.

In 2016, the value of Novo A/S' holdings in Novo Nordisk and Novozymes decreased by 35% to DKK 198.0 billion, whereas the value of Novo A/S' holding in NNIT increased by DKK 0.09 billion. Novo received dividends of DKK 6.9 billion – an increase of 84% over 2015, helped by the interim dividend pay-out from Novo Nordisk in August 2016. As in 2015, we decided not to participate in Novo Nordisk's share buyback programme in 2016. At the end of the year, we held 537,436,000 A shares and 163,814,000 B shares, equivalent to 27.5% of the share capital and 75.0% of the votes in Novo Nordisk.

As announced in January 2014, Novo A/S has informed Novo Nordisk that it intends to consider its participation in the Novo Nordisk share repurchase programme on a caseby-case basis. For 2017, Novo A/S has informed Novo Nordisk that it does not plan to participate in the share repurchase programme. Novo A/S currently owns 27.5% of Novo Nordisk, with 25.5% being the targeted minimum and historical ownership level, and the additional 2.0%-point of the current ownership being part of the liquidity reserve of Novo A/S.

Novo A/S has the ambition to build on its position as a world-leading life science investor. This will primarily be pursued via larger investments in life science companies. To fund this strategy, Novo A/S might in the future consider reducing its holding of Novo Nordisk B-shares. Over time, this could bring the current ownership towards the minimum targeted and historical ownership level of 25.5%.

As part of Novozymes' share buy-back programme, we sold 765,000 B shares, yielding DKK 0.2 billion. At the end of the year, we held 53,743,600 A shares and 25,306,400 B shares, equivalent to 25.5% of the share capital and 70.9% of the votes in Novozymes.

The value of the Investment Portfolio increased during 2016 to DKK 76.5 billion, up from DKK 69.8 billion in 2015. This was primarily due to the allocation of significant investments in SYNLAB, a market leader in laboratory services, and in ERT, a leading clinical trial cloud platform provider, as well as increased activity within venture investments in the US. In 2016, eight of Novo A/S' venture portfolio companies undertook a public listing.

Our cash inflow from the Novo Group in 2016 amounted to DKK 7.1 billion, which is the highest inflow Novo A/S has received since its establishment. Novo A/S' cash inflows primarily comprised dividends from Novo Nordisk and Novozymes and participation in Novozymes' share buy-back programme.

In 2016, Novo A/S paid DKK 3.0 billion in dividends to the Novo Nordisk Foundation, which, in accordance with its statutes, provides grants for scientific, humanitarian and social purposes. Since 2010, the Foundation has issued more than DKK 10.0 billion in grants, primarily for public research, education, innovation, treatment, social and humanitarian purposes in Denmark and Scandinavia.

#### **INVESTING IN LIFE SCIENCE FOR FUTURE GROWTH**

As part of Life Science Investments, we provide both seed and venture capital to development-stage companies and take significant ownership positions in well-established companies. It is Novo A/S' vision to build on its position as a world leading life science investor, with a focus on creating long-term value.

Novo divides its Life Science Investments into three distinct areas: Large Investments focuses on established companies; Novo Ventures focuses on venture investments primarily in the US and Europe; and Novo Seeds focuses on early start ups primarily in the Nordic region. By the end of 2016, Novo had DKK 37.7 billion allocated to life science investments.

#### LIFE SCIENCE INVESTMENTS VALUE BY YEAR END

DKK billion	2016	2015
Large Investments	31.5	27.8
Venture Investments	5.9	3.9
Seeds Investments	0.3	0.3
Total Life Science Investments	37.7	31.9

### LARGE INVESTMENTS

Since 2013, more of Novo A/S' investments have been directed towards well-established, cash-flow positive companies. These investments are made in publicly listed as well as privately owned companies with a mix of minority and majority positions.

LARGE INVESTMENTS		
DKK billion	2016	2015
Value at the end of the year	31.5	27.8
Investments during the year	6.5	1.2
Cash proceeds during the year	0.7	2.1
Unrealised and realised gains/losses during the year	-2.1	6.6

Large Investments made two major investments in 2016 – both as minority stakes with private equity firms as the controlling shareholder. The first investment was made in eResearch Technology Inc. (ERT), in which Novo A/S acquired a 30% stake with Nordic Capital as the controlling shareholder. ERT is incorporated in the US and offers software-enabled solutions for the collection of clinical data.

The second investment was made in German-based SYNLAB, the European market leader in clinical laboratory services. Novo A/S initially acquired a minority equity stake of over 10% in SYNLAB and, since the initial acquisition, we have increased our holding in the company. The majority owner is the British private equity firm, Cinven, with whom our Large Investment unit has a close working relationship.

In 2016, unrealised and realised returns for Large Investments were negative, primarily due to the unfavourable development in the share prices of Chr. Hansen Holding A/S and Ophthotech Corp. In December, Ophthotech announced that FoVista® did not achieve the primary endpoint in its pivotal phase 3 study. As a consequence, the result for 2016 for Large Investments was negatively impacted. It should be noted, however, that while the share price of Ophthotech dropped significantly in 2016, the overall investments into Ophtotech have delivered a positive, albeit small return.

By the end of 2016, our Large Investments portfolio comprised 10 companies of which eight are located in Europe and two in the US. The portfolio consists of majority positions in Sonion and Xellia, both headquartered in Denmark, and minority positions in Chr. Hansen, Symphogen, SYNLAB, Orexo, Veloxis, BTG (all European) and ERT and Inogen (both in the US). Following an extensive strategic review in 2016, we intend to continue to allocate significant funds to Large Investments in the years to come.

### VENTURE INVESTMENTS

In 2016, Novo A/S continued with its high level of activity in life science venture capital investing, thus consolidating its position as a world-leading venture investor.

VENTURE INVESTMENTS		
DKK billion	2016	2015
Value at the end of the year	5.9	3.9
Investments during the year	2.1	1.7
Cash proceeds during the year	0.8	3.6
Unrealised and realised gains/losses during the year	0.7	1.9

Novo A/S added four public and 10 private companies to its venture portfolio; the companies are all located in the US except for two that are located in the UK. Novo A/S was a lead or co-lead investor in eight companies that went public in 2016.

Of the DKK 2.1 billion invested by Novo Ventures in 2016, DKK 1.8 billion was invested in the US and DKK 0.3 billion in Europe – DKK 1.2 billion in new companies and DKK 0.9 billion as follow-on investments in existing portfolio companies. In 2016, six of our portfolio companies were sold, eight were publicly listed. Exit proceeds totalled DKK 0.8 billion. At the end of the year, the total book value of our venture investments was DKK 5.9 billion, and the venture portfolio consisted of 52 companies, of which 39 are located in the US. The share of listed companies increased from 56% in 2015 to 64% in 2016 as a result of initial public offerings of a number of portfolio companies and new investments in listed companies.

It is the intention of Novo A/S to continue to increase the allocation of resources towards the private and public US venture market in the coming years.

## SEED INVESTMENTS

Novo A/S runs a seed investment programme that supports early-stage life science companies, primarily in the Nordics. In addition, Novo A/S assists the Novo Nordisk Foundation in a pre-seed programme that aims to identify and support academic research with commercial potential. This programme provides managerial and strategic support to early-stage projects, and funding is given as grants in the same manner as other grants awarded by the Novo Nordisk Foundation.

Novo A/S has made a strategic decision to contribute to the strengthening of the Nordic biotech environment. We will continue to build on the success of our seed investment portfolio and make the most of the opportunities generated by the preseed programme, not only in the Nordic countries but also in the rest of Europe. In this way, we hope to attract international investors to the Nordic life-science sector.

#### SEED INVESTMENTS

DKK million	2016	2015
Value at the end of the year	291	250
Investments during the year	149	75
Cash proceeds during the year	26	129
Unrealised and realised gains/ losses during the year	-81	56

# FINANCIAL INVESTMENTS DELIVERS HEALTHY RETURN

By investing in non-health care assets, Novo A/S ensures diversification, which provides a healthy relationship between risk and return on the Novo Nordisk Foundation's capital. The financial investments are also to a large extent liquid, which is important for Novo A/S in order to finance the grant-giving activities of the Novo Nordisk Foundation and to be able to support Novo Nordisk or Novozymes financially, if the need should arise.

At the end of 2016, the value of our financial portfolio (including the Novo Nordisk Foundation's share) was DKK 38.8 billion.

Since equities comprise the vast majority of the financial portfolio, the return on Financial Investments is closely linked to the performance of global equity markets. During 2016, financial markets had another strong year, resulting in a return of 8.1% on the liquid part of Financial Investments. Financial Investments has delivered a return of approximately DKK 15 billion since its inception and a highly attractive Time-Weighted Rate of Return (TWR) of 11% and 8% has been realized over a five- and 10-year period.

FINANCIAL INVESTMENTS		
DKK billion	2016	2015
Value at the end of the year	38.8	37.9
Unrealised and realised gains/ losses during the year	2.8	2.9

In 2016, we raised our ownership stake in the Danish engineering company, FLSmidth A/S and in the private Danish real estate company, Dades A/S.

### INVESTMENT CRITERIA AND CSR

Novo A/S carries out extensive due diligence when we invest in new companies. In addition to financial, legal, scientific and business-related issues, our due diligence efforts establish whether a company operates according to values and principles that correspond to those of the Novo Group. A bioethical perspective helps to evaluate whether the relevant companies – in connection with clinical trials and potential use of biological material – comply with ethical standards and international conventions. Please turn to page 54 to see the 2016 CSR report. As of yet, Novo A/S' Board of Directors has no female members. In 2016, the Board decided to set out the target that by 2020 the Board will consist of at least one member of each gender. To achieve this goal, the Board will work to identify suitable candidates.

### GOVERNANCE

Novo A/S puts great emphasis on representative ownership. We strive to have board representation in the companies in which we invest, and, through this, to contribute to the major strategic initiatives that our portfolio companies take. We also take an active interest in the composition of the board and the executive leadership team in the companies, and keep close track of their performance. However, when it comes to daily management and more operational issues, we rely on and entrust the company's management and board.

We are keen that the companies in our portfolio observe the value-based standards defined in the Charter for Companies in the Novo Group.

### STRATEGY

Our guiding strategy is based on the commercial objectives of the Novo Nordisk Foundation.

Novo A/S will continue to be a strong owner of the companies in the Novo Group and will invest its capital in the life science sector to optimise value creation and to support development in the industry in general.

Due to our extensive experience and expertise, we are particularly well positioned to play an active role in the life sciences. We invest across the entire spectrum of life science companies, from early seed investments through to traditional venture investments and investments in large, established companies. We have a flexible investment approach enabling us to take both minority and majority ownership stakes.

In the years to come, Novo A/S plans to further increase investments in life science companies, with a focus on US and European markets.

It is also our aim to maintain an adequate liquidity reserve, which we allocate to more traditional portfolio investments, primarily in global equities.

### **KNOWLEDGE RESOURCES**

Novo A/S relies on highly specialised expertise, particularly within the areas of life sciences and investments. For this reason, the professional competences of our employees are of great strategic importance. We focus on training and education to allow the individual employee to increase his or her value to Novo A/S and the labour market in general.

To serve our portfolio companies with the best combination of competences, our life science teams include individuals whose professional experience has been gained inside as well as outside the Novo Group. In addition to the Board of Directors, Novo A/S has an advisory group of external life science professionals, who provide Novo A/S with feedback and advice on life science investment projects.

## **BUSINESS AND FINANCIAL RISKS**

Novo A/S' most important risks are related to the business risks of the two operating companies, Novo Nordisk and Novozymes. The business risks vary in the two subsidiaries as a consequence of their different activities.

There are inherent risks associated with investing in Novo Nordisk. A rigorous enterprise risk management approach is in place to mitigate the potential adverse impacts and protect long-term value creation. Risks that have an impact on the company's performance may materialise as delays or failure of products in the pipeline, supply disruptions, competition and market developments, compromises to product quality and safety, information technology security breaches, currency impact and tax disputes, breach of legislation or ethical standards, and loss of intellectual property rights. In 2016, the most prominent risk that did materialise was a more challenging business environment in the US, caused by a combination of factors that put the US business under pressure. In turn, the overall R&D profile improved considerably with results of key clinical trials that were better than expected.

Novozymes is exposed to a range of risks throughout the value chain and has implemented measures to mitigate these. Based on risk analyses, Novozymes' Board of Directors has identified four key risks that may impact the company: competition in industrial enzymes, volatility of the starchbased ethanol business, loss of knowledge, and delay of BioAg commercialisation. To mitigate the risk of competition from existing and new competitors in industrial enzymes, Novozymes focuses on its strong innovation pipeline and delivering novel solutions tailored to the needs of customers operating in different local market conditions. To address the risk of a persistent low-price environment in the starch-based ethanol business, Novozymes is continuously investing in R&D to develop even better enzyme solutions for improving yield and profitability to ensure that biofuels are a commercial alternative to traditional fossil fuels. To ensure protection of knowledge and mitigate the risk of cyber-attacks, Novozymes pursues an active patent strategy and continuously implements key security procedures and behaviours to prevent theft of e.g. production strains and data. Novozymes' Board of Directors continues to place The BioAg Alliance high on its agenda, and prioritises and follows developments closely. Although a merged Bayer-Monsanto could cause a delay in BioAg commercialisation, the new entity could also be an attractive alliance partner for Novozymes in the long term, sharing its vision and commercial commitment, and increasing the commercial reach of the Alliance. In the short term, Novozymes' priority is to ensure the success of the Alliance, and its focus is on getting full value from the recent launch of Acceleron  $^{\rm \otimes}$  B-300 SAT.

For more information about Novo Nordisk and Novozymes and their approach to risk management, please consult the companies' annual reports.

In 2016, a new financial risk framework from the Novo Nordisk Foundation has become effective. The Novo Nordisk Foundation has decided upon a number of risk tolerances regarding shortfall risk for growth in grant pay-outs, portfolio volatility, idiosyncratic risk and access to liquidity. Novo A/S and its investments must adhere to this risk framework.

More specifically, Novo A/S should allocate its capital in a way which ensures that: (i) the Novo Nordisk Foundation should generally be able to increase its grants by at least the growth in nominal GDP; (ii) a maximum loss on the invested portfolio, excluding Novo Nordisk and Novozymes, in exceptional, negative markets conditions has been defined; (iii) no single investment should represent more than a certain percentage of the invested portfolio, excluding Novo Nordisk and Novozymes; and (iv) the Novo Nordisk Foundation should at any time be able to liquidate assets without incurring losses from forced disposals, for a value corresponding to the actual commitment as well as expected five-year grant pay-out obligations plus additional buffer.

Novo A/S is adaptive and has a range of strategic levers available for meeting these risk objectives.

#### THE FUTURE

Novo A/S' financial prospects are partly dependent on the results of Novo Nordisk and Novozymes. For further information on the outlook for 2017 for these two companies, please consult their annual reports.

Although pricing and healthcare reforms are adding pressure to the life science industry, we believe that the underlying long-term trends are positive. Positive developments in the Life Science Investments portfolio, combined with a number of strong exits and public offerings in recent years, provide the basis for our continued optimism.

At their Annual General Meetings, Novo Nordisk and Novozymes approved dividends for 2016 of DKK 4.6 per share and DKK 4.0, respectively. Consequently, Novo will receive DKK 3.5 billion in March 2017 from the two companies. In August 2017, Novo expects to receive additional interim dividends from Novo Nordisk. ■

# LARGE INVESTMENTS

evercare ::::

Value creation through long-term ownership

# Investing in innovation and growth



e are looking to invest in life science companies whose key source of value creation is innovation and growth. Our investment comes with an engaged and supportive approach, to help the company board and management realise their growth ambitions.

We provide access to funds across the entire capital structure. Our investment may be of a permanent nature, making Novo A/S a true long-term partner.

In addition to capital and engagement, an investment from Novo also provides access to our extensive network within the life science industry.

# **AN EXPANDING PORTFOLIO**

At the beginning of 2016, Novo's Large Investment portfolio comprised eight companies, of which six were direct investments undertaken as large investments and aligned with the current strategy – in addition to certain equity positions representing legacy investments.

During 2016, we completed two major large investments. In March, we issued a convertible bond to Cinven, which in December was converted into an ownership of more than 10% of SYNLAB Ltd, a leading European laboratory services provider. In May, we partnered with Nordic Capital and acquired 30% of eResearch Technologies (ERT), a leading cloud platform solution provider for the collection of outcomes data in clinical trials.

### **AMBITIONS GOING FORWARD**

During 2016, an extensive review of the Large Investment strategy was completed, leading to a redefined framework for our future investments in this area. During the coming decade, the principal purpose of Large Investments is to pursue investments into, or actually build, four to six lighthouse positions – i.e. major leading life science companies with strong operational and financial performance, as well as global commercial presence.

# *Large Investments in brief 2016*

Large Investments covers Novo A/S' direct investment efforts in wellestablished life science companies. These companies are characterised by their strong market position, attractive growth prospects, and an ambitious innovation agenda.

Large Investments was established as a separate entity in 2013. Following an extensive strategic review in 2016, this area was highlighted as one where Novo will place significant further investments in the years to come.



**PORTFOLIO COMPOSITION** 

# Large Investments in DKK million





# Large Investments



# eResearch Technology

# Global leader in solutions for clinical outcomes data capture

In May 2016, Novo A/S acquired a minority stake in eResearch Technology Inc. (ERT), a leading global provider of electronic clinical outcomes data collection for the pharmaceutical industry. The minority share was acquired from Genstar Capital for USD 1.8 billion. The acquisition was lead by private equity partner, Nordic Capital.

RT is the leading global provider of electronic data collection solutions for clinical development programmes. ERT's cloud-based solutions capture quality efficacy and safety endpoints, harmonise

data from any clinical source system, and deliver real-time insights for optimal trial performance while ensuring patient safety.

# >50%



of FDA drug approvals in past three years were based on ERT-supported studies. studies with 3 million patients have relied on ERT solutions.

Novo holds 30% of the institutional equity in ERT plus a portion of the debt. We partnered with Nordic Capital for this transaction, which was our first investment in a US-headquartered company with global business activities.

# ADVANCING DATA COLLECTION, ANALYSIS AND REPORTING

ERT's combination of technology, services and consulting increases the accuracy and reliability of patient data and improves the efficiency of the clinical development process throughout the product lifecycle.

The company operates in three main business areas:

• Electronic clinical outcomes assessment (eCOA) comprises electronic questionnaires (e.g. probing on degree of pain) to track patient health status. Questionnaires are administered by phone or tablet to track and collect patient-reported metrics. Digital solutions are increasingly used over paper due to low costs, improved data quality and subject compliance as well as dynamic functions (e.g. suicide risk alerts).

• Cardiac safety involves the collection and interpretation of cardiac data using a connected ECG for use in drug safety testing. Centralised digital solutions are increasingly taking over from paper data capture due to the higher data quality in automated readings (e.g. detection of short 10 milliseconds abnormalities that ~80% of cardiologists miss). ERT delivers ECG readings supported by proprietary analytics software and in-house cardiologist data evaluation.

• Respiratory includes the collection and interpretation of respiratory data from connected spirometers for testing of the efficacy and safety of drugs. Respiratory data is used as key end point to determine efficacy in respiratory diseases (asthma, COPD, CF, IPF). It is also used for lung safety in other therapeutic areas.

### **POSITIVE PREDICTIONS**

ERT has consistently been growing both revenues and profits by more than 10% per year, and the company is well positioned to continue benefitting from significant and rapid shifts in the market.

Three key factors account for ERT's positive prospects. First, regulatory and payer requirements to clinical trial sponsors are becoming ever more stringent and expansive. Demand is increasing for further data elements – many patient as well as physician reported – to demonstrate patient benefits and overall cost effectiveness.

Second, electronic data capture improves accuracy, speed and cost. More than 80% of patient-reported data is still collected on paper, representing an enormous opportunity for ERT. Additionally, the US FDA has issued guidelines stipulating that only electronically collected data can be used for labelling purposes.

Finally, clinical trial sponsors increasingly need scalable, dynamic and trusted solutions. At the same time as sponsors need additional functionality to interact with patients and physicians, the overall cost of clinical trials has never been higher, which increases operational risk. ERT is the only large IT solutions provider with a track record of zero failed studies.

"Increased regulations, greater complexity and a highly competitive market are exponentially raising the level of risk for our customers. By investing in advanced technology platforms, providing superior customer service, and identifying problems before they occur, we are helping pharmaceutical and biotech companies bring life-saving therapies to market faster and more cost effectively than ever." — Jim Corrigan, CEO, ERT

# Fast facts

• Established in 1972

• Headquarters: Philadelphia • 1,000 employees in five countries

Open pc

Ent

Inta Ertao

EST

• Jim Corrigan, CEO

# **SYNLAB**

# *– European #1 in clinical laboratory services*

In March 2016, Novo A/S acquired a minority share in SYNLAB, Europe's largest laboratory services provider. This was achieved by means of a convertible debt instrument, which was subsequently converted in December 2016.

S YNLAB is the undisputed European market leader in the field of laboratory services, performing approximately 450 million test results per annum for customers across the entire healthcare sector – including practicing doctors, clinics and the pharmaceutical industry. The company holds a top three position in all of its key markets.

Novo acquired its shares in SYNLAB from Cinven, a UKbased private equity company, which remains the majority shareholder in the Cinven Group.

### **INNOVATIVE MEDICAL LABORATORY SERVICES**

SYNLAB offers a full range of medical laboratory services for human medicine, including routine and specialty clinical pathology tests; anatomic pathology tests covering histological and cytological tests; and diagnostic imaging tests using medial and molecular imaging technologies. SYNLAB also offers testing services for veterinary medicine and environmental analysis such as food, water and air.

Although laboratory medicine represents only approximately 2% of the European healthcare budgets, it plays a key role in the diagnosis and the validation of therapeutic interventions and paves the way for implementation of personalised medicine. In the future, the role of laboratory medicine is expected to become even more important, and SYNLAB attaches great importance to the advancement of medical diagnostics. SYNLAB focuses on the implementation of innovative laboratory technologies and on leveraging its Europeanwide network of specialist diagnostic competences. Through its leadership position, SYNLAB benefits from its pan-European scale and organisational structure, achieving low costs while providing high quality and short turnaround times to its customers.

These benefits also position SYNLAB as one of the most successful consolidators of the highly fragmented European clinical laboratory services market – with significant potential for scale and competence synergies. Continued consolidation through acquisitions remains a cornerstone in SYNLAB's strategy of accelerating its growth and strengthening its leadership position in the European market.

## A FOOTHOLD IN THE HEALTHCARE SERVICE INDUSTRY

Through the investment in SYNLAB, Novo has diversified its large investment portfolio and obtained exposure to the healthcare services industry in a segment that benefits from classic industrial business drivers, solid fundamental growth drivers, high entry barriers, and a stable competitive environment.

Moverover, the co-investment with Cinven provides Novo access to a partner with a proven track record within large-scale, post-merger integration efforts, and industry consolidation through buy-and-build strategies. ■ "Two major drivers are shaping the global market for medical laboratory diagnostics: innovation as a prerequisite for organic growth on the one hand: and a highly fragmented market with huge potential for consolidation on the other. SYNLAB plays – and will continue to play – a major role in this market. By continuing our proven M&A strategy and by focusing on innovative tests and services, we will maintain and further strengthen our position as Europe's leading provider for medical diagnostics." — Bartl Wimmer CEO, SYNLAB

Fast facts

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 Established through a combination of Labco and SYNLAB in 2015 Present in more than 30 countries across four continents

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15.000 employees performing approximately 450 million test results per annum

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- Sales revenues of approximately EUR 1.6 billion
- Dr Bartl Wimmer, CEO and cofounder

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# Large Investments portfolio companies

## **NEW INVESTMENTS IN 2016**



eRESEARCH TECHNOLOGY (ERT) is the leading global provider of electronic clinical outcomes data collection for the pharmaceutical industry through cloud platform solutions for clinical development programmes. www.ert.com

# SYNLAB

**SYNLAB** is the largest laboratory services provider in Europe, offering a full range of medical laboratory services for clinical practice and the entire healthcare sector. www.synlab.com

## **PRIVATE COMPANIES**

# SOUISU

**SONION** is a leading provider of micro acoustical and micro mechanical technology solutions to the hearing aid industry. www.sonion.com



**SYMPHOGEN** is a biopharmaceutical company that develops therapeutics based on antibody mixture for the treatment of cancer. These therapies are based on a proprietary technology platform. www.symphogen.com



XELLIA PHARMACEUTICALS is a leading provider of complex anti-infective products used in treatment of serious and often life-threatening infections. www.xellia.com

### **PUBLIC COMPANIES**



**BTG** is focused on building a platform of innovative therapies and diagnostic within interventional medicine - combining medicines and device technologies to deliver targeted treatments.

www.btgplc.com

# CHR\_HANSEN

Improving food & health.

**CHR. HANSEN** is a global bioscience company that develops natural solutions for the food, nutritional, pharmaceutical and agricultural industries. www.chr-hansen.com

# inøgen

**INOGEN** leads the market within the development, manufacture and marketing of innovative portable oxygen concentrators, which deliver supplemental long-term oxygen therapy to patients suffering from chronic respiratory conditions.

www.inogen.com

# orexo

**OREXO** is a specialty pharmaceutical company focused on the therapeutic areas of opioid addiction treatment and pain management.

www.orexo.com



**VELOXIS PHARMACEUTICALS** is a specialty pharmaceutical company focused on the commercialisation of Envarsus XR (extended release Tacrolimus), an immunosuppressant for kidney rejection treatment. www.veloxis.com

# *Portfolio company achievements in 2016*

## BTG

- completed the acquisition of Galil Medical, a leading provider of cryoablation products used in the treatment of kidney and other cancers.
- launched the ßETA™ Radiation Safety programme, a new initiative designed to reduce the risk of radiation exposure when performing selective internal radiation therapy (SIRT) with 90Y microspheres.

# CHR HANSEN

- launched a new coagulant, CHY-MAX<sup>®</sup> Special a true game changer for soft cheese manufacturers and the food service sector.
- acquired LGG<sup>®</sup> business from Valio OY to further strengthen its microbial platform.
- acquired Nutritional Physiology Company and expanded its business in probiotics to the livestock industry.

# eRESEARCH TECHNOLOGY

- completed the acquisition of UK-based Exco Intouch, a leading provider of patient engagement and digital health solutions for clinical trials.
- integrated the market-leading fractional exhaled nitric oxide (FeNO) measurement device by Aerocrine – a Circassia-owned subsidiary – into ERT's diagnostic platform for e.g. spirometry and ECG home monitoring of clinical trials endpoints.

# INOGEN

 released innovative Inogen One G4<sup>™</sup> Oxygen Concentrator. The ultra-portable device is the smallest and lightest oxygen concentrator that the company has ever produced.

#### OREXO

 and Mundipharma announced the submission of a regulatory Marketing Authorisation Application (MAA) for Zubsolv (buprenorphine and naloxone) sublingual tablet to the European Medicines Agency (EMA), seeking approval for the treatment of opioid dependence.

### SONION

 and InvenSense announced the release of the O-series MEMS microphone in two very small form factors, thereby completing a critically important development programme.

### **SYMPHOGEN**

 and Baxalta announced a broad strategic immuneoncology collaboration. Symphogen received USD 175 million upfront, in addition to potential future milestone payments and royalties.

### **SYNLAB**

- announced a successful re-financing of its debt by issuing a EUR 940 million senior secured floating rate notes at par.
- completed integration of the merger process between Labco and SYNLAB.

## **VELOXIS PHARMACEUTICALS**

 announced that once-daily Envarsus XR<sup>®</sup> (tacrolimus extended-release tablets) received US Food and Drug Administration (FDA) approval for label enhancements. These enhancements are related to pharmacokinetics.

## **XELLIA PHARMACEUTICALS**

- reached agreement with US Food and Drug Administration (FDA) on modifications for the newly-acquired Cleveland site, and subsequently received approval for its use as a packaging facility
- expanded Croatian anti-infective product and innovation capabilities to tackle antimicrobial resistance crisis.

# NOVO VENTURES

*Investing in biotech to bring innovative products to patients* 

# A unique approach to venture investments

N ovo Ventures is a specialised life science venture capital investor. We focus on building and realising financial value in our portfolio. In addition to generating financial return, we strive to invest in companies that develop drugs, medical

devices and diagnostics that can improve the health and lives of people around the world.

Novo A/S' approach to venture capital investments is unique due to our special ownership structure. Novo has significant shareholdings in Novo Nordisk A/S and Novozymes A/S, but our venture investments are fully independent of the two major Novo Group companies.

Our venture investments are structured as an open evergreen fund with Novo as the only investor. This unique funding structure allows us to assume a long-term perspective when we make our investments.

# AN INTERNATIONAL INVESTOR

With people on the ground in Copenhagen, London, San Francisco and Boston, Novo is positioned to reach the major global life science hubs and can quickly respond to new, interesting investment opportunities wherever they emerge.

Our team also supports our portfolio companies through participation on the board of directors and by leveraging the experience gained from our diverse life science portfolio.

## A STRONG TRACK RECORD

During our 17 years in the business, we have invested DKK 10 billion in 138 companies and successfully exited 44 companies – primarily through trade sales to large pharmaceutical and medical device companies, and through IPOs that have provided liquidity. Today, we have a diversified portfolio of life science companies and a history of successful exits that have delivered positive financial results.

With annual investments of over DKK 2 billion in 2016, Novo's ventures investments have reached their highest level ever.

### **INVESTMENT APPROACH FOR 2017 AND BEYOND**

Novo is expanding its venture investments in both private and public market investing. In 2017, we will continue with a high level of investing and allocating more resources to our teams in Copenhagen, San Francisco and Boston.

While increasing the level of private investing, we will have a greater focus on public investments. We will continue to focus on development and regulatory stage companies that address unmet therapeutic needs.

Within medtech investing, we will be deploying specific resources to identify new opportunities. We will continue to focus on US-marketed, revenue-stage, high-growth companies that use innovation to address underserved patient populations.

For more information about Novo's ventures investments, please visit novo.dk



The loaded embrace between a dendritic cell and a lymphocyte is the focus for the next generation immunotherapeutics. Source: Nature Biotechnology.

# *Novo Ventures in brief 2016*

Novo A/S is one of the largest life science venture capital investors in the world. We currently invest more than DKK 2 billion on an annual basis. Since 2000, we have invested in 138 companies, and successfully exited 44 companies through trade sales and IPOs.

We have activities in Copenhagen, San Francisco, Boston and London. Through our international network of scientific, development and commercial expertise, we cover the major life science hubs.

Investments in 2016

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**DKK 0.3** billion in EUROPE **DKK 1.8** billion in the US

4 New public companies (1 billion DKK invested) 10 — New pi compa

New private companies (1 billion DKK invested)

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Geographical allocation by number of companies









# Selected portfolio company achievements in 2016

### **BUSINESS NEWS**

ANOKION completed an option deal with CelGene in December 2016. ..... APOLLO ENDOSURGERY completed a reverse merger and was listed on Nasdag in December 2016. ..... CORVUS PHARMACEUTICALS was listed on Nasdag in March 2016. CRISPR was listed on Nasdag in October 2016. ..... **iRHYTHM** was listed on Nasdaq in October 2016. ..... KALVISTA completed a reverse merger and was listed on Nasdag in November 2016. ..... MERUS was listed on Nasdag in May 2016 and completed a major collaboration with Incyte in December 2016. RA PHARMACEUTICALS was listed on Nasdag in October 2016. ..... **REATA PHARMACEUTICALS** was listed on Nasdaq in May 2016. TOBIRA THERAPEUTICS was acquired by Allergan in a

buy-out valued up to USD 1.7 billion.

### PRODUCT NEWS

ACACIA achieved positive phase 3 data in two trials in post-operative nausea and vomiting with amisulpride.

**ALLAKOS** completed a phase 1 study with AK002, an antibody under development for treatment of immunologic diseases and demonstrated clinical activity with depletion of eosinophils in healthy volunteers.

**ANAPTYS** completed a phase 1 trial of anti-IL33 antibody, achieving three months suppression of IL-33 for three months with a single injection.

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**COLUCID PHARMACEUTICALS** met the primary and secondary end points in a phase 3 pivotal study for acute migraine.

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**RA PHARMACEUTICALS** completed a successful phase 1 study with an sc-administered inhibitor of C5-mediated hemolysis.

**SPECTRANECTIS** successfully completed a randomised study with the Stellarex drug-coated balloon, meeting the end points of the study.

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**TOBIRA THERAPEUTICS** missed the primary end point but met an important secondary end point for reduction of fibrosis in the phase 2b NASH study.

# Introducing the class of 2016

uring 2016, Novo added four public and 10 private companies to its venture portfolio. In the majority of the private financings, Novo A/S was lead or co-lead investor.

Our new portfolio companies develop therapies for a variety of indications, including anti-infectives, cancer immunotherapy, genetics, respiratory diseases, endocrinology, urology, gynecology and hematologic diseases.

All the companies are located in the US, except for two (F2G Ltd. in Manchester and Verona Pharma in London, both UK).

### **ANTI-INFECTIVES**

**ENTASIS THERAPEUTICS**, a spin out from Astra Zeneca, is developing a pipeline of antibiotic products.

**F2G LIMITED** is focusing on the discovery and development of novel drugs to treat life-threatening fungal diseases.

#### **CANCER IMMUNOTHERAPY**

**BATTERSEA BIOTECH** develops alternative cell types and technologies to overcome the shortcomings of current CAR-T and TCR technologies.

**BOLT THERAPEUTICS** is developing two immune-oncology technologies.

**RGENIX** is developing first-in-class drugs that target key pathways in cancer progression.

**TARVEDA THERAPEUTICS** is a pre-clinical stage biotechnology company that is developing novel drugs for the treatment of cancer.

#### **RESPIRATORY DISEASES**

**VERONA PHARMA** is a clinical stage biopharmaceutical company focused on the development of innovative prescription medicines to treat respiratory diseases with significant unmet medical needs (such as COPD, asthma and cystic fibrosis).

#### GENETICS

**CRISPR THERAPEUTICS** is developing transformative genebased medicines for patients with serious diseases. The therapeutic approach is to cure diseases at the molecular level using the breakthrough gene-editing technology called CRISPR-Cas9.

#### **ENDOCRINOLOGY**

**SPRUCE BIOSCIENCES** is a clinical-stage biopharmaceutical company with programmes in development to serve the chronic and acute needs of patients with orphan disease affecting the neuroendocrine axis.

#### UROLOGY

**OUTPOST MEDICINE** is developing novel therapeutics for the treatment of urologic and gynecologic disorders. OP-233 is currently in phase 2 for the treatment of stress urinary incontinence.

#### **GYNAECOLOGY**

**MINERVA SURGICAL** focuses on women's healthcare. Currently, Minerva Surgical's development projects are aimed at delivering next generation products for the treatment of abnormal uterine bleeding.

# HAEMATOLOGY

ACCELERON PHARMA is a clinical-stage biotechnology company developing ligand traps that target the endogenous ligands for the TGF superfamily of serine/threonine protein kinase receptors. The company's lead compound, luspatercept is in phase 3 clinical trials for the treatment of anemia associated with myelodysplastic syndrome (MDS) and thalassemia.

#### DERMATOLOGY

**DERMIRA** focuses on the development and commercialisation of novel therapies for the treatment of dermatological conditions.

### **MEDICAL DEVICES**

**SPECTRANETICS** develops, manufactures, markets and distributes single-use medical devices used in minimally-invasive procedures within the cardiovascular system.

# Investing in next generation oncology therapies

One of the significant breakthroughs within cancer research is immuno-oncology – using the body's own immune system to fight cancer. Novo A/S has made several investments in immunooncology companies, providing capital and support to transform innovative research into therapies that work.

mmuno-oncology is the principle by which a patient's immune system attacks and clears malignant cells.

Recent clinical advances have demonstrated that pharmacological interventions – through mechanisms that lead to the activation of immune cells – can control certain cancers (Fig. 1).

Emerging data indicate that multiple immune cell types as well as numerous immune-suppressive pathways represent therapeutic opportunities to induce synergistic anti-tumour responses. However, researchers need to push a number of scientific and clinical frontiers. These include developing strategies for neutralising tumour-promoting processes, broadening the repertoires of harmful antigens recognised by our immune systems, and targeting the mechanisms by which immune cells recognise and attack tumour tissues in particular. Such efforts are expected to pave the way for developing novel therapies that overcome resistance to current treatments and promote long-term control of cancer.

Our investments over recent years are creating opportunities that will impact the treatment of cancer in the future.



# TIOMA — activating the 'eat me' signal on tumours

Tioma is developing anti-CD47 antibodies for the treatment of solid and hematologic cancers.

Our immune system is organised into a layered defense system comprised of an innate response and an adaptive response. The innate immune system provides a rapid and robust response against foreign cells or pathogens. But it does not confer long-lasting or protective immunity. The adaptive immune system, however, is composed of highly specialised systemic processes and generates immunological memory. Targeting CD47 unleashes both the innate and adaptive arms of the immune system to fight cancer.

Up-regulation of CD47, a protein expressed on most tumour cells, acts as a 'don't eat me' signal, disguising the tumours as 'normal' tissue. Anti-CD47 antibodies thus have the potential to unmask the tumour and promote coordination of the innate and adaptive immune systems to act in concert to attack the cancer.

Tioma has generated a portfolio of anti-CD47 antibodies that have the potential to overcome the multiple checkpoints by which cancers evade the immune system.

# CORVUS — reprogramming of T-cells

Corvus Pharmaceuticals is a clinical-stage company that develops therapies blocking crucial immune checkpoints and reprogramme immune T-cells. The management team of Corvus helped develop Rituxan, Imbruvica and Zelboraf in the past.

### **IMMUNE CHECKPOINTS AND CANCER**

T-cells are constantly surveying the body by assessing cells as being normal or diseased using the identity of certain proteins on their surface. If the protein signature suggests that the cell is infectious or cancerous, the T-cell will initiate an attack.

A class of molecules known as immune checkpoints modulate the T-cell response to prevent damage to normal cells. Tumours use these molecules to evade the immune system. A number of recently approved drugs called checkpoint inhibitors interrupt this evasive mechanism, allowing the T-cells to attack the tumour.

Corvus is focused on modulating the adenosine-signalling (Fig. 2) axis for the treatment of cancers.

Adenosine is a signalling molecule used by the body to limit inflammation and immune responses. Many tumours

#### Fig. 2

#### The adenosine-cancer axis

The adenosine-cancer axis. The adenosine pathway participates in the generation of an 'immune-tolerant' niche for the tumour by regulating the function of immune and inflammatory cells, such as macrophages, dendritic cells, myeloid-derived suppressor cells, T-cells and NK cells. Each of these cell types expresses receptors that bind adenosine and thereby influence cell function. Tumours often express enzymes such as CD39 and CD73 that drive the increased production of extracellular adenosine. Source: Corvus Pharmaceuticals



# Continued from p. 33

produce and actively sustain high levels of adenosine within the tumour micro-environment.

The adenosine that tumours produce interacts with adenosine receptors on the surface of invading immune cells. A type of adenosine receptor known as A2A is expressed on several cells of the immune system, including T-cells, NK cells, macrophages and dendritic cells. Binding of adenosine to the A2A receptor has the effect of limiting the immune cells' ability to attack tumours. A significant body of scientific data indicates that blocking A2A receptor can promote anti-tumour immune responses, leading to tumour regression.

CPI-444 is an orally administered antagonist of the adenosine A2A receptor. The molecule entered a phase 1b study in early 2016. In collaboration with Genentech, this study is evaluating CPI-444 as a single agent and in combination with another promising checkpoint inhibitor.

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# NKARTA — harnessing the 'Natural Killing' capabilities of NK cells

NKarta Therapeutics is focused on developing therapies using Natural Killer (NK) cells. NKarta's core capability, developed by scientific founder Dario Campana, is the consistent expansion and genetic modification of primary NK cells for adoptive cell immunotherapy (for an overview of this process, please see Fig. 3). NK cells have an intrinsic ability to distinguish transformed versus normal cells. NK cells are unique based on the following attributes:

- They do not require activation to kill cells that are missing 'self' markers. This is especially important because harmful cells that are missing 'self' markers cannot be detected and destroyed by other immune cells, such as T-cells.
- They express both activating and inhibitory receptors that recognise multiple ligands, a potential advantage relative to the recognition of a single antigen seen with T-cells.
- They lack T-cell receptors (TCRs). TCRs from a donor can be recognised by the patient's immune system as 'foreign', resulting in a 'rejection' called Graft versus Host Disease (GvHD). Consequently, NK cells represent an opportunity for 'off-the-shelf' allogeneic approach versus an autologous approach.
- They have the ability to recruit and prime T-cells, generating a broad adaptive immune response as well.

NKarta is developing a best-in-class NK cell engineering platform that will allow for either allogeneic or autologous therapies.

# RGENIX

# - stopping tumour escape mechanisms

Rgenix is developing first-in-class drugs targeting key pathways in cancer progression. The company's lead programme is a small molecule that blocks the ability of tumours to evade the immune system.

# Fig. 3 Adoptive cell therapy

Adoptive cell immunotherapy typically involves at least four basic steps. 1) Peripheral blood mononuclear cells (PBMCs) are isolated from the patient or donor; 2) These cells are manipulated through various means to potentiate activity; 3) Modified cells are expanded ex vivo; 4) The modified cells are introduced into the patient.



### **REVERSING IMMUNE EVASION**

Tumours grow and escape the immune system either by taking advantage of cells known to suppress the immune system or recruiting healthy cells for growth. They do so by employing characteristic changes in lipid metabolism. Rgenix's lead programme, RGX-104 is a small molecule that targets a specific type of cell receptor known as LXR (Liver X Receptor). LXR is a master regulator of lipid metabolism and has been shown to play a role in tumour progression. Through selective activation of LXR, RGX-104 targets a key immune cell type in the tumour micro-environment, reversing immune evasion and generating robust anti-tumour immune activity.

RGX-104 has obtained FDA Orphan Drug Designation in several solid tumour types of high unmet need, and enters clinical trials in the second half of 2016.

# ARCELLX - engineering specificity and function

Arcellx is a pre-clinical company developing therapies using a proprietary binding domain directed against key tumour antigens.

Chimeric antigen receptors (CARs) (Fig. 4) are emerging as powerful tools for reprogramming T-cell specificity and function. These cells combine the antigen specificity of an antibody with the biologic properties of T-cells.

CAR-T therapy is a form of adoptive cell therapy (Fig. 3) in which T-cells from a patient are genetically modified to

express synthetic receptors targeting tumour-specific surface antigens (sparing healthy tissue). Due to their potentially long-lived nature, CAR-T cells can persist in the patient and provide long-term immune surveillance.

CARs are composed of a binding domain (Fig. 4) - typically a small fragment of an antibody that selectively targets a known tumour antigen. However, there are several challenges using the current methods. For example:

- Targeting of a single antigen doesn't always eliminate the cancer entirely, as tumours will escape by eliminating the targeted antigen; and
- The inability to turn the CARs on and off has certain safety consequences.

Arcellx aims to address these issues by pursuing an alternative binding domain technology (D-domain) developed in collaboration with the National Cancer Institute (NCI). The D-domain's small size allows for engineering CARs that bind and kill tumour through one or more target antigens, which should reduce recurrences due to antigen escape. In addition, D-domains can act as integrated functional switches, modulating the activity of CARs to help overcome safety issues.



# Fig. 4

body variable fragment (scFv) comprised of an extracellular domain linked through hinge and transmembrane domains to a cytoplasmic signaling region. Arcellx is developing a modified CAR that addresses current challenges in the field. Source: Kershaw, et al. Nature Reviews Cancer 2013.

# Novo Ventures portfolio companies

#### **PRIVATE COMPANIES**



Acacia Pharma focuses on the development of compounds for the prevention and treatment of nausea and vomiting following surgery and chemotherapy. The lead programme is in phase 3 clinical development.

www.acaciapharma.com



**Allakos** develops monoclonal antibody-based therapies to target eosinophils and mast cells. The lead programme is in pre-clinical development. www.allakos.com



**Bolt Therapeutics** plans to develop a novel format for T-cell mediated anti-tumour therapy.



F2G is focusing on the discovery and development of novel drugs to treat life-threatening fungal diseases. www.f2g.com



**Cianna Medical** is a medical device company that manufactures and markets the SAVI breast brachytherapy applicator for the delivery of radiation after lumpectomy surgery. www.ciannamedical.com



Galera Therapeutics is a clinical-stage company focused on the development of highly selective small molecule dismutase mimetics, targeting the prevention of radiation-induced mucositis. www.aaleratx.com



**AnaptysBio** is an antibody therapeutics company and a leader in antibody discovery and optimisation. www.anaptysbio.com



The company is developing novel antibiotics for treatment of severe Gram-negative infections. The focus is on developing new antibiotics to treat infections resistant to current treatments. www.entasistx.com

ENTASIS

# **≱KANYOS** BIO

**Kanyos Bio** is a spin out from Anokion. The company has the rights to develop celiac disease and T1D autoimmune programmes and an option deal with Astellas.

www.kanyos.com



**Anokion** develops novel peptide and protein therapeutic with very low immunogenicity. The company is focused on products for orphan diseases. www.anokion.com

# BATTERSEA BIOTECH

**Battersea Biotech** develops alternative cell types and technologies to overcome the shortcomings of current CAR-T and TCR technologies.



**Epsilon-3 Bio** develops compounds targeting the removal of cellular debris in chronic inflammatory and autoimmune disorders. The lead compound is in pre-clinical development. www.epsilon-3.com

#### E-SCAPE BIO

*E-Scape Bio* is developing a pipeline of ApoE4structure correctors for the treatment of neurodegenerative diseases, including Alzheimer's disease.



Karus Therapeutics develops innovative therapies for the treatment of inflammation and cancer. The lead programmes are in pre-clinical development and focus on histone deacetylase and phosphoinositide 3-kinase inhibitors. www.karustherapeutics.com



Minerva Surgical focuses on women's healthcare. Currently, Minerva Surgical's development projects are aimed at delivering next generation products for the treatment of abnormal uterine bleeding. www.minervasurgical.com


ObsEva develops innovative drugs for women's reproductive medicine. The lead project is in phase 2 clinical development for enhancing embryo implantation and increasing the pregnancy rate in connection with assisted reproductive technologies. www.obseva.com



Orphazyme develops novel therapeutics for the treatment of lysosomal storage diseases. The company is preparing the lead programme for a phase 2/3 registration-enabling clinical trial in Niemann-Pick disease type C. www.orphazyme.com

### RGENIX

Rgenix is developing first-in-class drugs that target key pathways in cancer progression. www.rgenix.com

# tioma

*Tioma* is developing drugs for life-threatening disorders driven by CD47-mediated signalling pathways.

www.tiomatherapeutics.com

### SI-BONE

SI-BONE is a revenue-stage medical device company, which develops and markets new therapies for patients with low back pain (related to sacroiliac joint disorders). www.si-bone.com

### CHAINED

Unchained Labs develops and markets a broad range of life science instruments to analyse protein stability and optimise protein formulations. www.unchainedlabs.com



Outpost Medicine is developing novel therapeutics for the treatment of urologic and gynaecologic disorders. OP-233 is currently in phase 2 for the treatment of stress urinary incontinence. www.outpostmedicine.com



Spruce Biosciences Spruce Biosciences is a clinicalstage biopharmaceutical company with programmes in development to serve the chronic and acute needs of patients with orphan disease affecting the neuroendocrine axis.



is developing antibody-coupled T-cell Unum technology platform to combine antibody with CAR-T killing mechanism for use in oncology. www.unumrx.com



PanOptica is developing a novel topical drug for wet age-related macular degeneration. The lead programme is in phase 1b clinical development. www.panopticapharma.com



Tarsa Therapeutics develops an oral calcitonin for the treatment of osteoporosis. www.Tarsatherapeutics.com

Vantia

Vantia Therapeutics develops small molecule agonists of vasopressin receptors. The lead asset is in phase 3 clinical development for the treatment of nocturia. www.vantia.com



Procent BioRobotics develops a new treatment for benign prostate hyperplasia based on image-guided and robotically-controlled water ablation of prostate tissue. The device is CE marked and a PMA study underway for US approval. www.procept-biorobotics.com



Tarveda Therapeutics is a pre-clinical stage biotechnology company that is developing novel drugs for the treatment of cancer. www.tarveda.com



Continued from p. 37

### **PUBLIC COMPANIES**



Acceleron Pharma (NASDAQ: XLRN) is a clinicalstage biotechnology company developing ligand traps that target the endogenous ligands for the TGF superfamily of serine/threonine protein kinase receptors. The company's lead compound luspatercept is in phase 3 clinical trials for the treatment of anemia associated with myelodysplastic syndrome (MDS) and thalassemia. www.acceleronpharma.com

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Apollo (NASDAQ: APEN) markets Orbera® and Lap-Band® for the treatment of obesity. The company is a leader in flexible endoscopic surgery via OverStitch<sup>™</sup> and other endoscopic devices. www.apolloendo.com

# Colucid

**CoLucid Pharmaceuticals (NASDAQ: CLCD)** develops lasmitidan for the treatment of acute migraine. Positive phase 3 data has been announced. www.colucid.com

### CORVUS Pharmaceuticals

**Corvus Pharmaceuticals (NASDAQ: CRVS)** develops drugs that harness the immune system to fight cancer in a new area of medicine known as immuno-oncology.

www.corvuspharma.com



CRISPR Therapeutics (NASDAQ: CRSP) is developing transformative gene-based medicines for patients with serious diseases. The therapeutic approach is to cure diseases at the molecular level, using the breakthrough gene editing technology called CRISPR-Cas9. www.crisprtx.com



Dermira (NASDAQ: DERM) focuses on the development and commercialisation of novel therapies for the treatment of dermatological conditions. www.dermira.com



Flexion (NASDAQ: FLXN) is a specialty pharmaceutical company focused on the development and commercialisation of novel, local therapies for the treatment of patients with musculoskeletal conditions, beginning with osteoarthritis (OA) – a type of degenerative arthritis. www.flexiontherapeutics.com

### **HTG** Molecular

HTG Molecular Diagnostics (NASDAQ: HTGM) is developing and marketing its Edge instrument and assays for quantification of gene expression. They are used for clinical diagnostics and in research. The Edge instrument is being launched in the US. www.htamolecular.com

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Invuity (NASDAQ: IVTY) is a commercial stage medical technology company pioneering the use of advanced photonics to provide surgeons with improved direct visualisation of surgical cavities during minimally invasive and minimal access surgical procedures. www.invuity.com

# iRhythm

*iRhythm Technologies (NASDAQ: IRTC)* is a medical device company that develops and markets the ZIO<sup>®</sup> Service – an innovative cardiac monitoring and diagnostic solution, which uses a single-use wearable patch to detect cardiac arrhythmias. www.irhythmtech.com

KalVista

KalVista Pharmaceuticals (NASDAQ: KALV) develops plasma kallikrein inhibitors for the treatment of diabetic macular oedema. Their lead programme is in phase 1 clinical development. www.kalvista.com



Merus (NASDAQ: MRUS) is a Dutch biotechnology company developing fully human bi-specific antibodies for various oncology treatments. Their two lead programmes are for solid tumours and AML. www.merus.nl



Nabriva Therapeutics (NASDAQ: NBRV) is focused on the research and development of novel antiinfective agents to treat serious infections. Nabriva's lead product candidate, lefamulin is entering phase 3 clinical trials for the treatment of moderate to severe community-acquired bacterial pneumonia. www.nabriva.com

RaPharma

Ra Pharmaceuticals (NASDAQ: RARX) develops drugs for treatment of complement dysregulation diseases. The lead programme is an anti C5 complement inhibitor. www.rapharma.com

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Reata Pharmaceuticals (NASDAQ: RETA) develops new drugs for the treatment of inflammatory diseases and cancer. The lead programmes are in phase 2 clinical development. www.reatapharma.com

# **O** Spectranetics

Spectranetics (NASDAQ: SPNC) develops, manufactures, markets and distributes single-use medical devices used in minimally invasive procedures within the cardiovascular system. www.spectranetics.com



Verona Pharma (LSE: VRP) is a clinical stage biopharmaceutical company focused on the development of innovative prescription medicines to treat respiratory diseases with significant unmet medical needs, such as COPD, asthma and cystic fibrosis. www.veronapharma.com



Xenon Pharmaceuticals (NASDAQ: XENE) is a genetics-based drug development company. The lead compound is in clinical development for the treatment of pain. www.senon-bharma.com

# *Selected exits* 2007–2016

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### TRADE SALES AND INITIAL PUBLIC OFFERINGS

**Adaptimmune** Initial public offering in 2015

**Aerie Pharmaceuticals** Initial public offering in 2014

**Akebia Therapeutics** Initial public offering in 2014

**Alder Biopharmaceuticals** Initial public offering in 2014

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**Alios BioPharma** Acquired by Johnson & Johnson

**Amira Pharmaceuticals** Acquired by Bristol-Myers Squibb

BioMimetic Therapeutics Acquired by Wright Medical Group

 Elevation Pharmaceuticals

 Acquired by Sunovion Pharmaceuticals

*Funxional Therapeutics* Sold lead asset to Boehringer Ingelheim

FoldRx Pharmaceuticals Acquired by Pfizer

Gloucester Pharmaceuticals
Acquired by Celgene

InSound Medical Acquired by Sonova Holding

*Intersect ENT* Initial public offering in 2014

**NeoMend** Acquired by C R Bard

**Nevro** Initial public offering in 2014 **Novexel** Acquired by AstraZeneca

**Otonomy** Initial public offering in 2014

**Protein Forest** Acquired by ProteinSimple

**ProteinSimple** Acquired by Techne Corporation

**PTC Therapeutics** Initial public offering in 2013

Santaris Pharma Acquired by Roche

Sapphire Therapeutics Acquired by Helsinn Healthcare

**Spinifex Pharmaceuticals** Acquired by Novartis

*Synosia Therapeutics* Acquired by Biotie Therapies

**Tetraphase Pharmaceuticals** Initial public offering in 2013

*Thiakis* Acquired by Wyeth Pharmaceuticals

**Tobira Therapeutics** Initial public offering in 2015

**Tokai Pharmaceuticals** Initial public offering in 2014

**ZymoGenetics** Acquired by Bristol-Myers Squibb

*ZS Pharma* Initial public offering in 2014



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Creating companies from innovative life science

# Growing tomorrow's biotech successes

t is Novo Seeds' vision to create an even stronger Nordic biotech industry. We do this by building and investing in startup companies founded on strong science and innovative products with the potential to transform patient treatment.

In close collaboration with leading researchers, academic institutions, entrepreneurs and leaders in the biotech industry, we turn promising life science discoveries into viable businesses. The commercial value is developed and matured through two routes: pre-seed grants for concepts that need maturation and capital investment in projects with a solid plan.

Since 2007, we have built and exited three companies and created a pipeline of biotech startups that are currently developing their portfolio towards commercialisation and success. Today, our portfolio consists of 19 active seed companies and 19 pre-seed projects, primarily from the Nordic region. We cover the spectrum from early-stage discovery through to clinical-stage companies.

### AN EXCITING YEAR

In 2016, the Seeds unit invested in seven new startups and invested about DKK 100 million in our portfolio companies. In Scandinavia, new startups such as NMD pharma (DK), Hoba (DK) and Merozyne (SE) were launched with Novo Seeds as company creator and lead investor. These companies are prime examples of how we turn advanced science into exciting new spinouts. We also lead larger series A financings in the immunooncology startup, Macrophage Pharma (UK); the medical device company, Corwave (FR); the liver regeneration company, Heparegenix (DE); and the medical imaging play, AMRA (SE).

Overall, we have increased investments outside the Nordics, thereby leveraging our approach to building new biotech companies. Furthermore, we are continuously expanding the investor network, bringing commercial competence to the region. Through our investment activity in 2016, we raised capital by attracting 10 new co-investors to portfolio companies.

In addition, we awarded on behalf of the Novo Nordisk Foundation eight pre-seed grants to promising early-stage research in the Nordics. These grants focus on developing the commercial potential of ambitious academic discoveries. In the coming years we will increase our investment activities in both the Nordics and other parts of Europe.

A key part of building a biotech company is the management. Therefore, in 2017, we plan to establish an Entrepreneur in Residence programme with the goal of having strong management competencies available to biotech startups.

As our portfolio matures, we will focus on delivering more biotech successes that will illustrate the ability of the Nordic biotech industry to translate innovative science to products. Products that attract the pharma industry, and will drive exits and value creation.

### SEED INVESTMENTS

The most promising early-stage biotech companies are developed and financed through seed investments. Through our hands-on approach, we transform innovative science into products that address unmet healthcare needs and improve quality of life.

As access to capital is always a challenge for early-stage companies, we place great emphasis on working closely with other regional and international venture funds. This relation not only brings capital; it also gives access to talent and network, which are a critical success factors. Significant investment represents an important validation for a biotech company. In 2016, co-investors contributed more than twice as much capital to our portfolio compared to Novo Seeds – a significant recognition of quality.

### **PRE-SEED GRANTS**

One way in which we identify and develop new startups is through the pre-seed grant programme. Awarded on behalf of the Novo Nordisk Foundation, our pre-seed grants are given to early-stage, highly qualified academic research projects with promising commercial potential.

Before and during the grant phase, we work closely with each project to help them sharpen their plan and grow. In this way, we begin to set the team for a future spinout company, and provide each project with the best conditions to develop into attractive seed investments. Novo Seeds in brief 2016

Novo Seeds vision is to create an even stronger Nordic biotech industry. We do this by building and investing in startup companies, which are founded on great science and that develop products with the potential to transform patient treatment.

### Seed companies Pre-seeds projects



**Acesion Pharma** Adenium Biotech Avilex Pharma **Biosyntia HOBA Pharmaceuticals IO Biotech MinervaX NMD** Pharma Reapplix Antag AntibioTx **BioProtect** ChildTreat DARE Diacure **GlyProVac** Glia **ISD-Immunotec** LOX miRana NonCodania Reticare **RSK Inhibitors** TONSL

- 2 SWEDEN
- AMRA Galecto Biotech Merozyne RSPR Pharma ApoA-I derived peptides Biopetrolia

### **3** FINLAND

Forendo Pharma PeptiCRAd

4 NORWAY Zinchel

5 FRANCE Corwave Lysogene

6 SWITZERLAND Inthera Bioscience

**7** GERMANY Heparegenix

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8 UK Macrophage Pharma

• 2016 • 2015

### Novo Seeds investments in DKK million





2014

2013

2012

2011

2010

2009

2008

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# Innovative treatment for rare muscular diseases

NMD Pharma is a new drug development company that develops new treatment for chronic muscle wasting diseases such as Myasthenia Gravis and Amyotrophic Lateral Sclerosis, better known as ALS. A pre-seed grant and, this year, a seed investment lead by Novo Seeds helped to build this pioneering company.

reathing, walking, running. These are physical activities that most people perform without even thinking. Although they might seem basic, such actions are the result of complex signal

transmissions between our nerves and muscles, all of which are activated and controlled by our nervous system. In a range of neuromuscular diseases and in some clinical conditions, however, this critical transmission from the nervous system to the muscles fails. Such signal failure reduces mobility, compromises quality of life, and can lead to life-threatening muscle weakness.

NMD Pharma is developing a novel treatment that strengthen this critical communication between nerve and muscle. The company's main focus is rare neuromuscular disorders with clear unmet medical needs, such as Myasthenia Gravis and Amyotrophic Lateral Sclerosis, also known as ALS. But the treatments may work across a wide range of other neuromuscular diseases too.

### A NEW TREATMENT APPROACH

The research that led to the discovery of the new treatment was conducted in the muscle physiology laboratory of NMD Pharma's founders, Associate Professor Thomas Holm Pedersen and Professor Ole Bækgaard Nielsen – in close collaboration with senior researcher and co-founder Claus Elsborg Olesen at Aarhus University, Denmark.

The decisive soft funding for NMD Pharma's groundbreaking discoveries originally came from a pre-seed grant from Novo A/S in 2014. This enabled the three scientists to develop a proof-of-concept data package. They demonstrated that NMD Pharma's treatment approach could produce a fivefold increase in physical performance (running) in an animal model of Myasthenia Gravis (MG). A result that far exceeded current treatment options.

The NMD Pharma treatment is highly original in that it engages a target not previously used in neuromuscular disorders. In addition, the target is muscle specific, allowing it to be pharmacologically modulated with minimal side effects.

### FROM PRE-SEED GRANT TO SEED INVESTMENT

Having seen the impressive results that the initial pre-seed grant had helped to achieve, Novo's Seeds engaged with the founders to prepare a seed financing round. In May 2016, we led a DKK 20 million financing round in NMD Pharma, together with Lundbeckfond Emerge and Capnova. This round will fund further medicinal chemistry development as well as the testing of the company's compounds in animal models of muscoskeletal disease such as MG, Amylotrophic Lateral Sclerosis (ALS) and Spinal Muscle Atrophy (SMA).

If successful, this will lead to a large financing that could take the treatment to test in human subjects by 2019. "Novo Seeds is excited to be working with the founder team behind NMD Pharma", says Stephan Christgau, Partner at Novo Seeds. "This company is an excellent example of a prominent scientific group with an idea to address a major unmet medical need – where a pre-seed grant has catalysed initial commercial development, and where we have been able to support the company in orchestrating the first financing round."

Novo Seeds looks forward to continue working with the NMD Pharma team, providing them with the support they need to provide better treatment for people with neuromuscular diseases.

> "NMD Pharma is an excellent example of how access to crucial early-stage soft funding can transform academic discoveries into vibrant and specialised biotech startups." Thomas Holm Pedersen, CEO at NMD Pharma.

# A seed investment in CorWave

Heart failure is one of the leading causes of death globally. With their unique blood pump technology, Parisbased medtech, CorWave is working to reverse these critical figures. Novo Seeds is on board as part of a EUR 15.5 million Series B fundraising.

eart transplant is the most effective treatment for end-stage heart failure. However, such an intervention is only relevant or possible in a minority of cases. The majority of cardiac patients get a mechanical pump implanted.

Left Ventricular Assist Devices (LVADs) are mechanical pumps that are implanted below the native heart. They can restore blood flow to normal levels and correct the main symptoms associated with heart failure. LVADs can add up to 10 years of additional life to patients.

### **NEED FOR NEW GENERATION BLOOD PUMPS**

The problem with current pump technologies – based on rotor technologies – is that they create a non-physiological flow; they are also associated with a high risk of serious adverse events. After two years of support, more than 80% of patients will be affected by at least one debilitating complication caused by the pump itself – mainly stroke, bleeding or infection.

The French medtech company, CorWave has developed a disruptive technology that could overcome the limitations of the current rotary pump LVADs.

### FAST FACTS ON CORWAVE'S 'FISH TAIL' TECHNOLOGY

The wave membrane technology developed by CorWave is a unique and disruptive technology protected by seven patent families. It is the result of more than 10 years of research led by academic laboratories and AMS R&D. This unique 'Fish Tail' technology enables a gentle pumping of the blood, and Corwave's LVAD has the potential to become the only fully pulsatile device on the market, mimicking heart beats.

### AN INNOVATIVE MOTION MEMBRANE

CorWave was founded in 2011 by Paris-based incubator, MD Start. The company won the World Innovation Challenge in 2016.

The CorWave LVAD utilises an undulating disc wave pumping mechanism, which replaces the high speed, high shear impeller of the current continuous flow rotary pumps. This mechanism causes much less trauma to the blood, reducing clotting and bleeding complications. The high frequency actuation of the CorWave pump generates a pulsatile flow that mimics the action of the native heart, whereas current LVADs provide only continuous flow with no significant pulsation, due to the high inertia of their rotors. In addition to low power consumption and small size, the CorWave pump combines total implantability with the incorporation of benefits from a wireless energy transfer system.

### SUPPORT FROM AN INTERNATIONAL SYNDICATE

CorWave has recently raised a EUR 15.5 million in a financing round led by Novo Seeds, with the support of an international syndicate of new and existing investors, including Ysios Capital, Sofinnova Partners, Bpifrance and Seventures.

With this funding in place, CorWave now has the resources to prepare their LVAD pump for the first-in-man study, bringing this pioneering technology into the hands of clinicians.

"We have proven through in vitro physiologic models and in vivo experiments that the CorWave pump can faithfully replicate the native heart pulse and successfully restore blood circulation. Our talented team of engineers and scientists is now working hard to take the technology to the next stages: turn our pump into a qualified product and bring it to patients." Louis de Lillers, CEO

# Selected portfolio company achievements in 2016

### ACHIEVEMENTS IN PORTFOLIO COMPANIES IN 2016

Galecto completed its first clinical phase IIa study in Idiopathic Pulmonary Fibrosis (IPF) patients. The Galecto treatment was found to be effective and well tolerated.

Minervax has successfully concluded their phase Ib study of the GBS vaccine.

**IO Biotech** entered into a broad collaboration agreement with Center for Cancer Immunotherpy (CCIT) at Herlev University Hospital in Copenhagen. Through this collaboration, IO Biotech has gained access to several new clinical stage programmes, the first of which is a PD-L1 based vaccine, which is now being advanced to clinical proof of concept.

Acesion has obtained a new EUR 4.2 million financial commitment from the Wellcome Trust. This occurred concurrently with the selection of a clinical candidate for further development.

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### NEW PRE-SEED GRANTS IN 2016

Antag project focuses on the role of the gastric inhibitory polypeptide hormone in diabetes and obesity.
<b>ChildTreat project</b> focuses on the development of a novel treatment to prevent procedural pain in children.
ISD-Immunotech project focuses on systemic lupus erythematosus (SLE). SLE is an autoimmune disease, characterised by systemic chronic inflammation.
LOX project focuses on the tumour secreted Lysyl Oxidase, LOX, that is closely correlated with cancer progression and metastasis.
<b>NonCodania project</b> focuses on therapeutic application of non-protein coding RNA molecules.
Reticare focuses on neuroprotection in eye disorders.
<b>TONSL project</b> is developing a novel DNA Damage Response (DDR) cancer therapy.
Glia project focuses on the commercial aspects of

**Glia project** focuses on the commercial aspects of pioneering cell therapy for Central Nerve System (CNS) diseases.

# Novo Seeds portfolio companies

### **CLASS OF 2016**

### **EXISTING PORTFOLIO**



**AMRA** is a healthcare IT startup. The company is developing an automated image analysis platform for a full body MRI scan. The platform will be able to quantify fat and muscle volumes across the body.

### CorWave

**Corwave** is a French medical device company. Corwave is developing a unique left ventricular assist device (LVAD) for congestive heart failure (CHF). http://www.corwave.fr/

HepaRegeniX

Heparegenix GmbH is a German company that is developing a new treatment to promote liver regeneration.

#### HOBA THERAPEUTICS

Hoba Therapeutics is developing a treatment for neuropathic pain.



**Macrophage Pharma** is a new UK immune-oncology company that is working on improving the response rate to a range of cancers.

### merozyne

*Merozyne Therapeutics AB* is developing a pharmaceutical treatment against MDC1A, a rare and severe form of muscular dystrophy. http://merozyne.com/

### NMOPHARMA

**NMD Pharma** is developing novel treatments for neuromuscular diseases such as Myasthenia Gravis and ALS.

### aesion

Acesion Pharma ApS develops new therapies for the medical treatment of atrial fibrillation, the most common type of cardiac arrhythmia. www.acesionpharma.com

#### Adenium Biotech 🏠

Adenium Biotech ApS focuses on the development and commercialisation of novel antibiotics for the treatment of multi-drug resistant bacterial infections. www.adeniumbiotech.com



Avilex Pharma ApS develops dimeric peptides that target PSD95 for the treatment of ischaemic stroke. www.avilexpharma.com

# Biosyntia

**Biosyntia** is a biotech startup within synthetic biology and metabolic engineering. The company develops biocatalysts at an unprecedented speed and efficiency by employing a patent pending highthroughput screening technology. http://biosyntia.com/

### INTHERA

**Inthera Bioscience** is a Swiss biotech company targeting HPV+ head and neck cancer (HNSCC) and/ or HPV+ genitourinary cancer as initial indication(s).

FORENDO P H A R M A

Forendo Pharma Ltd develops drugs for tissue-specific regulation of sex hormone effects. www.forendo.com

### Galecto Biotech

Galecto Biotech AB develops anti-fibrotic and antiinflammatory treatments based on small molecules of galectin modulators. The company's lead programme is in development for idiopathic pulmonary fibrosis. www.qalecto.com



IO Biotech ApS is developing a novel immunotherapy for cancer by targeting a mechanism used by tumour cells to evade immune responses. http://www.iobiotech.com/

### LYSOGENE

Lysogene SA is a clinical-stage biotech company working in the field of gene therapy. The company's therapies target severe genetic pathologies of the central nervous system in children. www.lysogene.com

### **MINERVAX**

MinervaX ApS is developing a novel vaccine candidate against Group B streptococci, which is the leading cause of life-threatening bacterial infections in newborn babies. www.minervax.com

# 🞯 Reapplix

**Reapplix ApS** is developing a device that produces a fully autologous dressing for wound care, particularly difficult-to-heal diabetic foot ulcers. www.reapolix.com



**RSPR Pharma** is developing an oral anti-asthmatic drug that provides mast cell control by inhibiting both induced and basal release of asthma mediators. http://www.rsprpharma.com/

# FINANCIAL INVESTMENTS

A global multi-asset class portfolio

# 2016 – a strong year for Financial Investments

uring 2016, the value of the Novo A/S' financial investment portfolio yielded DKK 2.6 billion. By the end of the year, the total value of the financial investments portfolio reached DKK 38.8 billion.<sup>1</sup>

During the year, US interest rates increased while Danish interest rates decreased. Our fixed income assets were not significantly affected by the changes as we continue to have a very low interest rate risk in our credit and bond portfolio. However, the increase in the US interest rates led to higher earnings expectations for some of the large US banks and insurance companies in which we are shareholders.

Credit spreads narrowed across the entire asset class in 2016. Particularly low-rated and energy-related credits experienced significant returns. Our credit portfolio has little energy exposure and is generally less risky than the average high yield market. Consequently, our credits did not benefit from the appreciation of those assets.

Equity market returns were broadly flat until the US election. Following the election, equities appreciated significantly, in particular within the energy, materials and financial sector. We have an overweight position in the financial sector, which contributed positively to our relative performance, but an underweight position in energy and materials, which contributed negatively.

The total liquid financial investments portfolio delivered a return of 8.1% and a total profit of DKK 2.6 billion. The weighted benchmark of the portfolio returned 9.3%. As such, this was the first year of underperformance since the initiation of the financial investment activities in 2005.

We look back on a year where financial assets remained expensive; interest rates were at a historically low level; credit spreads stayed below historical average levels, and market values of equities remained high relative to their fundamental earnings power. As a result, we expect portfolio returns over the next three to five years to be somewhat lower than they have been over the past seven years.

 $\longrightarrow$  Continues on p. 50

<sup>1</sup> Including illiquid financial investments and the Novo Nordisk Foundation's share of the liquid financial investment. Continued from p. 49

### INVESTMENT APPROACH

Novo's financial investment portfolio consists of equities, credits, bonds and illiquid investments. Some of these investments are managed by external firms and some are managed in-house. Regardless of asset class or management structure, all of our financial investment adhere to a number of investment principles:

- Buying businesses not ticker symbols: Focus on the underlying business fundamentals and values. Invest in high-return businesses managed by shareholderorientated people.
- Long-term investment horizon: Attempt to buy businesses that are out of favour for reasons that we consider temporary.
- Avoid permanent loss of capital: Don't pay too much for the asset in the first place and understand the fundamental risk of each asset.
- Cyclicality in valuations, earnings and credit spreads: Opportunities arise due to 'human herd' behaviour that creates cyclicality in financial markets.
- Conservative: Only pay for the expected outcome and keep a margin of safety. Do not buy into optimistic management cases and leave room for upside potential.

### **EQUITIES**

Novo's equity portfolio is liquid and diversified. Around 15% of the equity portfolio is currently allocated to highly liquid index products. The remaining 85% is invested in about 250 different listed companies that have been carefully selected by our active managers (the 20 largest externally managed holdings account for a third of the equities).

By the end of 2016, our actively managed equities were split between 13 external managers in a mix of global, regional and country-specific mandates. Common to these managers is that they:

- invest in durable cash-generative business;
- invest for the long-term;
- have a strong focus on management and shareholder orientation;

- invest only in companies that they understand;
- base their investments on in-depth fundamental analysis; and
- are only willing to pay a reasonable price, even for an excellent business.

In order for us to become an active partner rather than a passive client for our external managers, it is important that our team understands the theses for the majority of the securities that the external managers invest in. To ensure this, a significant amount of team resources are devoted to following the companies in question and discussing investment theses with our current managers.

We are constantly screening the capital management universe for new talent that match our investment philosophy and values. We only consider managers who have a coherent and well-defined investment strategy, invest with passion and integrity, are sceptical of conventional wisdom, and whose interest are strongly aligned with ours. In 2016, we introduced a new manager to the portfolio, who is regarded as one of the best longterm value investors in Asia.

A part of the equity portfolio is managed internally. The internally managed liquid equity investments are primarily comprised of our investment in the Danish engineering and machinery company FLSmidth, but the portfolio also includes a few smaller stakes in other listed companies.

In the beginning of 2016, we increased our stake in FLSmidth where we became a major shareholder in 2015. On January 21th, we announced that our holdings corresponded to 15.02% of the share capital. FLSmidth supplies equipment and services to the mining and cement industries. These industries were not in favour on the stock market at the time of our investment, and we were able to acquire the shares at an attractive valuation

In 2016, our liquid portfolio returned 8.1%. This should be viewed relative to the benchmark (MSCI World Index), which returned 9.3%. Over the past five years, the equity portfolio has returned 11.3% p.a. versus a benchmark return of 9.8% p.a.



Novo's financial investment equity portfolio by geography and sector. The allocation is a result of bottom-up investment opportunities in individual companies within these regions and sectors rather than a top-down allocation strategy.





Continued from p. 50

#### CREDITS

Novo's credit portfolio is diversified across several types of underlying risk sources. These assets can be broadly classified into the following categories:

- Emerging market debt
- Senior secured loans issued by corporations
- Commercial real estate debt
- High-yielding debt issued by corporations
- Subordinated debt issued by financial institutions

The management of our emerging market debt assets is carried out by an external manager, who pursues a bottomup approach in global credit markets. The firm is exclusively engaged in this activity and has extensive experience in dealing directly with sovereign and corporate entities in non-G7 countries. The emerging markets strategy accounts for about 30% of Novo's credits.

The majority of our senior loan assets are managed by two managers – one specialises in European, the other in US senior loan assets. We also have a few senior loans in our internally managed credit portfolio. Our senior loan assets are typically 1st lien floating rate notes, issued by large international companies with an appreciable degree of debt on their balance sheets. Our senior loans accounts for about 30% of the credit portfolio.

Our real estate debt assets are overseen by an external manager, who focuses on commercial mortgage-backed securities. The vast majority of the underlying real estate assets are located in the US. The credit portfolio also includes a European High Yield Bond strategy, which is conducted by an external manager.

Our internally managed credits primarily consist of subordinated debt issued by Danish financial institutions. We also have a number of investments in debt issued by corporations in various industries. These bonds or loans typically carry a yield that reflects that the security is either subordinated or that the market perceives the issuer to be risky.

Our high proportion of floating rate loans means that our credit portfolio is less sensitive to changes in interest rates as compared to fixed rate high yield bonds. The absolute return of Novo's credits from year to year is highly dependent on the global capital flows either into, or away from risky assets. The relative performance relies on the ability to invest in securities that carry a significant yield while avoiding losses. All of our credit investments, internally and externally managed, are based on a business-oriented investment approach, in-depth fundamental analysis, and a long-term perspective.

In 2016, our credit portfolio returned 11.3%. This should be viewed relative to the benchmark (a blend of Merrill Lynch Global High Yield Index and J.P. Morgan Emerging Market Bond Index) that returned 12.6%. The relative underperformance is largely due to our underweight in lowrated and energy-related corporate credits. Over the past five years, the credit portfolio has returned 9.5% p.a. versus a benchmark return of 6.9% p.a.

### BONDS

Novo's bonds are managed in-house. A large bulk of our bonds are covered bonds issued by Danish mortgage institutions. Our fixed-rate covered bonds typically have a few years to maturity, which makes them less sensitive to changes in interest rates. The bond portfolio also consists of investments in the safest tranches of securitised pools of international corporate loans. Finally, we have a few minor positions in bonds issued by corporations with high credit ratings. In short, the bond portfolio has a high liquidity, low credit risk and low interest rate risk. By the end of 2016, the bonds amounted to DKK 6.4 billion.

Bonds that have a high liquidity and low default risk, such as the bonds in Novo's portfolio, offer yields that are only slightly above yields of risk-free government bonds. Therefore, the absolute return of Novo's bonds is primarily determined by the Danish interest rate environment, which is currently trading at historically low yields. In 2016, our bond portfolio returned 1.4%. This should be viewed relative to our benchmark (EFFAS 1-3 Index) that returned only 0.2%. Over the past five years, the bond portfolio has returned 1.7% p.a. versus a benchmark return of 0.4% p.a.

#### ILLIQUID INVESTMENTS

Novo has invested a certain amount of its financial investments in illiquid assets. We have an opportunistic, value-driven approach to this pool of the financial investments, which consists of:

- a significant share of the private Danish real estate company, DADES A/S; and
- limited partnerships in a number of private equity funds.

DADES is one of Denmark's largest real estate companies with a special focus on commercial properties primarily in the Copenhagen area as well as shopping centres all over Denmark. Our first shares in DADES were acquired in 2015 for a sum of DKK 1.7 billion. The investment exposes Novo to a new asset class and a platform for making new real estate investments in the future. In 2016, DADES made a number of investments; most predominantly, Nykredit's headquarter in the harbour of Copenhagen. To finance these investments, DADES exercised a part of Novo's additional capital commitments, which increased Novo's ownership from 38% to 44% of the share capital in DADES.

Our private equity commitments consist of a number of funds that were raised in the period 2005 to 2008. We are frequently evaluating the attractiveness of illiquid investment opportunities relative to liquid investments. It is our view that an illiquid asset should provide a significant yield premium in order to compensate for lack of liquidity.

### **PORTFOLIO PERFORMANCE**

Novo's financial investment portfolio is based on bottom-up investment ideas. Consequently, exposures to certain sectors, countries and currencies may deviate from our benchmark and lead to short-term fluctuations in relative performance. However, we believe that this approach pays off in the long run, as it allows us to deploy a more long-term perspective when evaluating our investments.

Since the inception of the financial investment portfolio in 2005, the portfolio return has been 7.8% p.a. and the profits have been DKK 17 billion. The weighted benchmark has returned 5.3% p.a. in the same period. The outperformance of 2.54% p.a. corresponds to excess profits of DKK 5.5 billion. ■

# Corporate Social Responsibility

orporate Social Responsibility (CSR) is an integral part of Novo A/S' value-based heritage. Novo is a wholly owned subsidiary of the Novo Nordisk Foundation. The vision of the Foundation is to contribute significantly to research and development

that improve the health and welfare of people. In 2016, the Foundation awarded more than DKK 4 billion, primarily for research and diabetes treatment at public research institutions and hospitals as well as for humanitarian and social purposes.

In recent years, the Foundation has become one of the largest private contributors of funding to biomedical and biotechnological research in the Danish public sector.

Novo is responsible for managing the Foundation's assets. The mission of Novo is:

- to ensure that the Foundation receives sufficient dividends to cover its grants.
- to ensure that the Foundation obtains a competitive return on its holdings in Novo Nordisk A/S and Novozymes A/S, as well as from the other companies and financial assets in which Novo invests.
- to support the application of life sciences by investing in seed and venture portfolio companies.
- to maintain the Charter for Companies in the Novo Group

The Charter describes a shared set of values that all companies in the Novo Group must comply with. This includes that the companies must strive to make sure that company products and services make a significant difference to improve the way people live and work. It also includes continuous improvement on financial, environmental and social performance.

### **REPORTING ON CSR**

For 2016, Novo has selected four CSR focus areas that represent the most important areas in which CSR can impact the company's overall business performance.

For each focus area, Novo reports its policies, activities and the effect of these activities. To align our CSR reporting with our overall business performance, Novo re-evaluates and, if necessary, adjusts the focus areas, policies and activities each year. ■



CSR FOCUS AREAS	WHY IS THIS IMPORTANT?	POLICIES / ASPIRATIONS	ACTIVITIES	RESULTS
Impact on society through investment activities	Novo's impact on society depends on how well it deploys its financial re-	To leave a positive foot- print on society.	Ensuring funds for the Foundation's philanthropy.	The Foundation awarded DKK 4.2 billion within its three areas of support through 340 grants, both large and small.
	sources.		Starting new life science companies and developing the existing portfolio.	Novo helped start seven new companies, and we invested DKK 8.7 billion in 23 new and 41 existing portfolio companies. More than 30 new drugs and devices originating from Novo portfolio companies are on the market.
			Paying taxes.	The Novo Group paid company tax amounting to DKK 6 billion in Denmark.
Responsible investment process	Novo's core business is investing. This must be conducted in a socially and environmentally responsi- ble manner.	To be a responsible in- vestor by incorporating CSR into our investment processes.	Integrating and docu- menting CSR as part of our investment processes.	All new investment opportunities have been screened for potential CSR issues (including bioethi- cal and corporate governance issues).
Charter and Cornerstones	Novo is a value-based company. It is important to Novo's performance that all employees understand and adhere to Novo's Charter	To make sure all employees know, understand and adhere to the Charter and Cornerstone principles.	Monitoring that the or- ganisation adheres to the Charter and Cornerstone principles.	Charter: The Novo Group companies (Novo Nordisk A/S and Novozymes A/S) each adhere to the Charter, while the portfolio companies must not act against the Charter.
	and Cornerstones.			Cornerstones: Each employee has discussed the Cornerstones with his/her manager as part of their annual Dialogue Discussion, which also includes job description, targets, development plan and working conditions.
Brand and employees	Novo's main non-financial operational asset is its brand and its employees.	To be a well-reputed com- pany and a responsible and attractive employer.	All employees must help build the Novo Brand by adhering to and promoting the Novo values and culture	Novo receives informal feedback from stakeholders on an ongoing basis
			Assessing and redesigning the company's incentive scheme.	In 2016, Novo's long-term incentive scheme was redesigned for implementation in 2017.
			Conducting workplace assessments. Collecting key figures on sick leave and training.	Novo collects key figures on e.g. sick leave and resources/time devoted to training. Sick leave was less than 1.95% of total working hours. Internal and external training amounted to 1.34% of total working hours.
				In 2016, Novo welcomed 24 new colleagues incl. four Student Assistants. We handled more than 366 applications for vacancies, candidate profiles and

unsolicited job applications.

# novo nordisk fonden

he Novo Nordisk Foundation is an independent Danish foundation with corporate interests. Its history dates back to 1923.

The Foundation has two objectives – one commercial and one societal: 1) to provide a stable basis for the companies in the Novo Group; and 2) to support scientific, humanitarian and social purposes.

The vision of the Foundation is to contribute significantly to research and development that improves the health and welfare of people.

Foundation ownership ensures stable and long-term ownership of the companies in the Novo Group.

### **THREE AREAS OF SUPPORT**

The Foundation provides support within three main areas:

- physiological, endocrinological, metabolic and other medical research:
- research hospital activities within the field of diabetes in Denmark:
- other scientific fields including research on sustainable production, art history and nursing – as well as humanitarian and social causes.

The Foundation supports free and independent research, primarily at hospitals and universities in Denmark and the other Nordic countries.

The Foundation supports the entire value chain within research – from education to innovation – contributing to building bridges between the discoveries researchers make and their commercial applications. For this reason, the Foundation supports a range of initiatives, either directly or through Novo A/S, that aim to accelerate the use of innovative, researchbased knowledge. The ambition is to create added value by establishing new life science and bio-industrial companies that provide employment for people – ultimately benefiting society as a whole.

In 2016, the Foundation awarded DKK 4.2 billion within its three areas of support through 340 grants, both large and small.

The Foundation funds its activities primarily through the dividends received from Novo A/S, which manages the Foundation's assets. ■

For more information, please visit www.novonordiskfonden.dk







N ovo Nordisk A/S is a global healthcare company with more than 90 years of innovation and leadership in diabetes care. This heritage has given the experience and capabilities that make it possible to help people defeat other serious chronic conditions: haemophilia, growth disorders and obesity.

The company's values-based management framework is described in the Novo Nordisk Way. It spells out that the company's key contribution is to discover and develop innovative biological medicines and make them available to patients throughout the world. It also describes the behaviours that are expected of all employees. Decision-making is guided by the Triple Bottom Line principle, anchored in the company's Articles of Association, of always striving to be financially, environmentally and socially responsible.

#### FINANCIAL PERFORMANCE

Novo Nordisk's 2016 performance for sales and adjusted operating profit growth were both in line with the guidance provided in February 2016, although in the lower end of the ranges reflecting a more challenging competitive situation in the USA.

The free cash flow exceeded the outlook provided in February 2016, explained by a positive effect from settlement of tax cases related to prior years. Capital expenditure and other results were in line with the latest guidance provided in October 2016.

Sales increased by 6% measured in local currencies and by 4% in Danish kroner. Sales growth was realised within both diabetes care and biopharmaceuticals, with the majority of growth originating from Tresiba<sup>®</sup>, Victoza<sup>®</sup>, Saxenda<sup>®</sup> and Norditropin<sup>®</sup> while sales of modern insulin and NovoSeven<sup>®</sup> declined.

Sales of diabetes and obesity care products increased by 6% measured in local currencies and by 4% in Danish kroner to DKK 88,949 million. Novo Nordisk is the world leader in diabetes care with a global value market share of 27%.

Sales of haemophilia products were unchanged in local currencies and decreased by 2% in Danish kroner to DKK 10,472 million.

All regions contributed to sales growth; however, the USA was the largest contributor with 37% share of growth measured in local currencies, followed by International Operations and Region China contributing 32% and 19%, respectively.

### **R&D PROGRESS**

2016 was a year in which Novo Nordisk made significant progress in its research and development pipeline and

reached several milestones. In Novo Nordisk's Annual Report, a pipeline overview shows all the compounds in clinical development, and further details on clinical trials can be found in the company announcements and press releases published by Novo Nordisk during 2016.

### **UPDATED R&D STRATEGY**

In October 2016, Novo Nordisk updated its R&D strategy and priorities to reflect the increasingly challenging payer environment, particularly in the US market, by applying an even higher innovation threshold for progressing R&D projects. Novo Nordisk will further intensify exploration of current assets in adjacent disease areas of high unmet need as well as identify new assets using our existing technology platform. In addition to the other areas, NASH (non-alcoholic steatohepatitis), diabetic kidney disease and cardiovascular disease are new areas to be pursued, both in research and development.

As a result of the updated R&D strategy and priorities, Novo Nordisk decided not to progress its current development projects within oral insulin and combinations involving oral insulin. In addition, a number of changes to the portfolio of early-stage projects were also implemented. Furthermore, Novo Nordisk intends to strengthen its activities for inlicensing of early- and mid-stage projects as well as external academic collaborations. Novo Nordisk's current late-stage development portfolio was not affected by the changes.

### THE PATIENT TARGET: 40BY20

Novo Nordisk's strategy for global access to diabetes care addresses a huge unmet need. The company's long-term target is to reach 40 million people with its diabetes care products by 2020 – double the 2010 base-line number. Novo Nordisk provided medical treatments to an estimated 28 million people with diabetes worldwide in 2016, compared with 26.8 million in 2015. Current projections show that it will not be possible to reach this target. This is due to a more challenging market environment than anticipated in 2013 when the long-term target was set. Novo Nordisk remains committed to continuing its efforts to reach more patients and improve diabetes care. ■

For more information, please visit Novo Nordisk's Annual Report 2016 at www.novonordisk.com/annualreport



N ovozymes A/S is the global market leader in biological solutions, producing a wide range of industrial enzymes and microorganisms used in the manufacture of numerous products in industries such as household care, bioenergy, agriculture, animal feed, and food and beverages.

To deliver on its purpose of finding biological answers for better lives in a growing world, Novozymes delivers new innovations to help customers produce more from less, adapt to market changes, make their products stand out, reduce costs and generate less waste.

More than 1,400 of Novozymes' employees work in R&D to create innovation that influences how customers work and succeed, and every year, around 13% of revenue is reinvested in R&D. In 2016, Novozymes launched eight new products aimed at the household care, agriculture, bioenergy and food & beverage industries.

### 2016: STRONG EARNINGS, BUT WEAK ORGANIC SALES GROWTH

Novozymes' financial results for 2016 showed strong earnings, and the company was able to expand its EBIT margin despite weak organic sales growth of 2%.

Sales growth was moderate across industries and, from a regional perspective, Novozymes saw growth in Europe and Asia Pacific, whereas sales in North America in particular proved challenging. Novozymes was able to deliver strong earnings due to very low cost expansion and continued efforts to optimise productivity in its facilities worldwide.

Total sales in 2016 were DKK 14,142 million. Sales grew by 2% organically and by 1% in DKK. Sales to the agriculture & feed and technical & pharma industries were the most significant contributors to organic sales growth in the period. The EBIT margin improved by 0.2 percentage points to 27.9%, and EBIT grew by 2%. Net profit increased by 8%.

Sustainability performance in 2016 was mixed, with good performance on several people targets, whereas Novozymes did not reach all of its environmental and occupational safety targets. The target for 24% use of renewable energy was reached, as was the target to reduce CO<sub>2</sub> emissions by 63 million tons through customers' use of Novozymes' products. Water efficiency, energy efficiency and CO<sub>2</sub> intensity performance were below the full-year targets. The water efficiency target was not met due to higher-than-expected water consumption as well as challenges in the water reuse system in Denmark. The energy

efficiency target was not met due to operational challenges in Novozymes' fermentation facilities and higher-than-expected energy consumption. The target for occupational accidents was not met, and several new initiatives with focus on safety improvements were undertaken in 2016.

### **GUIDED BY "PARTNERING FOR IMPACT"**

A growing global population with a rising need for food, water, energy and other necessities is pushing industries to get smarter and produce more from less. It is around these trends that Novozymes has defined its purpose and strategy - 'Partnering for Impact'. With the four strategic focus areas Rally for change, Lead innovation, Focus on opportunities and Grow people, Novozymes is reinforcing its commitment to help solve some of the pressing global challenges facing a growing world. The backbone of the strategy is the belief that Novozymes makes the biggest impact through partnerships. For Novozymes, partnerships mean deep-rooted collaborations with mutual benefits and obligations. Impact is about creating healthier foods, better climate, cleaner air, nature in balance or more jobs. And it is about optimising a partner's processes, creating new products or reducing their environmental footprints.

### SUSTAINABILITY AND BUSINESS GO HAND IN HAND

Novozymes' products offer manufacturers more sustainable alternatives to traditional industrial processes. Sustainability is therefore evident in the company's agreements with suppliers, in its own production, and in partners' and customers' application of Novozymes' solutions in their production, increasing their operational efficiency and improving the performance of their products.

In 2016 alone, Novozymes' solutions helped its customers avoid an estimated 69 million tons of  $CO_2$ . That is equivalent to taking approximately 30 million cars off the road.

Novozymes sees long-term opportunities within industrial biotechnology and will continue to invest in innovation to realise the potential of its pipeline. Successful commercialisation of the pipeline will make a return to historical organic sales growth rates achievable. Novozymes now allocates additional resources to high-growth opportunities, primarily in emerging markets, while safeguarding profitability.

For more information, please visit Novozymes' Annual Report 2016 at www.report2016.novozymes.com

# ΠΠΙΤ

NIT A/S is one of Denmark's leading IT service providers and consultancies. NNIT offers a wide range of IT services and solutions to its clients, primarily in the Danish and international life

science sector, and to Danish clients in the public, enterprise and finance sectors. As a wall-to-wall provider, NNIT delivers services across the value-chain: advisory services, business solutions, application outsourcing and infrastructure outsourcing and support.

### 2016 FINANCIAL RESULTS

NNIT is a publicly listed company, and employs more than 2,800 people in 11 international offices around the world. In 2016, the company delivered organic revenue growth of 6.3% to DKK 2,765 million and an operating profit margin of 10.6% despite challenging market conditions. The Danish IT services market experienced growth around 3% (Gartner), hence NNIT remains competitive and continues to take market shares in all business areas.

NNIT's target level for revenue growth is at least 5% and reflects the expectation that NNIT will continue to outgrow the market by attracting new customers and continuing to deliver additional value to existing customer relationships. The 2016 results thus exceed NNIT's targets.

### STRATEGY - DEDICATED TO SUSTAINABLE GROWTH

NNIT is committed to being the preferred IT outsourcing partner for customers of Danish origin as well as a trusted provider of regulated IT for life science companies, globally. Based on quality and value-adding IT services, the company's main objective is to grow revenue and market share, while maintaining or improving operating profit margins.

### A TRUSTED PROVIDER OF REGULATED IT FOR LIFE SCIENCES

As a highly specialised IT services provider to life sciences, NNIT supports international life science companies in optimising their businesses, reducing cost and complying with regulatory requirements.

Based on NNIT's deep insights and industry experience within life sciences, the company creates value through IT

solutions and expertise while operating IT according to GxP (Good x Practice) pharma industry standards.

### THE PREFERRED OUTSOURCING PARTNER FOR CLIENTS OF DANISH ORIGIN

As a preferred IT outsourcing partner for clients of Danish origin, NNIT supports its clients during their internationalisation – essentially following the clients wherever they go.

NNIT is currently the third-largest IT services vendor in Denmark, with a total market share of 7% according to IDC.

### **CORE STRENGTHS**

Dedicated to its strategic ambition, and strongly founded in the company's three business cornerstones; loyal clients, compelling services, and highly skilled employees, NNIT is determined to continue to grow. The core strengths are:

- stable business model based on a focused strategy
- strong track record combined with profound experience
- integrated global delivery model
- prestigious customer base
- skilled and dedicated employees

NNIT's business model combined with its delivery centers and scale-driven operating leverage has secured robust operating profit margins over the past decade. At the same time, the diversification of the customer base and the long-term nature of many of the major contracts add to business transparency, mitigate operational risk and warrant long-lasting customer relationships.

For more information, please visit NNIT's Annual Report 2016 at www.nnit.com/pages/investor.aspx

# Charter for Companies in the Novo Group

### PRESENT AS WELL AS FUTURE COMPANIES IN THE NOVO GROUP MUST DEMONSTRATE WILLINGNESS, ABILITY AND RESOLVE TO MEET THE FOLLOWING CRITERIA:

- Company products and services make a significant difference in improving the way people live and work.
- The company is perceived to be an innovator in technology, in products, in services and/or in market approach.
- The company is among the best in its business and a challenging place to work.
- The company delivers competitive financial performance.

### **COMPANIES IN THE NOVO GROUP COMMIT TO:**

- value-based management
- open and honest dialogue with its stakeholders
- continuous improvement of financial performance
- environmental performance
- social performance
- reporting in accordance with relevant, internationally approved, conventions.

# A highly qualified team

s a life science holding and investment company, Novo A/S relies on the knowledge and expertise of its professionals, in the life science field and in the domain of investment management.

Many of our investment professionals have a background in science; several of them have worked as researchers and many have PhD degrees. Others have gained their scientific expertise through employment in research and management functions in Novo Group companies.

In addition to their scientific qualifications, all of our investment professionals have specialised knowledge of investments, relevant to their area of responsibility. This has typically been obtained through previous employment in the Novo Group, the life science industry or in the financial and consulting sectors.

Each member of our Board of Directors has comprehensive experience in investments or the management of life science companies, acquired through a long career in senior executive management at large international healthcare companies or financial institutions.

To support us in our investment decision-making, Novo has an advisory group of external life science professionals. We meet with them on a regular basis to receive feedback and advice on our investment projects.

Members of our management group have extensive international leadership experience. On the administrative front, our employees have relevant qualifications in accounting, auditing, administration, taxation, legal affairs, HR or IT.

As one of the leading investors in the life science sector, we have to continuously hone our knowledge base to fulfil our responsibilities towards our portfolio companies and make the right investment decisions. As such, ongoing learning is a high priority at Novo, allowing each of our employees to develop their skills and increase their value to our company – and the companies we invest in.

"The strong investment returns generated by Novo A/S is a testament to the life sciences expertise and investment management skills of our team." — Kasim Kutay, CEO



**COPENHAGEN** 



NOVO VENTURES (US) INC, SAN FRANCISCO



NOVO VENTURES (US) INC, BOSTON

Novo Ventures (US) Inc. is a separate legal entity that provides certain consultancy services to Novo A/S, mainly within the areas of identifying, analysing, and negotiating investment opportunities among life science and biotech companies in the US. They also conduct related follow-up activities, such as board memberships and control and reporting efforts.

# Leadership Team



### FROM LEFT TO RIGHT

THOMAS

DYRBERG

Managing Partner, Novo Ventures

PETER HAAHR

Officer

— Chief Financial SØREN MØLLER

\_\_\_\_ Managing Partner, Novo Seeds

— Head of People & Organisation

MADSEN

DORTE BARLEBO

MICHAEL SHALMI

> Managing Director, Novo Large Investments

KASIM KUTAY

Chief Executive Officer Managing Director, Novo Financial Investments

**MORTEN BECK** 

JØRGENSEN

# **Board of Directors**



### FROM LEFT TO RIGHT

### STEEN RIISGAARD

Born 1951, Danish national. Member of the Board since

2013. Chairman of the Board

of ALK-Abelló A/S, Cowi Holding A/S, Xellia Pharmaceutical A/S, Egmont International Holding A/S and WWF Denmark, and Vice Chairman of the Novo Nordisk Foundation and Willum Fonden. Member of the Board of Directors of Aarhus University, VKR Holding A/S and Corbion.

### GÖRAN ANDO

-

Born 1949, Swedish national. Member of the Board since 2006.

Senior Advisor to Essex Woodlands Health Ventures UK Ltd.

Chairman of the Board of Novo Nordisk A/S and Symphogen A/S, and member of the Board of Directors of Molecular Partners, EUSA Pharma and ICMEC.

### STEN SCHEIBYE

Born 1951, Danish national.

Member of the Board and Chairman since 2013.

Chairman of the Board of the Novo Nordisk Foundation, the Danish Industry Foundation, the Rich. Müller Foundation, RMIG Rich. Müller A/S and Knud Højgaard's Foundation.

### JEPPE CHRISTIANSEN

Born 1959, Danish national.

Member of the Board since 2009.

CEO (and co-founder) of MAJ Invest A/S.

Deputy Chairman of Novo Nordisk A/S, Chairman of the Board of Haldor Topsøe A/S and Emlika ApS, and member of the Board of Directors of Kirkbi A/S, Symphogen A/S and Det Kgl. Vajsenhus.

### PER WOLD-OLSEN

Born 1947, Norwegian national.

Member of the Board since 2011.

Chairman of the Board of GN Store Nord A/S and Medicines for Malaria Venture (MMV), and member of the Board of Directors of Gilead Sciences Inc.



# The following pages represent an extract from the Annual Report 2016, as submitted to the Danish Business Authority.

### **STATEMENT OF COMPREHENSIVE INCOME**

1 January to 31 December	2016	2015
	DKK million	DKK million
Income from Novo Group companies	7,142	4,271
Return from Life Science Investments	-1,534	8,592
Return from Financial Investments	2,758	2,895
Costs	-212	-383
Operating profit	8,155	15,375
Novo Nordisk Foundation's share of return of joint investment portfolio	-1,000	-527
Profit before tax	7,155	14,848
Income tax expense	-34	0
Net profit for the year	7,121	14,848
Proposed distribution of profit		
Proposed dividend	13	3,008
Retained earnings	7,108	11,840
	7,121	14,848

### **BALANCE SHEET**

As per 31 December	2016	2015
	DKK million	DKK million
Assets		
Novo Group companies	4,422	4,429
Life Science Investments	37,670	31,950
Financial Investments	38,078	36,787
Total non-current assets	80,170	73,166
Amounts owed by affiliated companies	7	4
Other receivables	99	141
Cash at bank	695	1,079
Total current assets	801	1,224
Total assets	80,971	74,390
Equity and liabilities		
Share capital	500	500
Retained earnings	66,562	62,449
Total equity	67,062	62,949
Joint investment portfolio Novo Nordisk Foundation	13,573	10,742
Trade payables	23	12
Amounts owed to affiliated companies	7	2
Tax payables	41	32
Other liabilities	45	22
Other provisions	220	631
Total current liabilities	13,909	11,441
Total liabilities	13,909	11,441
Total equity and liabilities	80,971	74,390

1 January to 31 December	2016	2015
	DKK million	DKK million
Net profit	7,121	14,848
Adjustment for non-cash items	-339	-11,322
Contribution from the Novo Nordisk Foundation to the joint investment portfolio	2,900	11,215
Repayments to the Novo Nordisk Foundation from the joint investment portfolio	-1,070	-1,000
Sale of shares relating to Life Science Investments	1,182	4,930
Purchase of shares relating to Life Science Investments	-8,723	-3,238
Sale of shares relating to Financial Investments	18,935	12,190
Purchase of shares relating to Financial Investments	-17,786	-22,223
Paid tax	-1	-1
Cash flow before change in working capital	2,219	5,399
Change in working capital		
Changes in accounts with affiliated companies	2	-2
Changes in other receivables	42	-1
Changes in other liabilities	34	-10
Cash flow from operating activities	2,297	5,386
Investment activities		
Proceeds from sale of shares in Novo Group companies	240	536
Purchase of shares in Novo Group companies	-	-797
Loans to subsidiaries	-	-66
Repayment of loans from subsidiaries	87	1,205
Cash flow from investment activities	327	878
Financing activities		
Bank loan (bridge financing)	-	-1,071
Dividends paid	-3,008	-4,715
Cash flow from financing activities	-3,008	-5,786
Net cash flow	-384	478
Cash and cash equivalents at the beginning of the year	1,079	601

Cash and cash equivalents at the end of the year 695 1,079



Graphic design: Kontrapunkt

Photos of Board of Directors and employees: Jon Norddahl

**Other photos:** 

Xellia (front page), Nature Biotechnology (p. 26), NASA Johnson Space Center (p. 48), Novozymes / Lasse Bech Martinussen (p. 54), Jon Norddahl (p. 10 and p. 69) Other photos were kindly made available by the portfolio companies.

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