# NOVO A/S ANNUAL REVIEW 2015

NOVO

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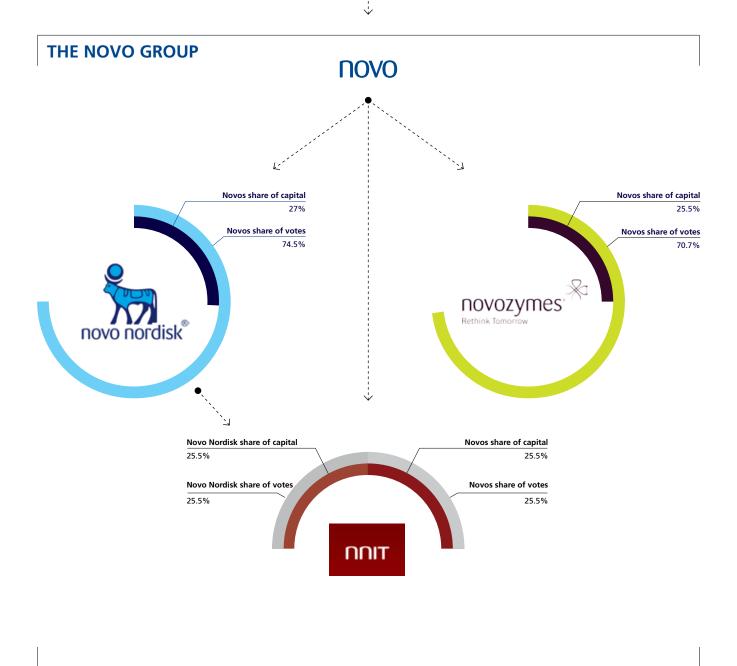
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# novo nordisk fonden

100% ownership



### **NOVO A/S**

ovo 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, as such, the controlling shareholder in the publicly listed companies, Novo Nordisk A/S, Novozymes A/S and 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'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; and
- always maintaining a material influence on Novo Nordisk and Novozymes.

By investing in the life science sector, Novo 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;
- the life science industry is financially attractive in a longterm perspective;
- Novo's capabilities as investor include life science investment competences, a strong industry network, financial strength, and a long-term investment horizon; and
- Novo may make select investments outside life science and maintains a liquid buffer to support any investment needs in the Novo Group.



Novo's investment objectives are to:

- generate competitive financial returns;
- gain the respect of its stakeholders as a responsible investor:
- help to address unmet medical needs; and
- generate a broader support for the life science industry.

The common denominator for all Novo'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's governance framework.

### 2015 IN BRIEF

#### THE NOVO GROUP

Novo A/S is the controlling shareholder in Novo Nordisk A/S and Novozymes A/S. Both companies achieved very good financial results in 2015. Novo Nordisk increased its profit after tax by 32%; and in Novozymes, the profit after tax increased by 12%. The value of shares in the two companies rose by 54% and 27%, respectively.

Novo A/S acquired 25.5% of the shares in NNIT when the company was listed on Nasdaq Copenhagen on 6 March 2015. As Novo Nordisk A/S has retained a 25.5% ownership of NNIT, Novo A/S is ultimately the controlling shareholder of the company. NNIT's IPO was very successful, and the company's performance has been satisfactory throughout 2015.

#### LARGE INVESTMENTS

In 2015, Large Investments added BTG and Inogen to its portfolio and divested its shares in Aerocrine AB. In addition, we focused our activities on the further development of our existing portfolio. Of the larger companies in the portfolio, Chr. Hansen A/S and the Sonion Group lived up to, or exceeded expectations, and Xellia Pharmaceuticals A/S made further progress towards fulfilling its market potential.

#### **VENTURE INVESTMENTS**

As in previous years, Novo worked to further consolidate its position as a major international investor within life science ventures. In 2015, Novo invested in 17 new companies, made follow-on investments in 30 of our existing portfolio companies, and successfully exited 13 companies. Our investments this year totalled DKK 1,733 million, and exit proceeds amounted to DKK 3,643 million. By the end of the year, the market value of our venture portfolio reached DKK 3.9 billion. Furthermore, Novo Ventures expanded its US footprint with the opening of a regional office in Boston, Massachusetts.

#### **SEED INVESTMENTS**

To enable early investments in the life science area, Novo runs a seed programme. In 2015, we invested DKK 75 million in 10 early-stage life science companies. This year, EpiTherapeutics, the flagship in the Seeds' portfolio, was acquired by the US biotech company, Gilead, and Novo Seeds made its first venture into industrial biotech with the investment in Biosyntia.

Novo assists the Novo Nordisk Foundation in a pre-seed programme that aims to identify and support academic research with commercial potential. In 2015, seven projects received grants from the pre-seed programme.

#### FINANCIAL INVESTMENTS

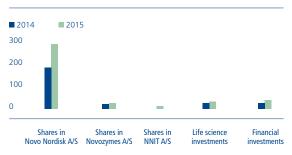
2015 was another good year for Novo's financial investments. The main purpose of these investments is to spread Novo's financial risk and, at the same time, maintain a substantial liquid financial reserve. In 2015, we continued the consolidation of our global financial portfolio. We expanded the scope of the financial investments to include larger direct investments in selected Danish companies, which resulted in two new investments: DKK 1,674 million in FLSmidth & Co. A/S and DKK 1,689 million in Dades A/S. In 2015, our portfolio of financial investments yielded a return of 10.5% and reached an accumulated value of DKK 38 billion.

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

In 2015, two of our top managers stepped down. Søren Carlsen, Managing Partner of Novo Ventures and Novo Seeds, retired after 36 years in the Novo Group. Thomas Dyrberg took his place as Managing Partner of Novo Ventures. Thorkil Kastberg Christensen, Novo's CFO since 2003, retired after more than 37 years in the Novo Group; he was succeeded by Bjarne Graven Larsen, former CEO of FIH Erhvervsbank, who, however, terminated his tenure by the end of the year. Finally, Michael Shalmi was appointed Head of Large Investments.

16 new colleagues joined the Novo team this year; 10 of these moved into newly created positions and four replaced colleagues who had taken employment elsewhere.

#### **DEVELOPMENT IN ASSETS (DKK BILLION)**







# LETTER FROM THE CHAIRMAN

The success of Novo A/S is measured by our ability to support the Novo Nordisk Foundation in the fulfilment of its objectives. To meet this obligation, we continually seek to strengthen our business by:

- preserving a strong balance sheet so that we are able to effectively assist the companies in the Novo Group;
- utilising our expertise within life science and investments to generate attractive returns, relative to the risks undertaken to finance our grant activities; and
- making investments that support the goals of the Novo Nordisk Foundation, which are the promotion of knowledge and world-class research.

2015 was a good year for Novo A/S, and we continue to strengthen our position as a key player in the international life science investment industry. Large Investments has had a very active year but did not conclude any significant new investments in 2015, as we in some instances found price levels too high. Novo Ventures, however, has made a series of new investments and successful exits, and we expect this high level of activity to continue in the coming year, with particular focus on early-stage publicly listed companies and defined exits. Novo Seeds remains a key player in the Nordic biotech space and will continue its efforts to build a Nordic life science hub through pre-seed grants and active investments.

In 2015, Novo Nordisk A/S and Novozymes A/S experienced strong growth in earnings, NNIT A/S went through a successful IPO, and our financial investments yielded great returns. In July, we acquired a large share of the Danish real estate company, Dades A/S – real estate being a complementary asset class in our finance portfolio.

In 2016, we will continue our strong focus on life science, and we expect to increase our direct investments outside this industry as well. We will direct particular attention to attractive long-term investments in leading and innovative companies with a Danish focal point – our recent investment in FLSmidth & Co. A/S being an example of this. Novo also expects to resume investments in other more illiquid assets in order to diversify our investments and reduce portfolio risks. This could include investments in private equity funds.

As an afternote, I would like to thank Eivind Kolding, CEO of Novo A/S, for his leadership and the results achieved during 2015. Eivind Kolding resigned from his position as of 29 February 2016, and the search process for a new CEO has been initiated. Until a new CEO is appointed, I have assumed working responsibilities as Executive Chairman on an interim basis.

Sincerely, **Sten Scheibye**Chairman of the Board

# BOARD OF DIRECTORS AND MANAGEMENT







**STEN SCHEIBYE**Chairman of the Board

Sten Scheibye was born on 3 October 1951 and is a Danish national. He holds an MSc in Chemistry and Physics from 1978 and a PhD in Organic Chemistry from 1981, both from the University of Aarhus, Denmark. In 1983, he obtained a BComm from Copenhagen Business School.

From 1995 to 2008, Sten Scheibye was President and CEO of Coloplast A/S, Denmark. Before joining Coloplast in 1993, he served as Senior Vice President, Sales & Marketing in Leo Pharma A/S, Denmark. He joined this company in 1981.

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

**GÖRAN ANDO**Board Member

Göran Ando was born on 6 March 1949 and is a Swedish national. Dr Ando is a specialist in General Medicine and a Founding Fellow of the American College of Rheumatology in the US. Dr Ando is former Executive Vice President and President of Research & Development of Pharmacia Corporation, which was acquired by Pfizer Inc. in 2003.

In April 2003, he was appointed CEO of the Celltech Group PLC in the UK until its acquisition in 2004 by UCB.

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

Dr Ando serves as a Senior Advisor to Essex Woodlands Health Ventures UK Ltd.

# JEPPE CHRISTIANSEN Board member

Jeppe Christiansen was born on 25 November 1959 and is a Danish national. He holds an MSc in Economics from the University of Copenhagen. Since 2004, Jeppe Christiansen has served as CEO of Maj Invest A/S, of which he is also a co-founder.

From 1986 to 1988, Jeppe Christiansen worked as an economist in Sparekassen SDS. He came to LD Pensions in 1988 where he became Head of Fund Management and later, as Executive Vice President, responsible for investments. From 1998 to 2004, Jeppe Christiansen worked as a Director in Danske Bank, responsible for international equity investments and corporate clients.

Jeppe Christiansen is Vice Chairman of the Board of Directors of Novo Nordisk A/S and Haldor Topsøe A/S, and a member of the Board of Directors of Kirkbi A/S and Symphogen A/S.







**STEEN RIISGAARD**Board Member

Steen Riisgaard was born on 22 March 1951 and is a Danish national. He holds an MSc in Microbiology from the University of Copenhagen.

Steen Riisgaard was President and CEO of Novozymes A/S from the demerger from Novo Nordisk A/S in 2000 until April 2013. He joined Novo Nordisk in 1979 in Enzymes Research & Development. In 1982, he moved to Tokyo to start up an enzymes R&D unit in the Novo Nordisk subsidiary, Novo Industri Japan Ltd. After his return to Denmark in 1985, he held a number of different positions in the company, before he was promoted to Corporate Executive Vice President in 1989 – with special responsibility for the Enzyme business.

Prior to joining Novo Nordisk, Steen Riisgaard was a research fellow at Statens Serum Institut (SSI) and a research microbiologist at Foss Electric, Denmark.

Steen Riisgaard is Chairman of the Board of Directors of ALK-Abello A/S, Cowi Holding A/S, Egmont International Holding A/S, Xellia Pharmaceuticals A/S and the World Wildlife Fund, Denmark. Furthermore, he is Vice Chairman of the Boards of the Novo Nordisk Foundation and the Villum Foundation, and serves on the Boards of Aarhus University, Corbion nv and VKR Holding.

### **PER WOLD-OLSEN**Board Member

Per Wold-Olsen was born on 6 November 1947 and is a Norwegian national. He holds an MBA in Economics and Administration from the Norwegian School of Management in 1972, and an MBA in Management and Marketing from the University of Wisconsin, US, in 1973.

Per Wold-Olsen joined Merck & Co. (MSD) in 1974. He became Managing Director of the Norwegian subsidiary in 1976 and Regional Director and Vice President of the Scandinavian region in 1986. In 1991, Per Wold-Olsen was appointed Senior Vice President for Worldwide Human Health Marketing of Merck & Co. Inc. in the US, and in 1994, he was appointed President of Human Health Europe of Merck & Co., Inc. In 1997, his region increased to include Eastern Europe, the Middle East and Africa, as well as Worldwide Human Health Marketing. In 2005, he was appointed President of the Human Health Intercontinental Region, Merck & Co. Inc. From 1994 to 2006, he was also a member of Merck's Management Committee.

Per Wold-Olsen is Chairman of the Board of Directors of GN Store Nord A/S and Medicines for Malaria Venture, and serves on the Board of Directors of Exiqon A/S and Gilead Sciences Inc.

### **EIVIND KOLDING** CFO

Eivind Kolding was born on 16 November 1959 and is a Danish national. He holds an MA degree in law from the University of Copenhagen and was admitted lawyer to the bar in 1986 and the High Courts in 1988.

In 1989, Eivind Kolding joined the A.P. Moller-Maersk Group. During his 22 years with the company he held a number of different positions. From 1991 to 1995, he served as Head of Corporate Secretariat, A.P. Møller-Mærsk A/S; from 1996 to 1998, he was Managing Director of Maersk Hong Kong Ltd.; and from 1998 to 2006, he served as CFO of the A.P. Moller-Maersk Group. Finally, from 2006 to 2011, he became Partner and CEO of Maersk Line.

In 2001, Eivind Kolding joined the Board of Danske Bank, became Vice Chairman of the Board in 2005 and its Chairman in 2011. From 2012 to 2013, he served as Group CEO of Danske Bank.

Eivind Kolding serves on the Boards of Novo Nordisk A/S, NNIT A/S and the Sonion Group.

Eivind Kolding resigned as CEO at the end of February, 2016.

# MANAGEMENT REPORT

# **CONTINUED SUCCESS FOR NOVO A/S IN 2015**

was a very good year for Novo A/S with all areas of activity yielding satisfactory results. Novo Nordisk A/S and Novozymes A/S, in which Novo is the controlling shareholder, experienced growth in both sales and earnings in 2015. Novo Nordisk's net profit increased by 32%, and in Novozymes net profit increased by 12%. The share price of the two companies increased by 54% and 27%, respectively.

In March 2015, a new independent member was admitted to the Novo Group, when NNIT A/S was officially listed on Nasdaq OMX Copenhagen. NNIT offers a wide range of IT services and solutions to its customers, which primarily come from the life science industry. The company was a wholly-owned subsidiary of Novo Nordisk prior to the IPO. The carve-out was a success, and Novo now holds 25.5% of the share capital in the listed entity. We welcome NNIT as a new member of the Novo Group.

Overall, 2015 rendered very satisfactory earnings. Novo's net result reached DKK 15 billion, compared to DKK 13 billion the previous year. The net result does not include price appreciations of our statute-bound shares in Novo Nordisk and Novozymes, and the result was achieved without participation in Novo Nordisk's share buyback programme.

DKK million	2015	2014
Returns from the Novo Group*	107,795	49,016
Returns from life science investments	8,592	7,336
Returns from financial investments	2,895	3,204

<sup>\*</sup> Returns from the Novo Group include unrealised appreciation of A and B shares based on the market value per B share.

Most of Novo's venture investments are made in the US and the USD/DKK currency ratio increased 12% from end of 2014 to the end of 2015. This appreciation contributed DKK 1.1 billion to our 2015 life science investment result.

#### **48% INCREASE IN TOTAL ASSETS**

By the end of the year, Novo's assets totalled DKK 378 billion, of which liquid and investment assets amounted to DKK 70 billion.

As a result of cash inflows, which primarily consist of dividends and exits from our investment portfolio and the returns from our financial portfolio, and cash outflows, primarily consisting of dividends to the Novo Nordisk

Foundation and investment in life science companies, our net cash flow in 2015 was DKK 478 million, which increased our financial reserves.

DKK million	2015	2014
Shares in Novo Group companies*	308,019	203,715
Life science investments	31,878	26,254
Financial investments	37,866	24,567
Total	377,763	254,536

\* Shares in Novo Group companies include unrealised appreciation of A and B shares based on the market value per B share.

In 2015, the value of Novo's shares in Novo Nordisk increased by 54% to DKK 280 billion. We received dividends of DKK 3,506 million – an increase of 11% compared to 2014. As in 2014, we decided not to participate in the share buyback programme in Novo Nordisk in 2015. As a consequence, our share of the capital in Novo Nordisk increased by 0.5%-points. At the end of the year, we held 537,436,000 A shares and 163,814,000 B shares, equivalent to 27% of the share capital and 74.5% of the votes in Novo Nordisk.

The value of Novo's shares in Novozymes increased by 25% in 2015. By the end of the year, the value of our holding in Novozymes amounted to DKK 26 billion. We received dividends of DKK 245 million – an increase of 20% compared to the previous year. As part of Novozymes' share buyback programme, we sold 1,708,500 B shares in Novozymes yielding DKK 537 million. As of 31 December 2015, we held 53,743,600 A shares and 26,071,400 B shares, equivalent to 25.5% of the share capital and 70.7% of the votes in Novozymes.

In 2015, Novo paid DKK 4,715 million in dividends to the Novo Nordisk Foundation, which, in accordance with its statutes, provides grants for scientific, humanitarian and social purposes. Since 2007, the Foundation has issued more than DKK 7 billion in grants, primarily to research within biomedicine and biotechnology in Denmark and the rest of the Scandinavian countries. These grants aim to strengthen the quality of research within these fields and advance future research by supporting talented scientists in their development.

We focus our investments on four main areas – three of which fall within life science and biotech and one within finance. Our life science/biotech investment activities are subdivided into three categories: large investments, venture investments and seed investments – each represented by their own business unit.

#### LARGE INVESTMENTS

Since 2013, Novo's investments in early-stage commercial companies have been redirected towards well-established, cash-flow positive companies with strongly positioned products and attractive long-term prospects. Our large investments complement our seed and venture portfolios by focusing on mature, well-established life science companies with a strong market position, attractive growth prospects, and an ambitious innovation agenda. The large investments can be made in publicly listed as well as privately owned companies and, depending on the situation, we may invest to take either a minority or a controlling position.

In 2015, Novo acquired a 3.24% share of equity in the UK-listed speciality pharma company, BTG plc. BTG licenses, develops and commercialises pharmaceuticals and has a pipeline of development programmes targeting neurological and other disorders, including varicose veins. In addition, Inogen was moved from our venture portfolio to Large Investments indicating our long-term interest in this company. By the end of 2015, our Large Investments portfolio consisted of Sonion, Xellia, Chr. Hansen, Symphogen, Orexo, Inogen, Veloxis and BTG.

2015 was a good year for Chr. Hansen Holding A/S with a share price increase of 57%.

LARGE INVESTMENTS				
DKK million	2015	2014		
Value at the end of the year	27,774	20,686		
Investments during the year	1,205	4,479		
Cash proceeds during the year	2,050	2,661		
Unrealised and realised returns during the year	6,577	3,092		

#### **VENTURE INVESTMENTS**

In 2015, Novo continued its strong commitment to life science ventures by making new and follow-on investments, consolidating our position as a recognised international investor within life science ventures.

As of 2015, the active venture portfolio consists of 42 companies of which 32 are located in the US.

VENTURE INVESTMENTS				
DKK million	2015	2014		
Value at the end of the year	3,854	5,331		
Investments during the year	1,733	1,096		
Cash proceeds during the year	3,643	2,590		
Unrealised and realised returns during the year	1,959	4,252		

We invested DKK 1,733 million as venture capital – DKK 1,077 million in new companies and DKK 656 million

In 2015 Novo Ventures expanded its US presence by opening a regional office in Boston, Massachusetts.



as follow-on investments in existing portfolio companies. In 2015, 13 of our portfolio companies were sold, four were listed in public offerings, and six were liquidated. Exit proceeds totalled DKK 3,643 million. At the end of 2015, the total book value of our venture investments was DKK 3,9 billion.

#### **SEED INVESTMENTS**

Novo runs a seed investment programme that supports earlystage life science companies, primarily in the Nordic region. In addition, Novo assists the Novo Nordisk Foundation in a preseed 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.

In May 2015, Gilead Sciences Inc., a global biopharmaceutical company, acquired EpiTherapeutics in which Novo Seeds was a lead investor. In the same month, the Novo Seeds portfolio company, Galecto Biotech initiated phase 2a studies with the company's galectin-3 inhibitor for the treatment of patients with idiopathic pulmonary fibrosis.

In 2015, Novo Seeds made a strategic decision to contribute to strengthening the Nordic biotech environment. Novo Seeds will continue to build on the successes of its seed investment portfolio and leverage the opportunities of the pre-seed programmes managed on behalf of the Novo Nordisk Foundation. Furthermore, Novo Seeds will work to increase the number of participants in the capital market for early-stage biotech. In the long run, the presence of more early-stage capital allocators will lead to improved exit opportunities for seed companies.

SEED INVESTMENTS				
DKK million	2015	2014		
Value at the end of the year	250	237		
Investments during the year	75	97		
Cash proceeds during the year	129	11		
Unrealised and realised returns during the year	56	-8		

#### **FINANCIAL INVESTMENTS**

The purpose of our financial investments is to diversify our entire investment portfolio, thereby spreading the risk while achieving high returns. These investments also serve as a liquidity buffer to cover the needs of the Novo Nordisk Foundation, the Novo Group and other portfolio companies. Since Novo is fully equity financed and our external

obligations minimal, we are in a position to adopt a longterm investment perspective.

We expanded the scope of our financial investments by including larger stakes in Danish companies. We acquired a 37% stake in the private real estate company, Dades A/S with additional capital commitments that can be used to make diversifying real estate investments through Dades as an investment platform. We also took a large direct stake in the public Danish engineering firm, FLSmidth & Co. A/S, which we view as a sound long-term investment.

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In the coming years, we will continue to be open to larger direct investments in the finance portfolio should such opportunities occur.

In 2015, our liquid financial investments generated a return of DKK 2.9 billion, equivalent to 10.5%, which was 3.76% better than the weighted benchmark. The total book value of the financial investments, including cash, reached DKK 38 billion by the end of the year. In addition, the Novo Nordisk shares that we could have sold in the share buyback programmes but preferred to keep, constituted an additional financial reserve of DKK 15 billion at the end of 2015.

FINANCIAL INVESTMENTS				
DKK million	2015	2014		
Value at the end of the year	37,866	24,567		
Unrealised and realised returns during the year	2,895	3,204		

#### **IMPACT**

Besides providing capital, Novo's investments support the life science industry in many other ways. By assisting in the commercialisation of new science and providing financial support to companies that bring new and more efficient treatments and technologies to market, we can help meet the medical needs of the global population – as well as contribute to identifying and addressing needs that are as yet unmet. This is made possible by our dedicated focus on R&D, innovation and product development.

In Scandinavia in particular, we support the dynamic life science environment with a view to strengthening the Scandinavian life science cluster.

#### **INVESTMENT CRITERIA AND CSR**

Novo carries out extensive due diligence in connection with investments in new companies. In addition to financial, legal, scientific and business-related issues, our due diligence inquiries establish whether the 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.

Social responsibility is an integral part of Novo's value-based governance framework. We believe that a responsible use of biotechnology will benefit society at large as well as Novo and its stakeholders. Social responsibility is a prerequisite for sustainable success and long-term value creation. It will increase transparency, accountability and trust – and thereby improve performance and reduce risk. Please turn to page 64 to see the 2015 CSR report.

#### **GOVERNANCE**

Novo puts great emphasis on active ownership. We strive to have board representation and hereby influence the major strategic initiatives that our portfolio companies take. We also have a real interest in the composition of the board and executive leadership team in the companies, and keep close track of company performance. When it comes to daily management and more operational issues, we believe such matters should be left to the company's management and board.

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

#### **STRATEGY**

Our strategy is based on the commercial objectives of the Novo Nordisk Foundation. Novo will continue to be a strong owner of the companies in the Novo Group and will invest its capital in the life science industry to optimise value creation and to support development in the industry in general.

Due to our long experience and extensive expertise, we are uniquely positioned to play an active role in the industry. We address the entire spectrum of life science companies – from early seed investments through traditional venture investments to investments in large, mature life science companies. We have a flexible investment approach enabling both minority and majority investments, which allows us to take a long-term perspective in all our investments.

We will also make select direct investments outside life science in attractive companies with a Danish focal point as well as investments in real estate and private equity funds. It is our aim always to maintain an adequate liquidity buffer, which we place as more traditional portfolio investments, primarily in global equities.

To be successful, Novo needs to make the right investment decisions and exert value-adding ownership of its portfolio companies.

#### **KNOWLEDGE RESOURCES**

As a life science investment company, Novo depends on highly specialised expertise – both within the field of life science and in the domain of investments. Most of our investment professionals have a background in science. Many of them have worked as researchers in the life science

industry and some have PhD degrees in fields relevant to life science (e.g. medicine, biochemistry, etc.). Others have gained their scientific expertise through employment in research and management functions in the Novo Group.

As one of the key players in the international life science investment industry, we have to ensure that our knowledge resources are always of an expert standard – so that we can fulfill our responsibilities towards our portfolio companies and make the right investment decisions. For this reason, continuing education 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 in which we invest.

#### **BUSINESS AND FINANCIAL RISKS**

Novo'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.

Novo Nordisk's performance is subject to a number of risks relating to activities throughout its value chain. Most of these risks fall into six categories: delays or failure of pipeline products, market risks, supply disruptions, quality and product safety issues, information technology risks as well as business ethics and legal risks. Product safety is directly linked to patient well-being, which means that safety and product quality are paramount concerns from both a financial and reputational perspective. While the gross risk is very high, with product safety having the potential to adversely affect operations, Novo Nordisk believes that vigorous efforts to manage and mitigate this risk effectively reduce the company's net risk profile.

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 three key risks that may impact the company: competition, volatility of the starch-based ethanol business and loss of knowledge. To mitigate the risk of competition from existing and new competitors, 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-margin environment in the starch-based ethanol business, Novozymes is continuously investing in R&D to develop more enzyme solutions for improving yield and profitability to ensure that the industry is a commercial alternative to traditional fossil fuels. To ensure protection of knowledge and mitigate the risk of cyberattacks, Novozymes continuously monitors and implements key security procedures and behaviours to prevent data theft. The risk is mitigated through a global information security strategy, IT governance, perimeter protection and access control.

For more information on 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 will become effective. The Novo Nordisk Foundation has decided upon a number of risk tolerances regarding shortfall risk for growth in grant payouts, portfolio volatility, idiosyncratic risk and access to liquidity. Novo and its investments must adhere to this risk framework.

More specifically, Novo 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 market 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 committed as well as expected five-year grant payout obligations plus an additional buffer.

Novo is adaptive and has a range of strategic levers available for meeting the new risk objectives.

#### THE FUTURE

Novo's financial prospects are highly dependent on the results of Novo Nordisk and Novozymes. For further information on the outlook for 2015 for these two companies, please consult their annual reports.

In 2016, we will continue our strong focus on life science, and we expect to increase our direct investments outside this industry as well.



Although pricing and health care reforms are putting pressure on the biotech industry, we believe that the underlying long-term trends are positive. Encouraging developments in the venture portfolio, combined with a number of strong exits and public offerings in recent years, provide the basis for our continued optimism.

In 2016, Novo expects to pay dividend of DKK 3,008 million to the Novo Nordisk Foundation and plans to invest significant amounts in small and large life science companies.

At their annual General Meetings, Novo Nordisk and Novozymes approved dividends for 2015 of DKK 6.4 per share and DKK 3.5 per share, respectively. Consequently, Novo will receive total dividends of DKK 4,767 million in 2016 from the two companies, equivalent to an increase of 27 % compared to 2015.



# LARGE INVESTMENTS

Value creation through long-term ownership

# INVESTING IN MATURE LIFE SCIENCE COMPANIES

arge Investments was established in 2013. Complementing our seed and venture portfolios, Large Investments focuses on mature, well-established life science companies with a strong market position, attractive growth prospects, and an ambitious innovation agenda. Our goal is to create value through active support and long-term ownership, particularly in industries and companies where we have networks and insights, and can contribute to making well-performing companies deliver even better results.

The long-term perspective of our investments provides a stable platform for the portfolio companies, helping them to make the right decisions for sustained long-term performance. Our large investments can be made in publicly listed as well as privately owned companies. Depending on the situation, we may invest to take either a minority or a controlling position.



Novo is looking to place substantial investments in the life science sector in the years to come.
In 2015, Novo invested in BTG plc and sold Aerocrine AB.

#### **DEVELOPMENTS IN 2015**

In 2015, Novo added BTG plc to our Large Investments portfolio. BTG is a UK-based company with a market-leading platform in interventional medicine. Our investment was motivated by the company's strategy to build a healthcare business within interventional medicine and high-margin specialist products. In addition, Inogen was moved from our venture portfolio to Large Investments indicating our long-term interest in this company. Inogen is a US-based medical technology company offering innovative respiratory projects for use in the homecare setting.

We divested our shares in Aerocrine AB – a medical technology company focused on improving the diagnosis and treatment of patients with inflamed airways. The divestment of Aerocrine is in line with our strategy of having a Large Investments portfolio that focuses exclusively on mature, cashflow positive companies. Aerocrine was acquired at a time when our focus was directed more at companies that were in the earlier phases of the commercialisation process.

Sonion Group, fully owned by Novo and a global leader in the manufacture of microelectronic components for the hearing aid industry, realised revenue growth above the underlying market growth of approximately 5% p.a. Xellia Pharmaceuticals, also fully owned by Novo, revised its long-term commercial plans. The company expanded its manufacturing footprint in the US with the acquisition of a major factory in Ohio. Xellia reported growth of 10% this year.

The other Large Investments, where Novo is a minority shareholder, realised very positive developments in 2015. Chr. Hansen Holding A/S experienced strong organic growth of 14% and is continuing its 'Nature's no. 1' strategy. Inogen continues to strengthen the company's direct-to-consumer model and growing brand awareness. Symphogen fully enrolled 240 patients in their phase 2b study for Sym004 in metastatic colorectal cancer — a product that was fully transferred from Merck Serono to Symphogen earlier in the year — and partnered with Baxalta to advance six immuno-oncology checkpoint inhibitors from discovery into clinical development. In August 2015, Orexo received FDA approval of Zubsolv for use at the initiation of treatment for opioid dependence. Finally, Veloxis Pharmaceuticals received FDA approval to use Envarsus for the prophylaxis of rejection in kidney transplant patients.

#### **GOING FORWARD**

To expand our existing portfolio, Novo is pursuing substantial investments in the life science sector in the years to come. Our areas of interest span broadly across the life science industry – from biopharmaceutical companies over med-tech manufacturers and healthcare service providers to industrial biotechnology. We strive to invest in companies that are market leaders, and where we believe our ownership can make a significant difference to the company's long-term performance.





**X** ellia Pharmaceuticals is a specialty pharmaceutical company that produces injectable anti-infective treatments against serious and often life-threatening infections

Xellia's range of anti-infective treatments combats most types of bacterial infections and certain fungal diseases. Some of these products can be used against antibiotic-resistant strains too. The company is the market-leading supplier of the anti-infectives, Vancomycin and Colistimethate Sodium. Vancomycin is used in the treatment of serious, life-threatening infections that have been unresponsive to other antibiotics. Colistimethate sodium is primarily used to treat lung infections, especially in patients with cystic fibrosis. In a world where the prevalence of multi-resistant infections is becoming more frequent, Xellia's portfolio of treatments offers a vital contribution to curing illnesses and saving lives.

Xellia has sales in more than 70 countries to more than 700 customers. The company is continually developing and expanding its product range to meet new treatment needs and customer requirements. This includes the development of new dosage forms. Xellia also offers contract manufacturing services and custom synthesis for clinical trial material supply.

#### **XELLIA**

Founded in 1903 in Norway

Headquartered in Copenhagen, Denmark, with manufacturing in Hungary, the US and China

Private company fully owned by Novo A/S (acquired in 2013)

Market leader in non-beta lactam antiinfectives, based on fermentation and aseptic manufacturing technologies

Revenue 2015: USD 220 million

Board member representing Novo A/S: Steen Riisgaard, Chairman and Aleks Engel, Asset Director

www.xellia.com

#### **NEWS**

Xellia announced the expansion of its Raleigh, NC site to enable the relocation of its North American headquarters from Grayslake, Illinois.

Acquired large finished dosage form manufacturing plant in Cleveland Ohio.

"Xellia's acquisition of a key manufacturing facility in Cleveland Ohio in 2015 is a great leap forward for the company. As Xellia's second manufacturing site in the US, this greatly expands its global manufacturing footprint, allowing it to meet the growing demand for sterile injectable products locally in the US, as well as address drug shortages of critical life-saving antibiotics globally."

Carl-Åke Carlsson CEO





**S** onion is a leading provider of technology solutions to the hearing aid industry. The company supplies microacoustic and micromechanical technologies and solutions to global manufacturers of hearing instruments, in-ear earphones and high-end communication headsets.

For more than 40 years, Sonion has provided components for the hearing aid industry that provide better hearing and more comfort for the hearing impaired. By making the components as small as possible, Sonion helps hearing aid producers to reduce the size of a hearing aid and increase comfort, ultimately with a view to improving quality of life for the end user.

Sonion supports their customers all the way from idea to high volume production. With a global base, experienced research and development departments, and a flexible production setup, the company strives to be their customers' preferred development partner and supplier of microacoustic and micromechanical solutions.

#### SONION

Founded in 1974 in Roskilde, Denmark

Headquartered in Switzerland with facilities in Denmark, Poland, the Netherlands, the US, China, Vietnam and the Philippines

Employs more than 4,000 people

Private company fully owned by Novo A/S and management (acquired in 2014)

Board members representing Novo A/S: Christian Salling, Asset Director

www.sonion.com

#### **NEWS**

Sonion announced the release of the RIC-4400 & RIC-E50D, a dual receiver for mild and moderate hearing loss.

Released their latest N-Series MEMS - the N11 omni/matched pair microphones.

Introduced the dual microphone, M20 with shared rear volume in one package. This product has been released for qualification.





hr. Hansen is a global bioscience company with leadership positions in a number of attractive niche markets, including cultures for the food & beverage, human health, animal health and plant protection industries; enzymes for the dairy industry; and natural colours for the food & beverage industry.

Chr. Hansen's solutions offer an attractive cost-to-value ratio for customers. The company has a strong R&D development platform, core capabilities in large-scale fermentation of cultures and strong application know how – all of which ensures successful integration with customers' products and processes.

Chr. Hansen's Nature's No. 1 strategy continues to guide the long-term direction of the company, and good progress in the strategic initiatives has been seen – both in established businesses and in new initiatives within biological plant protection and the human microbiome. Moreover, Chr. Hansen has taken an important step in its strategic venture into new generations of probiotic products and therapeutic microbes.

#### **CHR. HANSEN**

Founded in 1874 in Copenhagen, Denmark

Headquartered in Hørsholm, Denmark with development centres in Denmark, the US, France and Germany

Major investors include Novo A/S (from 2012), Capital Group Companies and APG Asset Management N.V.

Revenue in 2014/15: EUR 859 million

Public company listed on NASDAQ OMX Copenhagen since 2010. Code CHR

www.chr-hansen.com

#### **NEWS**

Launched a new generation of CapColors® Orange that enables conversion to stable and non-artificial colouration in the beverage market.

Launched the Direct Vat Set® solution, DVS® WhiteClassic culture, designed to match Greek Feta's balanced round flavours and creamy texture, while ensuring consistency and control.

Søren Westh Lonning was appointed new CFO.



### orexc

**S** ymphogen is a biopharmaceutical company that develops antibody mixture therapeutics for the treatment of cancer.

**O** rexo is a specialty pharmaceutical company focused on the therapeutic areas of pain and inflammation.

#### **SYMPHOGEN**

Founded in 2000

Headquartered in Ballerup, Denmark, with a clinical development unit in New Jersey, USA

Major investors include Novo A/S (from 2000), Essex Woodlands and PKA

Private company

Board member representing Novo A/S: Aleks Engel, Asset Director

www.symphogen.com

#### **NEWS**

Symphogen closed a EUR 67.5 million financing subscribed by existing investors.

Fully enrolled 240 patients in a phase 2b study for Sym004 in metastatic colorectal cancer. The product was fully transferred from Merck Serono earlier in the year. Sym004 is a novel antibody mixture targeting metastatic colorectal cancer, gliablastoma, and quamous cell carcinoma of the head and neck.

Established a strategic collaboration with Baxalta to develop six immuno-oncology antibodies.

#### **OREXO**

Founded in 1995

Headquartered in Uppsala, Sweden

Major investors include Novo A/S (from 2010) and HealthCap

Revenue 2015: SEK 228 million

Public company, listed on the Stockholm stock exchange since 2005. Code ORX

Board member representing Novo A/S: Michael Shalmi, Head of Large Investments

www.orexo.com

#### **NEWS**

Orexo received FDA approval for ZUBSOLV® for induction of buprenorphine maintenance therapy in patients with opioid dependence.

Announced the divestment of the subsidiary, Kibion that markets the products Heliprobe® System, Diabact® UBT and IRIS™ for the diagnosis of the gastric ulcer bacterium, Helicobacter pylori using breath test technology.

Initiated the launch of a new higher ZUBSOLV tablet strength (8.6 mg/2.1 mg buprenorphine/naloxone CIII sublingual tablets).

Entered into a settlement and license agreement with Actavis Laboratories FL, Inc. to settle the patent litigation regarding Abstral® in the US.

Received SEK 63.8 million milestone payment for Abstral® in Europe.

Eivind Kolding, CEO, Novo was appointed Chairman of the nomination committee.





V eloxis Pharmaceuticals is a specialty pharmaceutical company focused on the commercialisation of Envarsus XR (extended release Tacrolimus), an immunosuppressant for kidney rejection treatment.

nogen develops, manufactures and markets innovative, portable oxygen concentrators that deliver supplemental long-term oxygen therapy to patients suffering from chronic respiratory conditions.

#### **VELOXIS**

Founded in 2002

Headquartered in Hørsholm, Denmark with a subsidiary in New Jersey, USA

Major investors include Novo A/S (from 2003) and Lundbeckfond Ventures

Revenue 2015: DKK 16 million

Public company, listed on the NASDAQ OMX Copenhagen since 2010. Code VELO

Board members representing Novo A/S: Thomas Dyrberg, Managing Partner

www.veloxis.com

#### **NEWS**

Veloxis received FDA approval to use Envarsus for the prophylaxis of rejection in kidney transplant patients who require or desire conversion from other twice-daily tacrolimus products to once-daily Envarsus.

Envarsus® XR was granted orphan drug status by the FDA for prophylaxis of organ rejection in patients who convert from immediate-release tacrolimus.

Hired full commercial team in preparation for US launch.

Envarsus® XR demonstrated differentiated pharmacokinetic profile compared to twice-daily Prograf® or once-daily Astagraf XL® in stable kidney transplant patients.

Obtained unique J-code from Centers for Medicare & Medicaid Services (CMS).

#### **INOGEN**

Founded in 2001

Headquartered in Goleta, California, USA, with production facility/call centre in Dallas, Texas, USA

Major investors include Novo A/S (from 2006) and TimesSquare Capital Management

Revenue 2015: USD 159 million

Public company, listed on NASDAQ since 2014. Code INGN

www.inogen.com

#### **NEWS**

Inogen awarded as The Company of the Year at the South Coast Business & Technology Awards.

Brought to market an enhanced Inogen One G3 portable oxygen concentrator.

Deloitte's 2015 Technology Fast 500™ recognised Inogen as one of the fastest growing companies in North America



**B** TG is dedicated to finding smart, often unconventional solutions to complex medical problems. Many of the company's interventional medicine products combine medicines, device technology and new techniques in order to deliver more targeted minimally-invasive treatments.

#### BTG

Founded in 1981

Headquartered in London, UK

Major investors include Novo A/S (from 2015) and Invesco Ltd

Revenue 2014/15: GBP 368 million

Public company listed on the London Stock Exchange since 1995. Code BTG

www.btgplc.com

#### **NEWS**

BTG acquired US-based PneumRx in January 2015. PneumRx' main product, the RePneu Coil System, is a minimally-invasive device for treating severe emphysema.

Began selling its drug-eluting bead and embolization oncology products directly to customers in 11 European countries, taking back the license from Astellas in April 2015.

Announced positive safety and efficacy data in over 500 DC BeadM1 patients and compelling health economic data for TheraSphere.

Announced positive data from RENEW study of PneumRx® Coils.



# NOVO VENTURES

Investing in biotech to bring innovative products to patients

# A UNIQUE APPROACH TO VENTURE INVESTMENTS

#### SUCCESSFUL TRACK RECORD

Novo's venture activities have produced a positive track record and established Novo as an important player in the international life science venture capital industry.

During our 16 years in the business, we have invested DKK 8 billion in 121 companies and successfully exited 39 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. As 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.

#### **INVESTING UP TO DKK 2 BILLION ANNUALLY**

Novo's approach to venture capital investments is unique due to our special ownership structure. Novo has significant

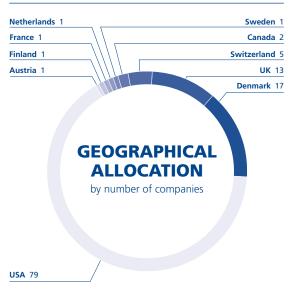
shareholdings in Novo Nordisk A/S and Novozymes A/S, but our venture investments are fully independent of the two major Novo Group companies.

Novo's venture investment activity has been geared up to an all-time high level of investment of up to DKK 2 billion annually. The 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; it also exempts us from the frameworks that are found in many traditional venture capital funds.

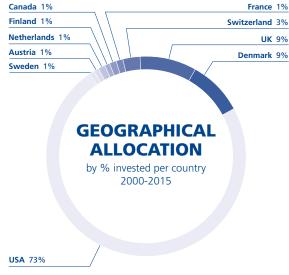
#### AN INTERNATIONAL INVESTOR

With people on the ground in Copenhagen, London, San Francisco and most recently Boston (see pp. 30-31), 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.

#### **PORTFOLIO 2000—2015**



#### **PORTFOLIO 2000—2015**



### **M&As AND IPOs IN 2015**

**2015** was another great liquidity year for Novo's private portfolio companies. During the year, we saw one company acquired by Novartis and four private portfolio companies become publicly traded companies on Nasdaq in the US.

#### 2015 public crop

- Adaptimmune (ADAP)
- CoLucid Pharmaceuticals (CLCD)
- HTG Molecular Diagnostics (HTGM)
- Tobira Therapeutics (TBRA)

#### A BUSY PUBLIC YEAR

Early May 2015 was a particular busy time for us. In just three days, four of Novo's portfolio companies became publicly traded companies. Tobira Therapeutics merged with Regado Biosciences on 5 May; Colucid Pharmaceuticals and HTG Molecular completed their initial offerings on 6 May; and Adaptimmune went public on Nasdaq on 7 May.

2015 was another great liquidity year for Novo's private portfolio companies. Spinifex was sold to Novartis for USD 200 million and four private portfolio companies went public on Nasdaq.



Number of successful exits per country invested	Number of ALL exits per country
Switzerland ①	Switzerland ①
France	France ①
Finland	Finland ①
Donmark (3)	Canada ①
Denmark	Sweden ①
UK (4)	UK 7
<b>USA</b> 29	<b>Denmark</b> 16
	USA 45

# ANATOMY OF AN EXIT: SPINIFEX PHARMACEUTICALS SOLD TO NOVARTIS FOR USD 200 MILLION

he angiotensin type 2 (AT2) receptor was discovered in the late 1980s when many big pharma companies researched the biology behind hypertension and the angiotensin type 1 receptor. It was quickly understood that the AT2 receptor has no role in the control of blood pressure, and all marketed angiotensin receptor blockers are highly-selective AT1 receptor antagonists.

For a long time, the function of AT2 remained unclear. But in 2004, Professor Maree Smith from University of Queensland, Australia discovered that AT2 receptor antagonists relieve symptoms of neuropathic and inflammatory pain in animal models. This discovery led to the formation of Spinifex Pharmaceuticals Pty Ltd. in Australia in 2005.

Neuropathic pain is a chronic condition with high unmet medical needs. Approximately 40 per cent of patients do not respond to current first-line treatments and a further 25 per cent do not respond to second-line treatment options. It is estimated that up to 7 to 8 per cent of the adult population suffer from chronic pain with neuropathic characteristics.

Leveraging peripheral targets, for example by using an AT2 receptor antagonist, is an emerging and promising approach to neuropathic pain treatment. Peripheral targets act outside the blood-brain barrier and are expected to be devoid of common side effects in the central nervous system, such as dizziness or confusion.

Novo Ventures' first dealings with Spinifex were in March 2010 when the company was conducting a financing round based on single and multiple ascending dosing in human volunteers. While the first meetings did not lead to an investment, we found the programme exciting and stayed in contact with Spinifex as the programme matured.

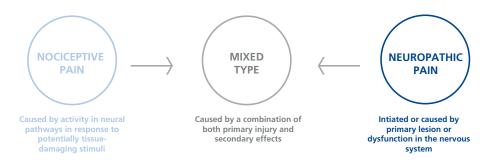
In early 2014, the positive results from Spinifex's phase 2 clinical trial of the lead programme EMA401 in post-herpetic neuralgia were published in The Lancet¹. Post-herpatic neuralgia is a painful condition that develops in some people following herpes zoster (shingles), and it is a condition that is difficult to treat with exiting pain medications. The side effects to the central nervous system that are common with other medications did not occur with EMA401.

After the promising early phase 2 data in post-herpetic neuralgia, Novo led a USD 45 million Series C financing in Spinifex in April 2014. At that time, Spinifex was still located in Melbourne, Australia but in connection with the financing, the company moved its headquarters to Connecticut in the US.

Spinifex had completed further phase 1 studies and was about to initiate several larger phase 2 pain studies when Novartis acquired Spinifex in June 2015 for USD 200 million upfront and undisclosed but very significant additional milestone payments.

1 Rice, A.S.C. et al. (2014), The Lancet, 383(9929): 1637-1647

#### **NOCICEPTIVE VS NEUROPATHIC PAIN**



The National Initiative on Pain Control® explains the difference and potential overlap of Nociceptive and Neuropathic pain.

# INTRODUCING THE CLASS OF 2015

**D** uring 2015, Novo added five public and 12 private companies to its venture portfolio. In most of the private financings, we played a key role as lead or co-lead investors.

Our new portfolio companies develop therapies for a variety of indications, including migraine, cancer immunotherapy, CNS, ophthalmology, glaucoma, immune diseases and anti-infective therapies.

Except for one, all the new companies are located in the US.

#### **ANTI-INFECTIVES**

**Nabriva Therapeutics** (NASDAQ:NBRV) develops novel anti-infective agents. The lead product candidate, lefamulin is in phase 3 for the treatment of community-acquired bacterial pneumonia. Novo invested in the company's IPO.

#### **CANCER IMMUNOTHERAPY**

**Corvus Pharmaceuticals** develops drugs that reprogramme T cells to restore the immune balance needed for tumour destruction. Novo participated in Corvus' two financing in 2015.

**Encarta Therapeutics** plans to develop novel T-cell therapies for cancer. Novo was a co-investor in Encarta's financing.

**Merus** closed a financing in August that was co-led by Novo. The company develops fully human bi-specific antibodies for various oncology indications.

**NKarta Therapeutics** is focused on developing Natural Killer (NK) cell-based therapies for use in the treatment of cancers. Novo co-lead the initial financing of the company.

**Unum Therapeutics** develops antibody-coupled T-cell receptor technology for use in cellular immunotherapies for cancer. Novo invested in its recent financing.

**Vasculox** develops a portfolio of anti-CD47 therapeutic antibodies for the treatment of cancer and pulmonary hypertension. Novo invested in its recent financing.

#### **CANCER SUPPORTIVE CARE**

**Galera Therapeutics** closed a financing in October that was led by Novo. Galera Therapeutics is a clinical-stage company with a lead product focused on radiation-induced mucositis.

#### **CNS**

**CoLucid Pharmaceuticals** (NASDAQ:CLCD) develops innovative therapies for CNS disorders and has initiated its first phase 3 pivotal trial to confirm Lasmiditan's safety and efficacy. Novo invested in the company's IPO.

**E-Scape Bio** closed a financing in August that was co-lead by Novo. The company develops a pipeline of ApoE4 structure correctors for the treatment of neurodegenerative diseases, including Alzheimer's disease.

#### **IMMUNE DISEASES**

**Kanyos Bio** is a spin-out from Anokion. The company focuses on autoimmune diseases (e.g. celiac disease and type 1 diabetes) under an option deal with Astellas.

**Ra Pharmaceuticals** closed a financing in July that was co-led by Novo. The company focuses on developing peptide-based drugs for treatment of diseases of complement dysregulation.

#### **MEDICAL DEVICES**

**Glaukos** (NASDAQ:GKOS) is focused on the commercialisation of medical devices to treat glaucoma. Novo invested in the company's IPO.

**Invuity** (NASDAQ:IVTY) is pioneering and commercialising the use of advanced photonics to provide surgeons with improved direct visualisation of surgical cavities during minimally invasive surgery. Novo invested in the company's IPO.

**Penumbra** (NYSE:PEN) develops and commercialises innovative medical devices primarily for the neuro and peripheral vascular markets. Novo invested in the company's IPO.

**Procept BioRobotics** closed a financing in July that was led by Novo. The company is developing a new treatment for benign prostate hyperplasia based on robot-controlled water ablation of prostate tissue.

**Unchained Labs** closed a financing in February that was led by Novo. The company develops and markets life science tools for analysing protein stability.

# PORTFOLIO COMPANY ACHIEVEMENTS IN 2015

#### **BUSINESS NEWS**

Adaptimmune was listed on NASDAQ in May 2015.

**Alder Biopharmaceuticals** raised more than USD 200 million in a follow-on offering in June 2015.

**Akebia Therapeutics** partnered Japanese and certain other Asian rights to Mitsubishi Tanabe Pharma for Vadadustat for USD 100 million, plus future milestone and royalty payments.

**CoLucid Pharmaceuticals** was listed on NASDAQ in May 2015.

**HTG Molecular Diagnostics** was listed on NASDAQ in May 2015.

**Kanyos** completed a build-to-buy option deal with Astellas to collaborate in the fields of type 1 diabetes and celiac disease.

**Nevro** issued a public offering resulting in an aggregate proceed of approximately USD 240 million.

ObsEva completed a CHF 60 million financing.

**Otonomy** closed a follow-on public offering for a total gross proceeds of approximately USD 86 million.

Spinifex Pharmaceuticals was sold to Novartis in 2015.

**Tobira** was listed on NASDAQ via reverse merger with Regado Biosciences and secured a USD 70 million financing.

#### **PRODUCT NEWS**

**Acacia Pharma** obtained positive phase 2b data in chemotherapy-induced nausea and vomiting with amisulpride.

**Apollo Endosurgery** received PMA approval for Obera® balloon.

**KalVista Pharmaceuticals** completed first-in-patient study in diabetic macular oedema with KVD001, a plasma kallikrein inhibitor.

**Nevro** received FDA approval for Senza®, the spinal cord stimulation system for chronic back and leg pain.

**Ophthotech** has completed enrolment of two phase 3 trials and top-line data are expected by the end of 2016.

**Otonomy** obtained FDA approval for OTIPRIO as a treatment of middle ear effusion.

**Tarsa Therapeutics** filed a NDA for oral calcitonin seeking an osteoporosis indication.

**Unchained Labs** acquired a portfolio of complementary products for protein formulation and stability analysis.

### NOVO VENTURES OPENS A NEW OFFICE IN BOSTON

With the opening of the regional office in Boston, Massachusetts, Novo Ventures has expanded its US footprint.

Over the past decade, Boston has become a major hub of biotech with the presence of world-class academic institutions, major pharma and biotech companies, and leading venture capital firms. This has resulted in prolific venture activities matched only by those taking place in the San Francisco area.

With our presence in Copenhagen, San Francisco, London, and now Boston, Novo Ventures stands out as one the few truly cross-Atlantic life science investors.

#### THE BOSTON INNOVATION ECOSYSTEM

Key to the emergence of Boston as an innovation hub is the simultaneous presence of world-class research, strong biotech industry and substantial venture capital, which together constitutes a very productive ecosystem.

The basic and clinical research performed at the universities and research hospitals in the area is key to driving the growth of the Boston biotech industry. For many decades, Harvard, MIT and several other leading academic institutions have attracted world-class research talent into the Boston community. Additionally, Boston is home to the highest-funded private research hospitals in the US, led by Massachusetts General Hospitals, Brigham and Women's Hospital, and Dana Farber Cancer Institute. With research budgets for these institutions exceeding USD 3 billion annually, the academic community will continue to feed the talent pool that drives the innovation economy.

Led by Novartis in 2002, large pharma and biotech have continued to build their presence in the Boston area. This trend has enabled cross-fertilisation between the academic, pharma and venture communities. Pfizer, Novartis, GSK, Amgen, Merck, Celgene, and Takeda/Millennium have all established major R&D operations in Boston. These R&D sites range from a few hundred researchers to several thousand employees.

During the past decade, we have also seen what was once small-scale start-ups mature into real large-scale biotech companies – e.g. Biogen, Genzyme (acquired by Sanofi) and Vertex. These companies have all focused on high medical need indications and let science and medical need be the driving force for their product development. They are now all generating billions of dollars in annual revenue from novel therapeutics, and driving public market valuations in the double-digit billion dollar range. These successes help to feed more investment dollars back into the biotech ecosystem; they also generate an enthusiasm for biotech and life science and create a conducive environment for the next generations of venture-backed and small cap public biotech start-ups.

The infusion of a significant amount of life science investment dollars into the Boston area has fueled an explosion of biotech in the region. More than 60,000 people work in the life science industry in the Boston area, and there are more than 180 life science companies incorporated here, many of which have been established within the last five years. Venture capital firms – including Novo – have contributed to this growth by investing nearly USD 6 billion in Boston-based biotech companies since 2010. Many of these private companies have transitioned to the public markets, with local biotech companies raising more than USD 2.6 billion in IPO proceeds since 2013.

With a healthy crop of well-financed young companies developing new drugs, there is reason to believe that some of these will succeed in getting blockbuster products to the market. These will become the next multi-billion dollar companies to infuse even more activity and growth into the Boston ecosystem.

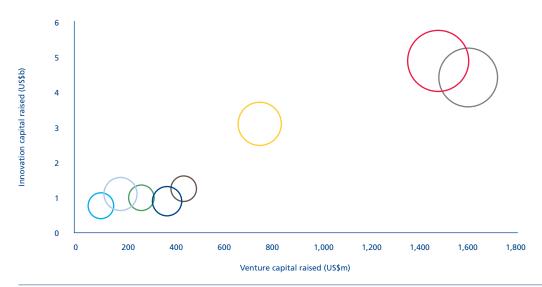


Source: EY, BioCentury, Capital IQ and VentureSource

#### **INNOVATION CAPITAL RAISED BY LEADING US REGIONS, 2014**



Size of bubbles shows relative number of financings per region. Innovation capital refers to the amount of equity capital raised by companies with revenues less than US\$500 million.

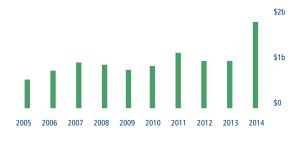


## BUILDING TOWARDS THE FUTURE WITH A STRONG START

Given the time necessary to successfully get a drug to market, life science investors need to take a long-term perspective if they want their investments to yield successful results. Novo Ventures opened its San Francisco office in 2006 with the intention of growing investment opportunities in the US through strong industry contacts and networks. Novo has opened its Boston office with this same long-term perspective – and we are off for a strong start.

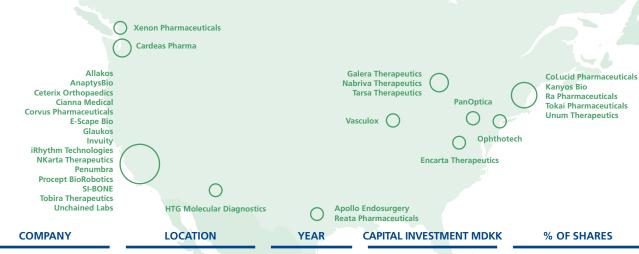
Since opening the Boston office in April 2015, we have added several new members to the Ventures team and completed three East Coast investments, including participation in a 65 million USD Series B financing of Unum Therapeutics; co-leading a USD 58 million Series B investment in RA Pharma; and leading a USD 37 million financing of Galera Therapeutics. For 2016 and beyond, it is Novo's goal to continue to expand our presence in Boston at a rate that matches the growth of high-quality investment opportunities in the area.

## VENTURE CAPITAL INVESTMENT IN MASSACHUSETTS BIOTECH COMPANIES, 2005-2014

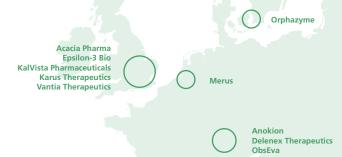




# **ACTIVE PORTFOLIO COMPANIES IN FIGURES**



				ata Pharmaceuticals		
	COMPANY	LOCATION	YEAR	CAPITAL INVESTMENT MDKK	% OF SHARES	
			of initial investment	0 50 100 150 200 >250	0% 25% 40%	
0	Allakos	San Carlos, CA, USA	2012			
0	AnaptysBio	San Diego, CA, USA	2007			
0	Apollo Endosurgery	Austin, TX, USA	2012			
0	Cardeas Pharma	Seattle, WA, USA	2011			
0	Ceterix Orthopaedics	Menlo Park, CA, USA	2012			
0	Cianna Medical	Aliso Viejo, CA, USA	2011			
0	CoLucid Pharmaceuticals	Cambridge, MA, USA	2015			
0	Corvus Pharmaceuticals	Burlingame, CA, USA	2015			
0	E-Scape Bio	San Francisco, CA, USA	2015			
0	Encarta Therapeutics	Germantown, MD, USA	2015	•		
0	Galera Therapeutics	Malvern, PA, USA	2015	11-		
	Glaukos	Laguna Hills, CA, USA	2015	1	1	
0	HTG Molecular Diagnostics	Tucson, AZ, USA	2011			
	Invuity	San Francisco, CA, USA	2015			
0	iRhythm Technologies	San Francisco, CA, USA	2014			
0	Kanyos Bio	Cambridge, MA, USA	2014	-		
	Nabriva Therapeutics	King of Prussia, PA, USA	2015		_	
0	NKarta Therapeutics	San Francisco, CA	2015	ı		
0	Ophthotech	New York, NY, USA	2007			
0	PanOptica	Bernardsville, NJ, USA	2014			
	Penumbra	Alameda, CA, USA	2015		1	
0	Procept BioRobotics	Redwood Shores, CA, USA	2015			
0	Ra Pharmaceuticals	Cambridge, MA, USA	2015			
0	Reata Pharmaceuticals	Irving, TX, USA	2006			
•	SI-BONE	San Jose, CA, USA	2014			
0	Tarsa Therapeutics	Philadelphia, PA, USA	2009			
	Tobira Therapeutics	South San Francisco, CA, USA	2010			
	Tokai Pharmaceuticals	Boston, MA, USA	2014		-	
0	Unchained Labs	Pleasanton, CA, USA	2015			
	Unum Therapeutics	Cambridge, MA, USA	2015		•	
0	Vasculox	St. Louis, MO, USA	2015			
	Xenon Pharmaceuticals	Burnaby, BC, Canada	2001	- :	1	



	COMPANY	LOCATION	YEAR	CAPITAL INVESTMENT MDKK	% OF SHARES
			of initial investment	0 50 100 150 200 >250 0	% 30% 60%
0	Acacia Pharma	Cambridge, Cambridgeshire, UK	2013		
0	Anokion	Lausanne, Switzerland	2014	. •	
0	Delenex Therapeutics	Zürich, Switzerland	2011		
0	Epsilon-3 Bio	Duxford, Cambridgeshire, UK	2011		
0	KalVista Pharmaceuticals	Porton Down, Wiltshire, UK	2011		
0	Karus Therapeutics	Abingdon, Oxfordshire, UK	2012	_	
0	Merus	Utrecht, Netherlands	2015	_	-
0	ObsEva	Geneva, Switzerland	2013		
0	Orphazyme	Copenhagen, Denmark	2011		
0	Vantia Therapeutics	Southampton Hampshire UK	2008		

Novo A/S on board **②**Denotes observer post **③** 

### **PRIVATE COMPANIES**



Acacia Pharma is focused 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



Ceterix Orthopaedics develops novel surgical tools for arthroscopic procedures. This technology has applications in numerous arthroscopic procedures in knees, hips and shoulders. The product is launched in the US. www.ceterix.com



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.



Allakos develops monoclonal antibody-based therapies to target eosinophils and mast cells. The lead programme is in phase 1 clinical development. www.allakos.com



Cianna Medical is a medical device company focused on breast surgery products. The company manufactures and markets the SAVI breast brachytherapy applicator and the Scout surgical guidance system. www.ciannamedical.com



Galera Therapeutics is a clinical-stage company focused on the development of highly selective small molecule dismutase mimetics, initially targeting the prevention of radiationinduced toxicity, including mucositis. www.galeratx.com



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



Corvus Pharmaceuticals develops drugs that harness the immune system to fight cancer in a new area of medicine known as immuno-oncology. www.corvuspharma.com



iRhythm Technologies is a medical device company that develops and markets the ZIO® Service – an innovative cardiac monitoring and diagnostic solution which uses a single-use wearable patch to detect cardiac arrhythmias. www.irhythmtech.com



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



Delenex Therapeutics develops therapeutic antibody fragments designed for local/topical use. www.delenex.com



KalVista Pharmaceuticals develops plasma kallikrein inhibitors for the treatment of diabetic macular edema and hereditary angioedema. The lead programme is in phase 2 clinical development. www.kalvista.com



Apollo Endosurgery markets Orbera® and Lap-Band® for the treatment of obesity. The company is a leader in flexible endoscopic surgery via OverStitch  $^{\text{TM}}$  and other endoscopic devices

www.apolloendo.com

#### **E-SCAPE BIO**

E-Scape Bio develops a pipeline of ApoE4 structure correctors for the treatment of neurodegenerative diseases, including Alzheimer's disease



Kanyos Bio is a spin-out from Anokion. The company focuses on autoimmune diseases (e.g. celiac diseases and type 1 diabetes) under an option deal with Astellas www.kanyos.com



Cardeas Pharma is developing a treatment for pneumonia in patients in intensive care units. The lead product is in phase 2 clinical development. www.cardeaspharma.com



Encarta Therapeutics plans to develop novel cell therapies

www.encartatx.com



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



**Merus** is a clinical-stage company developing fully human bispecific antibodies for various oncology treatments. The two lead programmes are for solid tumours and acute myeloid leukemia.

www.merus.nl



Ra Pharmaceuticals focuses on developing peptidebased drugs for treatment of diseases of complement dysregulation. The lead programme is an anti C5 complement inhibitor.

www.rapharma.com



Vantia Therapeutics develops a small molecule agonists of vasopressin receptors. The lead asset has completed phase 2 clinical development for the treatment of nocturia in men with prostatic hyperplasia and will enter phase 3 in 2016 following completion of a thorough Qt study. www.vantia.com

#### **NKARTA THERAPEUTICS**

**NKarta Therapeutics** is focused on developing Natural Killer (NK) cell-based therapies for use in the treatment of cancers.



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



**Vasculox** develops a portfolio of anti-CD47 therapeutic antibodies for the treatment of cancer and pulmonary hypertension. The lead programme is in pre-clinical development.

www.vasculox.com



**ObsEva** develops innovative drugs for women's reproductive medicine.

www.obseva.com



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



**Orphazyme** develops novel therapeutics for the treatment of lysosomal storage diseases. The company is undertaking a clinical trial in Niemann-Pick disease type C. www.orphazyme.com



**Tarsa Therapeutics** develops an oral calcitonin for the treatment of osteoporosis. The company submitted an NDA for TBRIA™ in 2015.
www.tarsatherapeutics.com



**PanOptica** develops a novel topical drug for wet age-related macular degeneration. The lead programme is in phase 1b clinical development.

www.panopticapharma.com



**Unchained Labs** develops and markets life science tools. The company focuses on analysing and predicting stability of complex protein therapeutics formulations. www.unchainedlabs.com



**Procept BioRobotics** develops a new treatment for benign prostate hyperplasia based on image guided and robot-controlled water ablation of prostate tissue. The device is CE marked and a regulatory study is underway in the US. www.procept-biorobotics.com



Unum Therapeutics develops proprietary antibodycoupled T-cell preceptor technology for use in new cellular immunotherapies for cancer. The lead programme is in clinical testing. www.unumrx.com

### **PUBLIC COMPANIES**



**CoLucid Pharmaceuticals** (NASDAQ:CLCD) develops innovative therapies for CNS disorders. The lead programme is in phase 3 clinical development for the treatment of migraine. www.colucid.com



**Glaukos** (NASDAQ:GKOS) is an ophthalmic medical technology company focused on the development and commercialisation of break-through products and procedures to transform the treatment of glaucoma, the second-leading cause of blindness. www.glaukos.com



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



**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



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



Ophthotech (NASDAQ:OPHT) is a biopharmaceutical company specialising in the development of novel therapeutics to treat diseases of the eye. The company has initiated a pivotal phase 3 clinical programme for its most advanced product candidate, Fovista™ anti-PDGF therapy. www.ophthotech.com



Penumbra (NYSE:PEN) is a therapy company that designs, develops, manufactures and commercialises innovative medical devices primarily for the neuro and peripheral vascular markets. www.penumbrainc.com



**Tobira Therapeutics** (NASDAQ:TBRA) develops products for the treatment of non-alcoholic steatohepatitis (NASH) and HIV. The lead compound, a CCR5 antagonist for the treatment of HIV infection, is in a phase 2b study for NASH and has completed phase 2b clinical development in HIV.

www.tobiratherapeutics.com



Tokai Pharmaceuticals (NASDAQ:TKAI) develops novel therapies for prostate cancer and other hormonally driven diseases. The lead candidate, galeterone is in phase 3 clinical development for the treatment of castration-resistant prostate cancer. www.tokaipharmaceuticals.com



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

#### **SELECTED EXITS**

#### **EXITS BY M&A**

#### ActivX Biosciences

Acquired by Kyorin Pharmaceutical in 2004.

#### Alios BioPharma

Acquired by Johnson & Johnson in 2014.

#### **Amira Pharmaceuticals**

Acquired by Bristol-Myers Squibb in 2011.

Acquired by Sosei Co. in 2005.

#### **BioMimetic Therapeutics**

Acquired by Wright Medical Group in 2012.

#### Cabrellis Pharmaceuticals

Acquired by Pharmion in 2006.

#### Combio

Acquired by Arpida in 2004.

#### **Conforma Therapeutics**

Acquired by Biogen Idec in 2006.

#### Corus Pharma

Acquired by Gilead Sciences in 2006.

#### **Elevation Pharmaceuticals**

Acquired by Sunovion Pharmaceuticals in 2012.

#### FoldRx Pharmaceuticals

Acquired by Pfizer in 2010.

#### **Funxional Therapeutics**

Sold lead asset to Boehringer Ingelheim in 2012.

#### **Gloucester Pharmaceuticals**

Acquired by Celgene in 2010.

#### **InSound Medical**

Acquired by Sonova Holding in 2010.

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#### NeoMend

Acquired by C. R. Bard in 2012.

#### Neurodan

Acquired by Otto Bock in 2005.

#### Novexel

Acquired by AstraZeneca in 2010.

#### **Protein Forest**

Acquired by ProteinSimple in 2009.

#### ProteinSimple

Acquired by Techne Corporation in 2014.

#### Salmedix

Acquired by Cephalon in 2005.

#### Santaris Pharma

Acquired by Roche in 2014.

#### **Sapphire Therapeutics**

Acquired by Helsinn Healthcare in 2009.

#### Spinifex Pharmaceuticals

Acquired by Novartis in 2015.

#### **Synosia Therapeutics**

Acquired by Biotie Therapies in 2011.

Acquired by Wyeth Pharmaceuticals in 2008.

#### ZvmoGenetics

Acquired by Bristol-Myers Squibb in 2010.

**EXITS BY IPO AND PUBLIC MARKETS** 

#### Adaptimmune

Shares sold in 2015.

#### **Aerie Pharmaceuticals**

Shares sold in 2015.

#### Akebia Therapeutics

Shares sold in 2015

#### Alder Biopharmaceuticals

Shares sold in 2015.

#### Arpida

Shares sold.

#### Flexion Therapeutics

Shares sold in 2015.

#### Intersect ENT

Shares sold in 2015.

#### Nevro

Shares sold in 2015.

**Otonomy** Shares sold in 2015.

#### **Panacos Pharmaceuticals**

#### PTC Therapeutics Shares sold.

#### **Tetraphase Pharmaceuticals**

Shares sold.

#### ZS Pharma

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# NOVO VENTURES INVESTS IN A EUROPEAN BIOPHARMACEUTICAL COMPANY. MERUS: BOOSTING NATURAL ANTIBODIES.

Bispecific antibodies are expected to play a key role in cancer immuno-therapy treatments in the future. The Dutch biotech, Merus is a leading player in this field, developing innovative bispecific antibody therapeutics to treat – and potentially cure – cancer patients.

**erus** is a clinical-stage immuno-oncology company that specialises in the development of bispecific antibodies for oncology. Its lead programme has entered clinical trials in solid tumours, and the second programme is getting ready to enter clinical trials in 2016 for the treatment of acute myeloid leukaemia.

#### **BISPECIFIC ANTIBODIES**

Natural monoclonal antibodies are symmetric and monospecific, i.e. both arms of the antibody bind to the same target. Merus' bispecific human antibodies have been modified to bind to two different targets to enable novel and more potent modes of action.

Bispecific antibodies can be designed to simultaneously block multiple receptors that drive tumour cell growth and survival. This approach has been used for the design of MCLA-128, Merus' HER2xHER3 bispecific antibody, which is in phase I/II clinical testing for the treatment of patients with HER2-expressing solid tumours.

In another approach, bispecific antibodies can be used to mobilise the patient's immune response by activating various killer cells to eradicate tumours. Micromet was the first company to truly advance this concept into clinical proof of concept, and their lead programme, blinatumomab was approved by the FDA in December 2014 for the treatment of acute lymphoblastic leukaemia. However, the problem with blinatumomab is that it is composed of antibody fragments and has a very short half-life of two hours.

Several other biotech and pharma companies are working on other bispecific formats with a view to improving half-life, reducing immunogenicity, and ensuring good manufacturability, high stability and tuneable immune activation. Merus is leading this field with Biclonics®, the first bispecific antibody format to represent a normal full-length human IgG antibody and meet all the desired attributes at the same time.

#### **BISPECIFIC ANTIBODY TREATMENT OF AML**

One of Merus' very promising programmes focuses on the treatment of patients with acute myeloid leukaemia (AML).

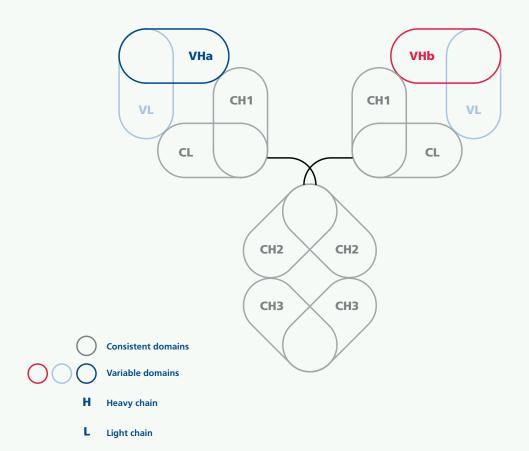
AML is a cancer of the myeloid line of blood cells, characterised by the rapid growth of abnormal white blood cells that accumulate in the bone marrow and interfere with the production of normal blood cells. As an acute leukaemia, AML progresses rapidly and is typically fatal within months if left untreated. Cause of death is often related to infections.

Merus' bispecific antibody, MCLA-117 could potentially treat more than 90 per cent of AML patients. MCLA-117 binds to two different targets: CLEC12A, whose expression is restricted to myeloid cells present in peripheral blood and bone marrow; and CD3, which is expressed on T cells. MCLA-117 brings the T cells in close proximity to the cancer cell to facilitate tumour cell killing. Pre-clinical data on patient tumour samples show impressive kill efficacy, while the bispecific antibody does not harm other cell types in vitro.

#### **MANY COMPLEMENTARY TECHNOLOGIES**

Merus uses its proprietary transgenic mouse, MeMo® and stateof-the art phage display libraries of human Fab fragments for the generation of panels of common light chain antibodies. Large and diverse panels of high affinity antibodies have been generated against a broad variety of targets.

- The MeMo® mouse. This technology has a knock-in of single human VL gene incapable of undergoing somatic hypermutation, and a knock-in of human VH locus capable of rearrangements and somatic hypermutation. The mouse also has a knock-out of endogenous murine immunoglobulin heavy and light chain loci. This results in the MeMo® mice generating high affinity, fully human mAbs encoded by the germline VL and a somatically mutated VH.
- Biclonics® high-throughput functional screening. The
  panels of target-specific human common light chain
  antibodies are introduced as pairs of DNA constructs into
  cells. The common light chain format and engineered
  CH3 domains of the antibody constant region ensure the
  secretion of essentially pure Biclonics® into the cell culture
  medium. The medium of thousands of cell cultures is
  harvested and used for rapid screening in cell- and tissuebased functional assays.



Human Bioclonics® The bispecific format with same light chain and different heavy chains. In the CH3 region, two specific mutations give electrostatic repulsion/attraction between the different backbones to ensure hetero-dimerisation.

#### A FIELD WITH GREAT PROMISE

In recent years, various cancer immunotherapy approaches have shown impressive clinical benefits to patients. Bispecific antibodies are poised to play an important role in cancer immuno-therapy since they hold the promise of effectively redirecting a patient's immune response to specific tumour cells with the convenience of easy to use 'off-the-shelf' antibody products.

To carry out its long-term vision, Merus requires a strong and committed financial base. This year, Sofinnova Ventures and Novo co-led the company's EUR 72.8 million Series C round to finance advancement into human clinical studies.

#### **FAST FACTS ON MERUS**

Privately held company

Number of employees: 36

Located in Utrecht, Netherlands

Raised Euro 100 million in VC and public financing. Novo led the Series C round of Euro 73 million.

# **IRHYTHM – A SILICON VALLEY MEDICAL DEVICE COMPANY. A GAME CHANGER IN CARDIAC CARE.**

iRhythm is setting a new standard in cardiac care. The company's innovative heart monitoring technology allows doctors to detect and diagnose cardiac arrhythmias far more effectively. This will help to significantly reduce the morbidity and mortality associated with these conditions.

ounded in 2006 based on technology and research from the Stanford Biodesign group, iRhythm Technologies in California developed the ZIO® XT Service – a long-term, continuous ECG monitoring service that detects cardiac arrhythmias. The ZIO® XT Service received FDA approval in 2009.

Cardiac arrhythmias are remarkably common. In fact, it is estimated that approximately 25 million patients in the US suffer from cardiac symptoms such as palpitations, dizziness, shortness of breath, etc. Since they are often passing and asymptomatic, these symptoms often go undiagnosed.

To identify whether a patient may have an arrhythmia, physicians commonly prescribe heart monitors, which are worn by the patient and continuously record the electrical heart trace (ECG) over a period of time. Recent studies have shown that a physician's ability to diagnose an arrhythmia increases when a heart monitor is worn between 48 hours and seven days, with optimal results achieved between seven and 10 days of wear. The most common heart monitor, the Holter, has been in use for more than 30 years. Due to its bulky profile, it is typically only worn for one or two days.

#### THE ZIO® XT SERVICE

The ZIO® Service is an easy-to-use and cost-effective alternative to a Holter monitor, event monitors, and other ambulatory monitoring technologies currently used to evaluate patients with suspected arrhythmias.

Fig. 1
The ZIO® Patch is a compact,
lightweight, single use,
FDA-cleared device.

The ZIO® XT Service includes:

- ZIO® Patch: A compact, lightweight, single use, FDAcleared device that is attached to the skin over the chest, providing continuous ambulatory cardiac monitoring for up to 14 days.
- Proprietary Algorithms: Proprietary software to identify arrhythmias from data downloaded from the Patch.
- ZIO® Report: A comprehensive and easy-to-read summary of the findings, based on both the proprietary algorithms and an analysis performed by certified ECG technicians.

Unlike common heart monitors – which are typically bulky, may have wires, and can interfere with daily activities – the ZIO® XT Patch is:

- discrete;
- water-resistant which means it can be worn in the shower); and
- small and lightweight which makes it easy for users to wear while they sleep or perform moderate exercise.

The ZIO® Patch continuously records heartbeats for up to 14 days. When finished, the patient simply mails the monitor to iRhythm in a pre-addressed, postage-paid envelope. Proprietary algorithms then analyse the entire data file to identify ECG waveforms of interest. The report (fig. 2) is structured to help the referring physician rule in or rule out the presence of arrhythmias. This enables timely and more accurate treatment, and ultimately improves patient outcomes and reduces healthcare costs.

The ZIO® XT Patch is not only designed to make patient compliance far easier, but being a small, single-use device, it is also ideal for use in cardiology offices, primary care offices and emergency rooms.

#### **HIGH QUALITY RESULTS**

The ZIO® XT Service is the only long-term, continuous cardiac monitoring option that is proven in multiple, peer-reviewed publications to produce a higher diagnostic yield and change patient management – sooner in the diagnostic pathway – compared to traditional approaches.

iRhythm's data warehouse is the largest ECG database in the world, containing over 51 million hours (that is 5,400 years!) of continuous ECG recordings. The company uses

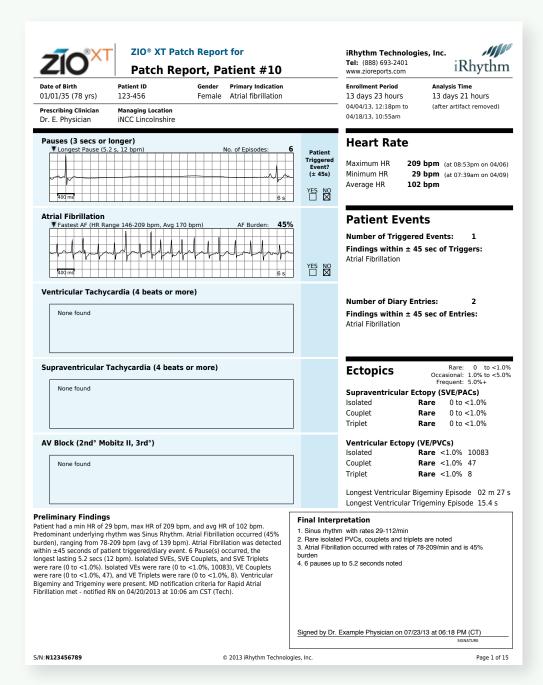


Fig. 2

The ZIO<sup>®</sup> XT Patch Report is a comprehensive easy to read summary of findings based on an analysis performed by ECG technicians.

this data to refine and enhance its algorithms, therefore providing the highest quality results, unmatched by any other cardiac monitoring service.

With the financial support of a strong investor base including Novo A/S, iRhythm has experienced 70 per cent growth in its revenues in the last year, with more than 400,000 patches sold since approval.

#### **FAST FACTS ON IRHYTHM**

#### Privately held company

Number of employees: Approximately 300 – the company continues to expand its sales force to enable growth.

Located in San Francisco, CA

Raised nearly \$100 million in equity from private investors. Novo led the company's Series E round.

# NOVO SEEDS

Creating companies from innovative Nordic life science

## INVESTING IN EARLY-STAGE LIFE SCIENCE

N ovo Seeds builds innovative Nordic biotech companies through early-stage investment. In close collaboration with leading researchers, academic institutions, entrepreneurs and leaders in the biotech industry, we help promising life science develop its commercial potential. This takes place through two programmes: pre-seed grants and seed investments.

Since 2007, we have built a pipeline of new biotech startups, developing portfolio companies towards commercialisation and success. Today, our portfolio comprises 16 active seed companies and 21 pre-seed projects, primarily from the Nordic region. These companies cover the spectrum from early-stage discovery through to clinical-stage companies.

#### AN EXCITING YEAR

In 2015, we not only saw a significant exit from our portfolio; we also took our first step into industrial biotech.

In May 2015, the flagship in Novo Seeds' portfolio, EpiTherapeutics was acquired by Gilead Sciences Inc., a major US biotech company, in a landmark deal for a Scandinavian biotech. EpiTherapeutics is based on the groundbreaking science conducted by world-leading epigenetic researcher, Professor Kristian Helin and his team at the University of Copenhagen (read more on pp. 46-47).

In April 2015, we made a seed investment in the Danish start-up, Biosyntia. The company specialises in the development of novel cell factories for the production of biomolecules by fermentation.

#### **SEED INVESTMENTS**

The most promising early-stage biotech companies based on advanced research are developed and financed through seed investments. While capital is a critical element, active involvement in building the team, selecting leading experts as advisors, and defining the milestones for the company

development plan, are equally important. Through our hands-on approach to seed investing, we aim to transform innovative science into products that address unmet healthcare needs and improve quality of life.

Novo Seeds has created a strong pipeline of early-stage biotech companies within drug development, medical devices and, as of 2015, industrial biotech. 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 collaboration not only brings additional capital; it also gives access to talent and networks, which is a critical success factor. Significant investment rounds represent an important validation of a biotech company. In 2015, Novo Seeds attracted more than a 2-1 ratio of co-investment in our portfolio companies.

#### **PRE-SEED GRANTS**

One way in which we identify and develop new biotech 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, state-of-the-art academic research projects with promising commercial potential.

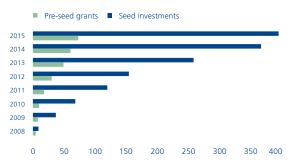
We work closely with each project to help them grow and draw on external experts and entrepreneurs who can contribute commercial experience and strategic directions to the individual projects. In this way, we begin to set the team for a future spinout company, and provide each project with the best conditions to develop into attractive seed investments.

Promising companies have already emerged from the preseed grant programme – with Galecto Biotech, Pcovery and Orphazyme as prominent examples. Today, Galecto Biotech and Pcovery are active Novo Seeds portfolio companies and have attracted strong investor syndicates with international participation.





#### ACCUMULATED COST OF PRE-SEED GRANTS AND INVESTMENTS (AS OF 31.12.15)



# ACTIVE SEED COMPANIES AND PRE-SEED PROJECTS

Forendo Pharma Seed companies O Pre-seed projects Denator **Galecto Biotech** Glionova **RSPR Pharma** ApoA-I derived peptides Pluvia 🔘 Biopetrolia Zinchel Metabogen **Acesion Pharma** Adenium Biotech Affinicon **BioProtect Avilex Pharma** DARE Biosyntia Diacure IO Biotech GlyProVac MinervaX **Immunitrack** Pcovery MAP1 miRana Reapplix MonTa **NMD Pharma RSK Inhibitors** Zentrix Lysogene 0 Inthera Bioscience 0

#### **ACHIEVEMENTS IN PORTFOLIO COMPANIES IN 2015**

**Biosyntia** closed a DKK 12.5 million financing round with Novo Seeds as lead investor. Biosyntia is one of the region's emerging start-ups. The company aims to deliver sustainable and biobased solutions, drawing on the extensive commercial experience and strong research based in Denmark.

**Galecto Biotech** started a phase 2a clinical trial for TD139 treatment of patients with idiopathic pulmonary fibrosis in the UK. The company expects to complete this study during 2016.

MinervaX observed strong antibody responses and good tolerability in the company's on-going phase 1 clinical study of a vaccine against invasive Group B strentococcus.

**IO Biotech** tested the new and improved version of the company's IDO-targeted vaccine approach in melanoma cancer patients.

RSPR Pharma completed their first clinical proof-of-concept studies.

#### **NEW PRE-SEED GRANTS IN 2015**

**ApoA-I** is exploring how to characterise short peptides and how to assess their potential as novel therapeutic agents.

**BioProtect** is developing cell factories for production of biocides by fermentation.

AA project JAK2 PeptiCRAd

**DARE** project has identified and investigated a novel target for the treatment of wet (advanced) AMD, microfibrillar-associated protein 4 (MFAP4).

**Diacure** is developing autologous stem cells for the treatment of type 1 diabetes.

**PeptiCRAd** has developed a novel technology for enhancing efficacy of oncolytic virotherapies.

**Zinchel** focuses on the development and characterisation of novel inhibitors of Metallo-Beta-Lactamases (MBLs).

#### **NOVO SEEDS INVESTMENTS AND PORTFOLIO 2015**

#### **PORTFOLIO**



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

#### affinicon

Affinicon ApS develops antibody-drug conjugate technology that targets macrophages for the treatment of inflammatory diseases and other indications where macrophages are involved (e.g. cancer). www.affinicon.com



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

#### denator

Denator AB develops, markets and sells instruments that help scientists stabilise biological samples, such as tissue sections or biopsies, from the moment of sampling www.denator.com



Forendo Pharma Ltd develops drugs for tissuespecific regulation of sex hormone effects. www.forendo.com

#### Galecto Biotech

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



Glionova AB is developing a small molecule drug for the treatment of glioblastoma multiforme, the most common and aggressive primary brain cancer. www.glionova.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/

#### **IYSOFNE**

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.lvsogene.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



Pcovery ApS develops first-in-class drugs for treatment of invasive fungal infections by targeting an essential and highly conserved component of the fungal cell membrane. www.pcovery.com



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



RSPR Pharma develops new medical approaches for the treatment of respiratory diseases, including early-onset allergic asthma. http://www.rsprpharma.com/

#### **NEW INVESTMENTS**



Biosvntia is a biotech start-up within synthetic biology and metabolic engineering. The company develops biocatalysts at an unprecedented speed and efficiency by employing a patent pending highthroughput screening technology. httn://biosvntia.com/



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

#### **EXIT**



**EpiTherapeutics ApS** develops novel innovative cancer drugs based on world-leading research in epigenetics. In 2015, the company was acquired by

www.epitherapeutics.com.

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# **EXIT EPITHERAPEUTICS**

In May 2015, one of the flagships in the Novo Seeds portfolio was acquired by one of the world's leading biopharmaceuticals in an important deal for a Scandinavian biotech. The development and exit of EpiTherapeutics is a best-case example of how Novo Seeds has helped realise the commercial potential of pioneering research.

piTherapeutics ApS was founded in September 2008 with Novo Seeds as the lead investor. The company was established based on seminal research conducted into the emerging field of epigenetics by Professor Kristian Helin and his team of scientists at the Biotech Research & Innovation Centre (BRIC), University of Copenhagen. The Helin group is one of the world's leading research teams within epigenetics.

Epigenetic targets are expected to offer new treatment options for a range of diseases, including cancer, inflammation and other debilitating conditions. In 2008, EpiTherapeutics set out to develop new drugs targeting specific epigenetic enzymes – the so-called histone demethylases.

#### FROM EARLY DISCOVERY TO SUCCESSFUL EXIT

Over the years, the talented team at EpiTherapeutics has skilfully converted their early scientific discoveries into solid drug development programmes and pre-clinical drug candidates. The results were so successful that the company's programmes and technology platform attracted the attention of Gilead Sciences Inc., an innovative and fast-growing biopharmaceutical company in California. Recognising the potential of EpiTherapeutics' pioneering work, Gilead put in a bid for the company. And in May 2015, the company acquired EpiTherapeutics for DKK 444 million.

Commenting on the acquisition, CEO of EpiTherapeutics, Martin Bonde explains: "I am very proud to be heading a team that has managed to transform ground-breaking research into a technology platform, and further translate this into a drug candidate that has attracted the attention of one of the world's leading biotech companies. We are confident that with Gilead's acquisition, our discoveries will have the best chance of developing into therapies that will benefit patients."

#### **BRINGING INNOVATIVE SCIENCE TO MARKET**

Martin Bonde is not the only one who is proud of EpiTherapeutics' progress. According to Søren Møller, Managing Investment Director at Novo Seeds, the sale of EpiTherapeutics captures the essence of what Novo Seeds works to achieve. "Working closely with world-class scientists and entrepreneurs, Novo Seeds was instrumental in launching EpiTherapeutics," says Søren Møller. "We helped put the management team and the board together, led the syndication efforts and the funding of the company, and finally, facilitated the trade sale to one of the world's leading biotechs. On top of all this, we generated an attractive return on our investment."

EpiTherapeutics illustrates how pioneering research, entrepreneurship and venture capital come together to create new jobs, financial returns and potentially new treatments for patients. We are positive that success stories such as this will influence further entrepreneurship and investments in the future, and strengthen a growing, successful life science industry in the Nordic region.

#### FAST FACTS ON EPIGENETICS AND EPITHERAPEUTICS' DISCOVERIES

The seminal epigenetic research conducted by Professor Kristian Helin and his team at BRIC, Copenhagen has led to an understanding of how normal cell biology is regulated and, by the same token, what goes wrong in cancer cells.

Professor Helin's discovery of a new protein family provided a unique opportunity to connect the basic research conducted into cancer with the development of pharmaceuticals. EpiTherapeutics' research could lead to important advances in the treatment of cancer and other serious illnesses.



# A SEED INVESTMENT IN MINERVAX

Group B streptococcal infection represents 50 per cent of life-threatening infections in newborns worldwide. There is an urgent need for an effective vaccine that can prevent these infections. Copenhagen-based biotech, MinervaX is addressing this need. And Novo Seeds is on board as leading investor.

The Danish biotech company, MinervaX is developing a vaccine for the prevention of infection with Group B Streptococcus (GBS), a Gram-positive bacterium that causes lethal infections or critical illness in newborns. These GBS infections occur as a result of mother-to-child transmission or from environmental sources.

The introduction of screening for GBS during pregnancy, as well as extensive use of antibiotics during labour, has greatly reduced the incidence of GBS infections. However, despite these efforts, GBS infection still remains a significant unmet need. An estimated 15 to 20 per cent of women carry GBS and run the risk of transmitting the infection to their unborn child – in the womb, during birth, or during the first months of the baby's life.

#### **SUCCESSFUL CLINICAL TESTING**

MinervaX was founded in 2010, based on research into GBS immunology at Lund University. At the end of 2013, Novo Seeds led the investment in MinervaX, supported by Sunstone Capital and Lauritzen Fonden. In addition, MinervaX received a grant from the European Commission's 7th Framework Programme (FP7), as part of a consortium of academic and SME partners, to fund clinical testing of the GBS vaccine.

These investments allowed MinervaX to start clinical testing in 240 healthy volunteers in the summer of 2015. The phase 1 trial represents a significant milestone for the company towards achieving clinical proof of concept by late 2016.

"We have excellent data for the vaccine in mice," explains Per Fischer, D.Phil. and CEO of MinervaX. "So we know that the vaccine works conceptually and protects against GBS infections, and we're expecting a high effect on immune response. By vaccinating with an antigen, we can measure how strong the immune response is, and thereby determine the therapeutic effect."

The initial part of the phase 1 clinical study, conducted in healthy, non-pregnant women, has shown that the vaccine is not only safe and well tolerated; it also generates a dose-dependent increase in antibodies against the bacteria. The next part of the trial will study the vaccine in a larger group of

women, and explore how long lasting the immune response is. This is important to know in order to determine when the vaccine should be administered, to give the baby the best protection during the critical time before and after birth.

Nanna Lüneborg, Investment Director in Novo Seeds, is impressed by MinervaX' progress – particularly that they've managed to take their vaccine candidate to the point of clinical testing already. "It's an enormous credit to the team to have developed the project, which started out as academic research at Lund University, to a point where it can be tested in humans. This vaccine has the potential to dramatically reduce the disease burden from GBS infection, and it's going to be really exciting to see the results from the trial next year."

#### **VACCINE IS KEY**

MinervaX is not alone in trying to develop a GBS vaccine. But Per Fisher is unfazed by the competition. "MinervaX's technology is superior and likely to cover a higher percentage of bacterial strains than the other vaccines in development. Our vaccine candidate is based on an innovative fusion protein, which induces a strong protective immune response against GBS infections."

Vaccination of pregnant women is a controversial issue, but the MinervaX team is convinced that it is the best way to address the disease burden of GBS infections.

The current practice of using widespread, broadspectrum antibiotics will eventually lead to the emergence of resistant strains of GBS, which will significantly impair the effectiveness of current preventive strategies and treatment options in the remaining GBS infections. That's why Per Fischer believes that all pregnant women should be vaccinated to prevent serious disabilities, and, in worse cases, death among infected newborns.

#### **FAST FACTS ON GROUP B STREPTOCOCCUS (GBS)**

GBS infection in the unborn child may lead to premature delivery or stillbirth, and GBS infection in the newborn child may result in sepsis, pneumonia or meningitis, all of which carry a significant risk of severe morbidity, long-term disability or death.

Annually, GBS is responsible for some 8,000 infections in newborns, 800 deaths and 1,000 life-long disabilities in Europe and US.



"We have excellent data for the vaccine in mice. So we know that the vaccine works conceptually and protects against GBS infections, and we're expecting a high effect on immune response. By vaccinating with an antigen, we can measure how strong the immune response is, and thereby determine the therapeutic effect."

Per Fischer, D.Phil. and CEO of MinervaX.



# NOVO FINANCE

Diversifying risk and generating long-term, attractive returns

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### CONTINUED PERFORMANCE ABOVE BENCHMARKS

or the fourth consecutive year, Novo's financial investments have yielded great results. The total return was DKK 2.9 billion, corresponding to a return of 10.5%.

Since the introduction of the current investment strategy 11 years ago, the portfolio has delivered a pro anno return of 7.8%. This should be compared to a benchmark return over the same time period of 4.9% per annum, corresponding to a yearly outperformance of 2.9% for the entire portfolio, equivalent to an excess return of DKK 5.3 billion. Since the financial crisis in 2008/2009, the portfolio has yielded an accumulated return of more than DKK 11.6 billion, equalling a pro anno return of 10.0%.

During 2015, the value of the financial portfolio increased by DKK 3.7 billion, of which DKK 0.8 billion were new inflows and DKK 2.9 billion were price appreciation of the portfolio.

As of 1 January 2015, we increased our strategic allocation to listed equities and credits and lowered our allocation to short-term bonds. Consequently, the majority of inflows were invested in listed equities and credit-related investments, while allocation to short-term bonds was reduced.

In the next three to five years, we expect portfolio returns to be somewhat lower than they have been over the past seven years. This is based on our assessment of the current valuation of the global equity markets – which we find high relative to its fundamentals – and further supported by the current low interest rate regime. In case of a sudden increase in interest rates, we see a risk of significant correction in the global equity markets.

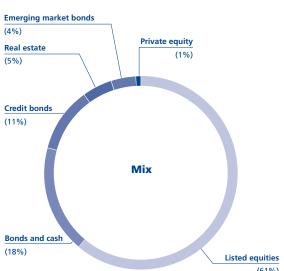
#### **OPPORTUNITIES**

2015 was the seventh consecutive year in the current bull market. The year was more volatile than we have seen in previous years. At the same time, performance in 2015 varied more. The greatest gainers were the equity markets in Europe and Japan, whereas the US equity market experienced the worst performance in 2015.

During the year, we saw a couple of macroeconomic events that triggered increased market volatility. Primarily, the uncertainty about the first interest rate hike from the Fed, and the whole issue about the economic slowdown in China.

The Fed was caught in the dilemma of when to raise interest rates. The market worried that increasing rates would have a negative impact on the equity market and the economic upswing. On the other hand, the Fed has to start increasing rates at some point. The economies in the US and EU are growing at a decent pace, creating new jobs and income growth, which, at the end of the day, is what is needed to stimulate consumption growth. On the other

#### MIX OF FINANCIAL INVESTMENTS



#### **EQUITY PORTFOLIO 2014**



hand, we are still seeing low inflation rates, which make central banks reluctant to raise rates, and the first interest rate hike was postponed until December.

The growth rate of the Chinese economy has been declining for some time. When China made a minor depreciation of the CNY against the USD to mitigate the slowdown in GDP growth, the financial market got really nervous. The Chinese economy is currently growing at its slowest pace in more than a decade. Since the growth of the Chinese economy is very commodity intensive, its slow pace has a negative impact on most commodity-producing countries.

As investors and capital allocators, we do not try to predict economic growth rates or market movements. Instead, we try to find companies that we understand and are able to analyse. If the company is cheap, based on conservative underwriting assumptions, we may invest in it. If it is not cheap enough, we will wait for market corrections and look elsewhere in the meantime.

Our investment decisions in listed equities and credits are based on a bottom-up analysis of the individual investment ideas, leaving short-term bonds as the residual in the portfolio. This means that we welcome short-term market volatility, as it enables us to invest our inflow or redeploy our investments. In 2015, we expanded the scope of the financial investments to also include larger stakes in Danish companies. This has resulted in two new investments. We invested DKK 1,674 million in FLSmidth A/S and DKK 1,689 million in Dades A/S. FLSmidth supplies the global minerals and cement industries with everything from engineering, single machines and complete processing plants to maintenance, support services and operation of processing facilities. Dades is a large Danish private real estate company that specialises in commercial real estate within office and shopping centres.

In the coming years, we will continue to be open to larger direct investments in the finance portfolio should such opportunities occur.

#### SIGNIFICANT OVERALL RETURNS

Looking back on 2015, we are satisfied with our overall returns – particularly the amount generated by our equity portfolio. Once again, our managers have done a great job. Eight out of 12 equity managers outperformed their respective benchmarks. Five out of six credit managers outperformed the relevant benchmark, including the portfolio managed in-house.

Despite the turmoil on the Chinese stock market and the generally poor performance on many Asian stock markets, our Asian equity managers did particularly well, with an outperformance of 15% compared to MSCI Asia. Besides Asia, several of our managers with a concentrated portfolio have delivered extraordinary performances in 2015.

By the end of the year, the S&P 500 Index was up 1.4% and the MSCI World Index by 10.6% compared to 2014. The Danish stock market, measured by OMXC20, was up by

40.2% during the same period. In December 2015, the US stock market was trading at a cyclically adjusted price/earnings ratio of 24.5 compared to a long-term average of 20.3.

The European bond yields continued their declining trend, with the 10-year German treasury rate hitting a new all-time low at 0.07bp in April and the two-year German treasury rate hitting a negative rate of 0.32bp in Q4. The US treasury rates were more stable throughout the year.

In general, the credit spread widened in 2015. The level of credit spreads for corporate credits is currently above the long-term average, whereas the spread for emerging market debt is closer to the levels before the financial crisis. Considering the low underlying yield, the all-in yield is still well below the long-term average for both credit classes.

# DEVELOPMENT IN THE VALUE OF FINANCIAL INVESTMENTS DKK billion 2015 2014 2012 2013 2012 2010 2009 2008 2007 2006 2008 2007 2006 2009 2001 1 0 10 20 30 40

#### ASSET MANAGEMENT AND BENCHMARKS

Novo's financial investments are managed both in-house and externally through portfolio managers. We carefully select the people we work with, as we wish to build long-term relationships with them. Our portfolio managers must have:

- a coherent and well-defined investment strategy that has proven successful over a number of years;
- a business-oriented investment approach with a longterm investment horizon;
- a passion for investments and a high level of professional integrity;
- a large part of their private wealth invested alongside Novo's;
- a limited amount of assets under management; and
- a fair fee structure.

By the end of 2015, our investments in equities were split between 12 active external managers in a mix of global, regional and country-specific mandates. In addition to the active managers, we have a portfolio of index mandates. By the end of the year, the global equity mandates amounted to

DKK 11.3 billion, while region or country-specific mandates amounted to DKK 3.5 billion. The index mandates totalled DKK 4.4 billion.

Our Danish bond portfolio consists mostly of short-dated covered bonds, and is managed in-house. By 31 December 2015, the bond portfolio and fixed-term deposits amounted to DKK 6.7 billion.

Novo's portfolio of credit-related investments consists of six separate mandates. One is managed in-house while five are externally managed. By the end of the year, the total amounted to DKK 5.6 billion; out of this total, the internal mandate was responsible for DKK 1.2 billion.

Novo's investment performance is evaluated against a number of benchmarks. We use the MSCI World Index to evaluate listed equities; Danish bonds are measured against the EFFAS 1-3 Index; and the Merrill Lynch Global High Yield Index is used as the benchmark for credit. We use the J.P. Morgan Emerging Market Bond Index to evaluate our performance for emerging market debt.

#### **ILLIQUID INVESTMENTS**

Novo has invested a minor percentage of its financial investments in illiquid assets. We have an opportunistic, value-driven approach to our illiquid financial investments. This means that we will mainly be allocating funds to this area if we see an investment opportunity that is not accessible through a liquid security. Such an opportunity occurred in 2015, when Novo bought a significant stake in the private real estate company, Dades A/S for DKK 1.7 billion.

Besides Dades, our illiquid financial investments consist of investments in private equity and real estate funds. Within private equity, we have invested DKK 947 million out of a total commitment of DKK 1,070 million. Within real estate, we have invested DKK 393 million out of a total commitment of DKK 472 million.

#### **RETURNS**

Novo's portfolio of financial investments outperformed the relevant benchmarks in 2015. This year, the return on the portfolio was 10.5%, against a weighted benchmark return of 6.7%. Since 2005, when Novo expanded the scope of its financial investments, the annual average return has been 7.8% against an annual benchmark return of 4.9% over the same period.

Novo's portfolio has performed better than the benchmark portfolio, mainly because our portfolio managers have performed better than their respective benchmarks – despite a risk profile that was lower than benchmark. The lower risk is explained by a periodical underweight in listed equities and an overweight in government and mortgage bonds. Moreover, the dividends from Novo Nordisk and Novozymes, as well as revenue from the sale of Novozymes B shares, have been invested at a gradual pace. This has contributed to an average underweight in shares.



ANNUAL REVIEW 2015

# NOVO NORDISK FOUNDATION AND THE NOVO GROUP

#### novo nordisk fonden

he Novo Nordisk Foundation is an independent Danish foundation that dates back to the 1920s.

The objectives of the Foundation are:

- to provide a stable basis for the commercial and research activities conducted by the companies in the Novo Group;
- to support scientific, humanitarian and social purposes.

Through its activities, the Foundation aims to promote worldclass research and innovation in medical, biotechnological and natural sciences and help to foster an education system of international standard.

The Foundation also aims to help develop a knowledge-based society that contributes to long-term economic activity and job creation for improved health and welfare, with Denmark as the Foundation's centre of gravity.

The ambition is that the Foundation's grants facilitate the emergence of new and pioneering research and help to create dynamic international research environments that can attract and retain the very best researchers.

By generating research-based products and services it is the Foundation's ambition that the Novo Group companies will position themselves as internationally recognized actors in the combatting of diseases and the more intelligent use of natural resources.

The Foundation finances its activities primarily through dividends from Novo A/S, which administers the assets of the Foundation.

#### SUPPORTING INDEPENDENT RESEARCH

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

The Board of the Foundation specifies the grant areas, grant types and the financial terms for funding. Within this framework, the Foundation ensures that each project application is assessed by independent research experts before a grant decision is made.

All grants awarded by the Foundation support free and independent research. The researchers decide their own research priorities; they can publish as they wish, and the IPR belongs to the public research institutions.

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.

#### **MAJOR GRANTS**

Since 2007, the Foundation has donated close to DKK 7 billion (€922 million) primarily for research purposes.

These grants include DKK 3.5 billion to establish and develop the Novo Nordisk Foundation's research centre cluster, which comprises a national biobank and four major research centres within the fields of stem cells, proteins, metabolism and biosustainability at universities or public knowledge institutions in the Greater Copenhagen area.

In 2015, the Foundation also announced its plan to award up to DKK 2.8 billion for the Steno Diabetes Center Copenhagen – a major new diabetes center which will be an international driving force for treatment of, and clinical research into diabetes.

#### **SELECTED GRANT ACTIVITIES 2015**

In 2015, the Novo Nordisk Foundation has awarded grants totaling DKK 1,159 million, including:

- DKK 235 million to strengthen and expand the activities of the Novo Nordisk Foundation Section for Basic Stem Cell Biology.
- DKK 572 million for individual research projects and scholar-/fellowships, awarded in open competition through the Foundation's expert committees, including DKK 120 million for the Novo Nordisk Foundation Challenge Programme which this year addresses microbiome research, and DKK 10 million for exploratory pre-seed grants.
- DKK 80 million for research into immunometabolism.
- DKK 25 million to pre-seed projects (in collaboration with Novo Seeds).
- DKK 20 million for an international mentor network to help develop promising early-stage commercialisation projects.
- DKK 7.6 million to art-related research.
- DKK 7 million for humanitarian and social causes.

The Foundation's total pay-out amounted to DKK 914 million in 2015.

For more information, please visit www.novonordiskfonden.dk



ovo Nordisk 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 key contribution is to discover and develop innovative biological medicines and make them available to patients throughout the world. This purpose is stated in the Novo Nordisk Way, which describes the ambitions and the values that characterise the company. The Novo Nordisk Way also emphasises the importance of accounting for financial, social and environmental performance in accordance with the Triple Bottom Line principle that is anchored in the company's Articles of Association.

#### FINANCIAL PERFORMANCE

In 2015, Novo Nordisk achieved its four long-term financial targets established in January 2013 and consequently, the Board of Directors has approved three updated long-term financial targets to guide Novo Nordisk's performance.

Novo Nordisk's 2015 performance on operating profit and free cash flow slightly exceeded the outlook for the year provided in the latest guidance from October.

Sales increased by 8% measured in local currencies and by 22 % in Danish kroner to 107.9 billion. Operating profit increased by 43% in Danish kroner to DKK 49.4 billion. In local currencies the growth was 21%.

Sales of diabetes and obesity care products increased by 22% measured in Danish kroner and by 9% in local currencies to DKK 85,590 million. Novo Nordisk is the world leader in diabetes care and holds a global value market share of 28% compared to 27% at the same time last year.

Sales of biopharmaceutical products increased by 19% measured in Danish kroner and by 6% in local currencies to DKK 22,337 million.

#### **R&D PROGRESS**

In March 2015, Novo Nordisk decided to resubmit New Drug Applications (NDA) of Tresiba® and Ryzodeg® 70/30 in the US. The resubmission was based on the interim analysis of the cardiovascular outcomes trial for Tresiba®, DEVOTE. In order to preserve the integrity of the ongoing DEVOTE trial, only a small team within Novo Nordisk had access to the data and made the decision to resubmit the NDA. Novo Nordisk management does not have access to the results of the interim analysis. The DEVOTE trial is expected to be

completed in mid-2016 and the results are expected to be announced in the second half of 2016.

The US Food and Drug Administration (FDA) approved Tresiba® and Ryzodeg® 70/30 for the treatment of diabetes in adults in September 2015. Following the approval, Tresiba® was introduced to diabetes care specialists in the US during November 2015 and was launched broadly in January 2016.

In August, Novo Nordisk decided to initiate a phase 3a programme with oral semaglutide; a once-daily oral formulation of the long-acting GLP-1 analogue semaglutide. The decision followed the encouraging results of the proof-of-concept phase 2 trial announced in February 2015 and the subsequent consultations with regulatory authorities. In January 2016, Novo Nordisk submitted the Marketing Authorisation Application (MAA) to the European Medicines Agency (EMA) for the approval of long-acting factor IX, nonacog beta pegol.

#### **THE PATIENT TARGET: 40BY20**

As part of Novo Nordisk's strategy for global access to diabetes care, the company has set a long-term target to reach 40 million people in 2020 with its diabetes care products, a doubling from the baseline number in 2010. The aim is to enable more people with diabetes to receive medical treatment. In 2014, Novo Nordisk provided medical treatments to an estimated 26.8 million patients with diabetes worldwide, compared with 24.4 million in 2014.

For more information, please visit Novo Nordisk's Annual Report 2015 at www.novonordisk.com/annualreport



N ovozymes is the world 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, food and beverages, biopharma, leather, pulp and paper, textiles and wastewater.

To deliver on its purpose to find biological answers for better lives in a growing world, Novozymes applies and delivers new innovation to the market, and launches new platforms that have an impact and create value for customers – improving performance, while saving energy and generating less waste.

#### 2015: STRONG EARNINGS, BUT MODERATE SALES GROWTH

In 2015, Novozymes delivered double-digit growth in earnings and a substantial improvement in the EBIT margin, but only moderate sales growth. The long-term organic sales growth target has been revised to reflect the negative impact on sales growth of the uncertainties stemming from lower commodity prices and slower economic growth in emerging markets.

Total sales in 2015 were DKK 14,002 million. Sales grew by 4% organically and by 12% in Danish kroner. Sales to the agriculture & feed and food & beverage industries were the most significant contributors to organic sales growth in the period. EBIT grew by 15%, and the EBIT margin was 27.7%. Net profit grew by 12%.

Novozymes reached 11 of its 13 sustainability targets in 2015. Notably, Novozymes succeeded in improving its energy and  $\mathrm{CO}_2$  efficiency, whereas the rate of occupational accidents increased to 2.5 accidents with absence per million working hours. This remains a focus area for improvement at Novozymes.

#### **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 with 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 GOOD 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. Novozymes' focus on sustainability also provides a competitive advantage as more customers look for sustainability as a differentiator.

In 2015, the worldwide application of Novozymes' products helped its customers avoid an estimated 60 million tons of  $\mathrm{CO}_2$  emissions, the equivalent of taking approximately 25 million cars off the road.

For more information, please visit Novozymes' Annual Report 2015 at www.report2015.novozymes.com

#### **NNIT**

NIT is one of Denmark's leading IT service providers and consultancies. NNIT offers a wide range of IT services and solutions to its customers, primarily in the life sciences sector in Denmark and internationally, and to Danish customers in the public, enterprise and finance sectors. The company is a wall-to-wall provider, delivering services within all categories: advisory services, business solutions, application outsourcing and infrastructure outsourcing and support.

#### **2015 FINANCIAL RESULTS**

In NNIT's first year as a listed company, the company delivered organic revenue growth of 7.9% to DKK 2,600 million and an operating profit margin of 10.3% despite a competitive market. The results exceed NNIT's long-term targets of at least 5% revenue growth and 10% operating profit margin.

#### **STRATEGY**

#### - DEDICATED TO SUSTAINABLE GROWTH

The company's main objective is to grow the revenue and market share in the IT services market in Denmark and the life sciences IT services market internationally, while maintaining or improving operating profit margins. By 2020, NNIT aspires to be:

- Denmark's preferred IT outsourcing partner
- A leading international IT partner dedicated to life sciences

In a fast-changing market with intense competition, the company must constantly focus on executing its strategy. NNIT's strategic approach towards 2020 is focused on competitiveness, delivery capacity and the global life sciences industry. NNIT continues to strengthen competitiveness by developing and implementing new services and solutions; it continues to explore and expand delivery capacity to fully meet the requirements of the customers; and it continues to leverage its extensive knowledge about the life sciences industry to fully optimize the company's potential – not only in Denmark, but more importantly internationally.

#### **KEY STRENGTHS**

As a high-quality IT services provider, NNIT competes in a global market with international competitors. Given the increasing standardisation of basic IT services, it is crucial to be able to differentiate through a focused portfolio of services.

NNIT's strong position in Denmark and internationally relies on the following key strengths:

#### TRACK RECORD

The company has a strong track record for delivering solid, organic revenue growth rates, consistently outperforming the growth of the Danish IT services market.

#### STABLE BUSINESS MODEL

NNIT's business model implies a close customer relationship combined with the company's global delivery centers and scale-driven operating leverage. NNIT has further diversified its customer base, and the long-term nature of many of the major contracts further adds to the transparency of the business.

#### PROFOUND EXPERIENCE

Coming from the pharmaceutical industry, NNIT understands and adheres to the regulatory requirements and the application landscape of the life sciences industry. This experience also allows the company to pursue other regulated industries such as finance and public, with strict focus on control and compliance.

#### INTEGRATED GLOBAL DELIVERY MODEL

The company's integrated local nearshore and offshore service delivery model enables provision of services and solutions in a comprehensive and well-managed way – with enhanced timely delivery, significant cost advantages, quality control and improved customer satisfaction, as well as overhead cost savings.

For more information, please visit NNIT's Annual Report 2015 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.

# NOVO'S CORNERSTONES - IN OUR INTERACTIONS

#### **INSIGHT**

In our interactions we strive to provide deep knowledge and innovative solutions.

#### **COMMITMENT**

In our interactions we strive to achieve groundbreaking and long-term results.

#### **PROFESSIONALISM**

In our interactions we will act in a proper manner emphasizing high integrity.

#### **TRUST**

In our interactions we emphasize building relationships based on mutual trust and respect.

#### A HIGHLY QUALIFIED TEAM

A s a life science investment company, Novo A/S depends on highly specialised expertise – both within the field of life science and in the domain of investments.

Most of our investment professionals have a background in science. Many of them have worked as researchers in the life science industry and some have PhD degrees in fields relevant to life science (e.g. Medicine, Biochemistry, etc.). Others have gained their scientific expertise through employment in research and management functions in the 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 sector.

At Novo A/S, our key goal is to add value to the life science industry. Highly qualified staff and specialised expertise in life science and investments help us to deliver on this ambition.

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 the senior executive management of large international healthcare companies or financial institutions.

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

In management and administration, all our employees are specialists within their area of responsibility. Members of our management group have extensive experience from senior executive management and board positions in some of Scandinavia's largest companies. Our employees in the administration have relevant qualifications in accounting, auditing, administration, taxation, legal affairs, HR or IT.

As one of the key players in the international life science investment industry, we have to ensure that our knowledge resources are always of an expert standard – so that we can fulfil our responsibilities towards our portfolio companies and make the right investment decisions. For this reason, continuing education 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 TEAM**



Jonas Ahm Investment Associate Large Investments



**Tiba Aynechi** Partner Novo Ventures (US) Inc.\*



Scott Beardsley Senior Partner Novo Ventures (US) Inc.\*



Peter Tuxen Bisgaard Senior Partner Novo Ventures (US) Inc.\*



**Johan Brønnum-Schou** Investment Director Finance



Raymond Camahort Associate Novo Ventures (US) Inc.\*



**Stephan Christgau** Investment Director Seeds



**Emmanuelle Coutanceau** Investment Director Seeds



**Christian Dahlfelt** Controller



**Dina Dohlmann** Personal Assistant Executive Office



**Kim L. Dueholm** Partner Ventures



**Thomas Dyrberg** Managing Partner Ventures



**Martin Edwards** Senior Partner Ventures



Aleks Engel Asset Director Large Investments



Shawnalea Frazier Associate Novo Ventures (US) Inc.\*



**Jonas Drachmann Gram** Associate General Counsel



Kenneth Harrison Associate Novo Ventures (US) Inc.\*



**Annemette Hessels**Coordinator
Seeds



**Brigid M. Hughes**Office Operations Manager
Novo Ventures (US) Inc.\*



**Kasper Sobfeldt Jahn** Business Associate Large Investments



**Sophie Jensen** Accounting Assistant



Merete Jepsen HR Coordinator People & Organisation



**Morten Beck Jørgensen** Senior Investment Director Finance



**Amy Kacprowicz** Venture Coordinator Novo Ventures (US) Inc.\*



**Jesper Kofod** HR Senior Specialist People & Organisation



**Simon Vesterby Kold** Financial Analyst Finance



Eivind Kolding CEO



Nilesh Kumar Senior Principal Novo Ventures (US) Inc.\*



**Heather Ludvigsen** Venture Auditor Ventures



**Nanna Lüneborg** Principal Ventures



Max Løwe Controller



**Dorte Barlebo Madsen** Director People & Organisation



Peter Moldt Partner Novo Ventures (US) Inc.\*



Søren Møller Managing Investment Director Seeds



**Jack Beck Nielsen** Senior Partner Ventures



**Lone Penby** Project Coordinator Large Investments



**Birgitta Ravn-Holm** Executive Assistant Executive Office



**Dorrit Ryd** IT Manager



**Jørgen Rønnow** General Counsel



**Christian Salling** Asset Director Large Investments



**Michael Shalmi** Head of Large Investments



**Eric Shiozaki** Principal Novo Ventures (US) Inc.\*



Sandra Tranbjerg Venture Coordinator Ventures



Nicole Zilveti Venture Coordinator Novo Ventures (US) Inc.\*

<sup>\*</sup> Novo Ventures (US) Inc. is a separate legal entity that provides certain consultancy services to Novo A/S, mainly within the areas of identifying, analyzing, 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.

#### **CSR IN NOVO A/S**

orporate Social Responsibility (CSR) is an integral part of Novo's value-based governance framework. The framework consists of four elements, which collectively set the direction for our company:

- Charter for Companies in the Novo Group
- Novo's Mission
- Novo's Cornerstones
- Novo's Investment Strategy

In addition to setting the overall direction for the company and its employees, this framework provides guidance in good business conduct and CSR.

The Charter describes the set of values shared by all companies in the Novo Group. Constituting the foundation for each company in the Group, the Charter acts as a professional framework for Novo Group employees. The Charter will drive the Group's long-term sustainable development and growth – and ensure its commitment to continuous improvement and reporting on financial, environmental and social performance.

Novo's Mission is to represent the economic interests of the Novo Nordisk Foundation. This includes management of the Foundation's assets, ensuring the Foundation sufficient dividends to cover its grant obligations, and maintaining our Charter for Companies in the Novo Group.

Novo's Cornerstones are Insight, Professionalism, Commitment and Trust. These values guide our interactions – internally and externally – and direct our approach to management.

Novo's Investment Strategy sets the guidelines for the allocation of financial resources to our investment areas. It also describes the investment objectives and the governance requirements for each investment area.

#### **OUR APPROACH TO CSR**

Novo has four core beliefs in CSR. Complying with Novo's Mission and the Vision of the Novo Nordisk Foundation, these beliefs describe our approach and commitment to CSR:

- Responsible use of biotechnology in its broadest sense will benefit society at large as well as Novo and its stakeholders.
- CSR is a prerequisite for sustainable success and longterm value creation.
- CSR will increase transparency, accountability and trust and thereby improve performance and reduce risk.
- CSR will benefit society at large as well as Novo and its stakeholders.

To support the governance framework and enable regular reporting and monitoring of performance, Novo has integrated CSR into its general business and investment processes. This ensures value-based governance on a day-to-day basis.

#### **REPORTING ON CSR**

For 2015, Novo has selected five CSR focus areas. The focus areas 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.

Our activities in Seeds, Ventures, and Large Investments help to translate academic life science research into viable commercial products as well as commercialising such products. In addition to our financial commitment, we are actively involved in supporting our portfolio companies in setting up and developing their businesses. As part of our CSR effort, we measure the financial performance as well as the progression of the research toward commercialisation – e.g. how many of the Novo portfolio companies' research projects have developed into marketed products.

CSR FOCUS AREAS	WHY IS THIS IMPORTANT?	POLICIES/ASPIRATIONS	ACTIVITIES	RESULTS
Responsible investment process	Novo's core business is investing. This must be conducted in a socially and environmentally responsible manner.	To be a responsible investor by incorporating CSR into our investment processes.	Integrate and document CSR as part of our investment processes.	All new investment opportunities have been screened for potential CSR issues (including bioethical and corporate governance issues).
Impact on society through investment activities	Novo's impact on society depends on how well it deploys its financial resources.	To leave a positive footprint on society.	Start new life science companies. Invest in life science companies. Pay taxes.	Novo helped start three new companies, and we invested 3,013 million in 20 new and 42 existing portfolio companies. More than 30 new drugs and devices originating from Novo portfolio companies are on the market.  The Novo Group paid company tax amounting to DKK 6 billion in Denmark.
Reputation	Reputation is of the utmost importance to Novo. It has an impact on all Novo Group companies, influencing e.g. market value, brand, hiring ability, etc.	To be a well-reputed company.	Act as a responsible company. This includes being a responsible shareholder for Group and portfolio companies.	Novo receives informal feedback from stakeholders on an ongoing basis, including feedback from board members and co-investors in portfolio companies.  Overall, Novo received favourable feedback in 2015.  The Novo Group companies have each performed internal board evaluations.
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 and Cornerstones.	To make sure all employees know, understand and adhere to the Charter and Cornerstone principles.	Monitor that the organisation adheres to the Charter and Cornerstone principles.	All Novo's investments 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's governance framework.  Charter: The Novo Group companies each adhere to the Charter. The portfolio companies do not act against the Charter.  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.
Employees	Novo's main non-financial operational asset is its employees. To ensure optimal workplace conditions, CSR is part of our management system.	To be a responsible and attractive employer.	Conduct workplace assessments.  Collect 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 0.9% of working days. Internal and external training amounted to 1.8% of working days.  In 2015, Novo welcomed 20 new colleagues incl. four students. We handled more than 804 applications for vacancies, and received 27 unsolicited job applications.

# ACCOUNTS, EXTRACTS

The following pages represent an extract from the Annual Report 2015, as submitted to the Danish Business Authority.

The tables below explain the relation between the figures in the Annual Report and the first two tables (returns and assets) in the Management Report.

Returns	Returns from the Novo Group	Returns from life science investments	Returns from financial investments
Annual Report figures:			
Result from subsidiaries	4.271	700	0
Result from associates	0	5.707	0
Result from other investments	0	1.870	2.360
Novo Nordisk Foundations share of result from joint investment portfolio	0	0	527
Costs	0	315	10
Financial income and expenses	0	0	-2
Revaluation to market value	103.524	0	0
Management Report	107.795	8.592	2.895

Assets	Shares in Novo Group companies	Life science investments	Financial investments	
Annual Report figures:				
Subsidiaries	4.501	2.446	0	
Loans to subsidiaries	0	3.931	0	
Investments in associates	0	14.606	0	
Other investments	0	10.895	36.787	
Cash at banks	0	0	1.079	
Revaluation to market value	303.518	0	0	
Management Report	308.019	31.878	37.866	

CASH FLOW STATEMENT		
1 January to 31 December	2015	2014
	DKK million	DKK million
Net profit	14,848	13,460
Adjustment for non-cash items	-11,322	-9,971
Contribution from the Novo Nordisk Foundation in the joint investment portfolio	10,215	-
Sale of shares in associates	-	159
Sale of shares relating to life science investments	4,930	5,145
Purchase of shares relating to life science investments	-3,238	-1,724
Sale of securities	12,190	5,755
Purchase of securities	-22,223	-6,974
Paid tax	-1	-22
Cash flow before change in working capital	5,399	5,828
Change in working capital:		
Changes in accounts with affiliated companies	-2	7
Changes in other receivables	-1	-94
Changes in other liabilities	-10	13
Cash flow from operating activities	5,386	5,754
Investment activities		
Proceeds from sale of shares in subsidiaries	536	319
Purchase of shares in subsidiaries	-797	-1,515
Loans to subsidiaries	-66	-3,062
Repayment of loans to subsidiaries	1,205	586
Cash flow from investment activities	878	-3,672
Financing activities		
Bank loan (bridge financing)	-1,071	1,071
Dividends paid	-4,715	-2,745
Cash flow from financing activities	-5,786	-1,674
Net cash flow	478	408
Cash and cash equivalents at the beginning of the year	601	193
Cash and cash equivalents at the end of the year	1,079	601

STATEMENT OF COMPREHENSIVE INCOME			
1 January to 31 December	2015	2014	
	DKK million	DKK million	
Result from subsidiaries	4,971	2,904	
Result from associates	5,707	2,134	
Result from other investments	4,230	8,492	
Result from investment activities	14,908	13,530	
Administration costs	-58	-66	
Operating profit	14,850	13,464	
Financial income	2	1	
Financial expenses	-4	-5	
Profit before taxation	14,848	13,460	
Corporation tax	-	-	
Net profit	14,848	13,460	
Proposed appropriation of net profit:			
Proposed dividend	3,008	4,715	
Retained earnings	11,840	8,745	

BALANCE SHEET		
As per 31 December	2015	201
	DKK million	DKK millio
Assets		
Investments in subsidiaries	6,947	6,16
Loans to subsidiaries	3,931	4,52
Investments in associates	14,606	9,28
Deferred tax assets	-	1
Other investments	47,682	33,89
Total non-current financial assets	73,166	53,88
Total non-current assets	73,166	53,880
Amounts owed by affiliated companies	4	:
Other receivables	141	14
Cash at bank	1,079	60
Total current assets	1,224	74
Total assets	74,390	54,63
Equity and liabilities		
Share capital	500	500
Retained earnings	62,449	52,31
Total equity	62,449	52,810
Other liabilities	-	;
Total non-current liabilities	-	:
Joint investment portfolio Novo Nordisk Foundation	10,742	
Bank loan	-	1,07
Trade payables	14	
Amounts owed to affiliated companies	1	
Tax payables	32	3
Other liabilities	21	4
Other provision	631	64
Total current liabilities	11,441	1,81
Total liabilities	11,441	1,814
Total equity and liabilities	74,390	54,630

Graphic design: Kontrapunkt

Photos of Novo A/S' Chairman: Henrik Sørensen

Photos of Board of Directors and employees: Jon Norddahl

Architectual photos: P. Wessel

Photo of Martin Bonde by Henriette Bonde

Other photos were kindly made available by the portfolio companies.

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Novo A/S Tuborg Havnevej 19 DK-2900 Hellerup Tel. +45 3527 6500 Fax. +45 3527 6510 www.novo.dk CVR no.: 24257630