Q4

### Karolinska Development

Karolinska Development AB (Nasdaq Stockholm: KDEV) is a Nordic life sciences investment company. The company focuses on identifying medical innovation and investing in the creation and growth of companies developing these assets into products that will make a difference to patients' lives and provide an attractive return on investment to its shareholders.

Karolinska Development has access to world-class medical innovations at leading universities and research institutes in the Nordic region, including the Karolinska Institutet. The Company aims to build companies around innovative products and technologies, supported by experienced management teams and advisers, and co-funded by specialist international life science investors, to provide the greatest chance of success.

Karolinska Development's portfolio now comprises nine companies focusing on the development of innovative treatments for life-threatening or serious debilitating diseases and other medical conditions.

The Company is led by a team of investment professionals with strong investment backgrounds, experienced company builders and entrepreneurs, with access to a strong global network.

### Financial Update

- The Total Portfolio Fair Value of Karolinska Development's portfolio at the end of December 2016
  was SEK 405.2 million, a decrease from the Total Portfolio Fair Value of SEK 410.5 million at the
  end of September 2016. Net Portfolio Fair Value of the portfolio at the end of December 2016
  was SEK 149.4 million, a decrease of SEK 1.6 million compared to the end of September 2016.
- The result of change in Portfolio Fair Value amounted to SEK -6.3 million. The decrease was
  mainly due to the planned divestment in first quarter 2017 of Inhalation Science Sweden AB
  through an earn-out agreement.
- Revenue amounted to SEK 3.7 million in the fourth quarter (SEK 0.5 million in the fourth quarter 2015), of which. SEK 3.3 million revenue was received as a dividend from BioArctic AB. Net loss amounted to SEK 23.0 million (SEK 121.6 million). Earnings per share amounted to SEK -0.4 (SEK -0.2).
- Karolinska Development's investments in portfolio companies during the fourth quarter amounted to SEK 4.8 million. Total investments in portfolio companies by other specialized life science investors during fourth quarter amounted to SEK 35.6 million.
- Personal Costs for the full year amounted to SEK 17.3 million, a reduction of 45% compared to SEK 31.2 million in 2015.
- Cash, cash equivalents and short term liquidity investments decreased by SEK 8.2 million during the fourth quarter and amounted to SEK 248.1 million as of December 31, 2016. Despite these

cash resources, equity in the Parent Company amounted to SEK 14.3 million at the end of December 2016

### Karolinska Development - Highlights

#### **Full Year Highlights**

- Karolinska Development continued to make excellent progress during 2016 executing its strategy as a focused Nordic life sciences investment company.
- Dr Viktor Drvota joined as Chief Investment Officer strengthening the Company's investment
  experience and ability to identify, access and manage new deals, while also strengthening its
  relationships with entrepreneurs and investors.
- SEK 610 million in total was raised by portfolio companies during 2016, whereof 91% came from new investors in the Nordic region and internationally. Aprea Therapeutics raised SEK 437 million from specialist life sciences investors in the largest round completed by a private life science company in Sweden in over a decade.
- Several companies advanced therapeutic pipeline candidates in Phase II studies, with multiple read-outs expected in 2018, including Aprea Therapeutics (with APR-246 in ovarian cancer), Modus Therapeutics (with sevuparin in sickle-cell disease) and Dilafor (with tafoxiparin in obstetric indications).
- Commercial-stage medtech companies in the portfolio, Promimic and OssDsign, made progress with their commercialisation plans, building distribution networks and manufacturing facilities.
- Promimic, Umecrine Cognition, Aprea Therapeutics and OssDsign added experienced leaders to their management teams and boards.
- Going into 2017, the majority of companies in Karolinska Development's portfolio are now wellfinanced and in a good position to deliver key value-generating, clinical or commercial milestones over the next 18-24 months.

#### **Q4 Highlights**

- Aprea Therapeutics treated the first patient in its Phase II trial of APR-246 in high-grade serous ovarian cancer (October 2016).
- Promimic and Danco completed the set up and validation phase of the US production facility for HA<sup>nano</sup> Surface coating technology (October 2016).
- Promimic elected Tord Lendau as Chairman of the Board of Directors, and Håkan Krook and Patrik Sjöstrand as Non-Executive Directors (October 2016).
- Dilaforette announced it has changed its name to Modus Therapeutics (October 2016).
- Modus Therapeutics extended its ongoing Phase II clinical study to include patients aged 12-18, and to increase sample size of the study from 45 to around 150 patients (November 2016).
- Umecrine Cognition announced positive Phase I data with GR3027 in hepatic encephalopathy and raised SEK 45 million in a private financing round (November 2016).
- Dilafor was granted a key US patent for tafoxiparin, which is in Phase II development for treating obstetric indications (December 2016).
- Trinity Delta, a UK-based equity research firm, initiated coverage of Karolinska Development and issued its first report on the Company (November 2016).

### Post Period Events

- Karolinska Development Board of Directors called for an Extraordinary General Meeting to approve on its decision on a set-off issue of shares, with the aim of a necessary strengthening of the Company's equity position, thereby reducing the Company's overall financial risk profile and ensuring that its current cash resources can be used to invest in new portfolio companies.
- Dilafor initiated a Phase IIb clinical trial with tafoxiparin in women with protracted labor (January 2017)
- OssDsign entered into new partnerships in Italy, Spain, Switzerland, Austria and The Netherlands for the commercialization of its medical implants for cranial and facial reconstruction, adding to existing partnerships in the UK, Nordic region and certain other non-European markets (January 2017). Furthermore, OssDsign received 510(k) clearance by the US FDA to market OSSDSIG<sup>N®</sup> Cranial PSI in the USA and is preparing to launch the product (January 2017) and OssDsign also entered an agreement for distribution of OSSDSIGN<sup>®</sup> Cranial PSI in the USA with Matador Medical Inc (February 2017).
- Promimic appointed Magnus Larsson as Chief Executive Officer, replacing Ulf Brogren, who
  relocates to the US to lead Promimic Inc., the Company's new sales operation in North America
  as Head of Sales (January 2017).
- KDev Investments (an investment fund jointly owned by Karolinska Development and Rosetta Capital) divested its entire shareholding in Inhalation Sciences Sweden AB (ISS) to the Swedish investment company Råsunda Förvaltning AB together with two other purchasers. Karolinska Development retains an economic interest in ISS through an earn-out agreement (February 2017).
- Oncopeptides AB made a successful initial public offering ("IPO") on Nasdaq Stockholm.
   Karolinska Development has a 5% earn-out agreement for Oncopeptides with Industrifonden that has a current market value of SEK 26.7 million based on Oncopeptide's market capitalisation at listing on February 22 (February 2017).

#### Jim Van heusden, CEO of Karolinska Development, comments:

"The progress that Karolinska Development has made in the past 24 months towards its ambition of becoming a leading Nordic life sciences investor has been significant. The Company has now finalized the strategic re-organization. The investment expertise has been strengthened and the portfolio has been focused on a smaller number of companies with exciting potential. Experienced leadership has been attracted to our portfolio companies, and we supported the financing of these companies through syndication with experienced international and domestic life science investors. We believe these companies are now well-positioned to deliver key value-generating, clinical and/or commercial milestones over the next 18-24 months.

In addition, the Board has decided (conditional of EGM approval) on a set-off issue of shares, which is aimed at strengthening the Company's equity position, reducing its overall financial risk profile and ensuring that cash resources can be used to make and support new investments that the Company has identified. The Board believes that successful completion of the set-off issue will enable Karolinska Development to leverage the progress it has made and begin executing its investment strategy with the aim of creating additional value for all share/bond holders."

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### Chief Executive's Report

#### Karolinska Development

Karolinska Development made excellent progress in 2016 executing its strategy as a Nordic investment company focused on building value for patients and shareholders.

During 2016, Karolinska Development saw its portfolio companies achieve multiple milestones, including raising new funds; advancing pipeline candidates through clinical development; progressing their commercialization plans; and attracting experienced leadership to management teams and boards of directors. As a result, the majority of companies in Karolinska Development's portfolio are now well-positioned to deliver key value-generating milestones during the next 18-24 months, while additional value potential is retained in divested companies through earn-out agreements.

#### **Investment Strategy**

Karolinska Development has during the two past years been reorganizing its business as an investment company. The organization has been streamlined. The Company's strategy is focused on identifying medical innovation and investing in the creation and growth of companies, developing these assets into differentiated products, that will make a difference to patients' lives and provide an attractive return on investment to its shareholders.

The investment team believes that some of the most innovative biomedical research and ideas in Europe originate at institutions in the Nordic region, and there is a substantial pool of unrealized value. At the same time, the Nordic region represents an under-ventured area for life science investments. The situation is rapidly improving with increasing international investment into the region from specialist life sciences investors highlighting its potential to become the next major life science cluster. Karolinska Development aims to be a focal point for this activity.

The Company's strategy is focused on identifying new investment opportunities across the Nordic region, to expand and diversify its portfolio into broader areas of life sciences with near-term value-inflection points, such as medical technologies, diagnostics or digital health. The Company will also seek to make investments in under-valued companies on the public markets in the region and in more mature investments, where returns may be realized more quickly than from early stage companies. Karolinska Development will look to syndicate deals with experienced life science investors.

Karolinska Development's ability to manage its existing portfolio and identify, access and manage new deals was considerably enhanced during the first quarter 2016 with Viktor Drvota, MD PhD joining the organization as Chief Investment Officer, following his appointment in December 2015. Dr Drvota is an experienced life science investor and joined Karolinska Development from SEB Venture Capital, where he was Head of Life Science since 2002. He has established a strong track record in identifying investment opportunities in the life sciences sector (biotech and medtech) in the Nordic region, building companies and fundraising.

The addition of Dr Drvota to the team means Karolinska Development can now call on a strong combination of local and international networks and expertise as it executes its investment strategy. This provides an opportunity to build truly international investor syndicates and intensify focus on the Nordic region as a source of future market-leading companies. In addition, the future success of such companies will serve to attract additional funding into the region; attract experienced leadership teams and board members to portfolio companies; and support entrepreneurs to develop their innovations into commercial propositions.

# An exciting portfolio with blockbuster potential – well-financed to deliver key milestones

At the end of December 2016, Karolinska Development's portfolio comprised ten companies; this has since become nine with the further re-focusing of the portfolio through divestment of Inhalation Sciences Sweden during the first quarter 2017. The portfolio companies are developing highly differentiated and commercially attractive products that have the potential to deliver compelling clinical and health economic benefits, as well as attractive returns on investment.

Important clinical development and/or commercialization milestones are expected for these companies in the next 18-24 months. A key objective for Karolinska Development is to ensure that its companies are financed to achieve these value-inflection points, and new funds have been raised through the syndication of deals with experienced international life sciences investors. During 2016, SEK 610 million was raised in Karolinska Development portfolio companies, 91% of which was from new investors.

Karolinska Development's portfolio companies that raised funds during the year include **Aprea Therapeutics**, which raised SEK 437 million in a Series B financing round in March from a syndicate of leading life sciences investors from the US, Canada and Sweden. This financing, to advance the clinical development of APR-246 in ovarian cancer among other uses, was the largest round completed by a Karolinska Development company and also by any private life sciences company in Sweden in more than a decade.

**Umecrine Cognition** raised SEK 60 million in a Series B financing round (SEK 15 million in March and SEK 45 million in November), in which several new Nordic investors participated alongside founder investor Karolinska Development. These funds are being deployed to advance GR3027 in Phase II studies in hepatic encephalopathy, a serious brain disorder and one of the primary complications in acute and chronic liver disease.

#### YEAR-END REPORT Jan – Dec 2016

### KAROLINSKA DEVELOPMENT

**Dilafor** raised SEK 50 million in September from new and existing investors including KDev Investments. The new funds will be used to facilitate a European Phase IIb dose finding trial of tafoxiparin, which is in clinical development to decrease the incidence of protracted labor both after induction of labor and after spontaneous onset of labor.

In addition, **Promimic** raised SEK 23.5 million in September from new and existing investors to finance the establishment of its commercial operations in the US targeting the US orthopedic and dental implant markets with novel products enhanced with Promimic's HA<sup>nano</sup> Surface coating technology.

Non-dilutive financing has also been received by certain companies to support the development of their businesses towards the next milestones partnerships. In February, **Dilaforette** (which has since changed its name to **Modus Therapeutics**) entered a clinical collaboration with the Arabian Gulf University in Bahrain, and is receiving up to SEK 10 million to support its Phase II trial of sevuparin in patients with sickle cell disease (SCD); **Promimic** received investment to support the establishment of a production line for its HA<sup>nano</sup> Surface process in the US from its partner Danco Anodizing – the companies announced the validation of the manufacturing line in October 2016; and **BioArctic** entered a strategic collaboration with AbbVie, a global biopharmaceutical company, to develop and commercialize BioArctic's portfolio of antibodies directed against alpha-synuclein for the treatment of Parkinson's disease and other potential indications.

### Portfolio News: pipeline progress

During 2016, several portfolio companies advanced their lead therapeutic pipeline candidates in Phase II studies, with multiple read-outs expected in 2018.

In October, **Aprea Therapeutics** announced that it had enrolled the first patients in the Phase II part of the PiSARRO clinical study, which aims to enroll up to 400 relapsed high-grade serous ovarian cancer patients in Europe and the US. The company also presented efficacy and safety data from a Phase Ib part of the same trial at the 2016 European Society for Medical Oncology (ESMO) Annual Meeting. The results showed that APR-246 combined with the standard chemotherapy is generally well tolerated and showed robust signals of efficacy, supporting earlier findings presented as the American Society of Clinical Oncology (ASCO) annual meeting in June.

In November, **Modus Therapeutics** announced that it was expanding its ongoing Phase II clinical study with sevuparin to include patients aged 12-18. Modus Therapeutics also decided to increase the sample size of the study from 45 to around 150 patients so that this study can play a more important role in the overall clinical program needed to register sevuparin. Patient enrollment is underway and top-line results are expected in the first half 2018. A poster highlighting the mechanism of action of sevuparin in treating SCD was presented at the European Hematology Association congress in June.

**Dilafor** initiated a 360-patient Phase IIb study of tafoxiparin as a potential new treatment designed to decrease the incidence of protracted labor (i.e labor that lasts more than 12 hours), which is the main cause of emergency surgical deliveries such as caesarian section. The first patient was enrolled into the study in January 2017.

In November, **Umecrine Cognition AB** announced encouraging Phase I results from a clinical study with GR3027, which is being developed to treat hepatic encephalopathy in liver disease patients. The first

patients have already been enrolled into the next clinical trials designed to support proof of concept of GR3027 in this indication.

In addition to development progress made with therapeutic candidates, the medtech companies within Karolinska Development's portfolio also reported encouraging clinical results with their products.

In September, **OssDsign** presented preliminary data at the European Congress of Neurosurgery from a retrospective study of patients undergoing cranioplasty using its OSSDSIGN® Cranial implants, the results of which indicate that this novel implant may provide a better, more permanent solution for cranioplasty, even in a complex patient population.

**Promimic** announced the results of an *in vivo* proof-of-concept study on medical implants coated with HA<sup>nano</sup> Surface in the *International Journal of Nanomedicine* in April. The results of this study show significant improvement of bone-to-implant contact and bone healing for the HA<sup>nano</sup> coated implants compared to uncoated controls at three weeks and 12 weeks follow-up.

#### Portfolio news: commercial progress

During 2016 **Promimic** also advanced its commercialization plans on several fronts: in January, the company announced that its strategic partner Sistema de Implante Nacional had initiated the launch in Brazil of the first dental implant coated with HA<sup>nano</sup> Surface. In March, Promimic entered a strategic partnership with Danco Anodizing whereby Danco will invest in a production line for the HA<sup>nano</sup> Surface process and become the preferred process partner for Promimic for the USA and China medical implant markets. In October, the companies announced that validation of the production line was complete.

#### Portfolio news: board and management teams strengthened

In October, **Promimic** strengthened its board through the elections of Tord Lendau (Most recently, General Manager at Sandvik MedTech) as Chairman of the Board of Directors, and Håkan Krook (Fund Manager at Chalmers Ventures) and Patrik Sjöstrand (Investment Manager at Almi Invest) as Non-Executive Directors – all bring significant and complementary leadership, operational and commercial experience from innovative, rapid growth companies.

In July, **Umecrine Cognition** announced the appointment of Dr. Bruce Scharschmidt as a new member of its board of directors and Senior Development Adviser. Dr. Scharschmidt most recently served as Senior Vice President and Chief Medical & Development Officer at Hyperion Therapeutics (acquired by Horizon Pharma Inc. in 2015), where he was responsible for the development of glycerol phenylbutyrate (GPB, RAVICTI®), approved for the treatment of urea cycle disorders in the US, Europe and Canada, and for the successful Phase II trial of GPB for hepatic encephalopathy.

**Aprea Therapeutics** appointed Christian S. Schade as its President and Chief Executive Officer in June 2016. Mr. Schade, who will be based in Boston, brings more than 30 years of private and public pharmaceutical and biotechnology industry experience, as well as broad corporate finance expertise from his tenure in the investment banking industry. Prior to joining Aprea, he was CEO of Novira Therapeutics (acquired by Johnson & Johnson in 2015), and held senior executive positions at Omthera (acquired by AstraZeneca), Medarex (acquired by Bristol-Myers Squib) and Merrill Lynch.

In April, **OssDsign** appointed Simon Cartmell as Chairman of the Board. Mr. Cartmell is an experienced entrepreneur in the life sciences industry and a Non-Executive Director / Chairman of a number European medical device companies. He was previously the CEO and architect behind the commercial success of

Apatech, a British medtech firm that developed ACTIFUSE, a novel bone void filler used to treat bone defects resulting from orthopaedic and spine surgery or traumatic injury. Apatech was acquired by Baxter International in March 2010 for USD 330 million.

#### Significant portfolio events after the year-end period

In January 2017, **OssDsign** announced a series of agreements designed to expand the European distributor network for its next generation implants for cranial and facial reconstruction. The new partnerships covering distribution of its products in Italy, Spain, Switzerland, Austria and The Netherlands, build on existing partnerships in Germany, the UK and the Nordic region, as well as selected non-European markets including Singapore and Israel.

In January, OssDsign received 510(k) clearance by the US FDA to market OSSDSIGN® Cranial PSI in the USA and is on track to launch the product in the US during the first half 2017. The Company is also undertaking regulatory and commercial activities in Japan.

In January 2017, Promimic announced the appointment of Magnus Larsson as Chief Executive Officer, replacing Ulf Brogren, who relocates to the US to lead Promimic Inc., the Company's new sales operation in North America as Head of Sales (January 2017).

In February 2017, KDev Investments divested its entire shareholding in Inhalation Sciences Sweden AB (ISS) to the Swedish investment company Råsunda Förvaltning AB and two other purchasers. Karolinska Development retains an economic interest in ISS through an earn-out agreement.

#### **Set-off Issue**

In February 2017, the Board of Karolinska Development resolved on set-off share issue directed to holders of convertibles, which is aimed at strengthening the Company's equity position, thereby reducing its overall financial risk profile and ensuring that its cash resources can be used to make and support a number of new investments that the Company is evaluating.

#### **Outlook**

Karolinska Development is making excellent progress in executing its strategy. The Company has a portfolio of exciting companies that are funded to deliver key value-generating milestones over the next 18-24 months, an investment strategy designed to generate further value from the most promising life science opportunities across the Nordic region, and key people in place with the necessary international experience and capabilities to drive its strategy forward. Furthermore, the Board believes that successful completion of the set-off issue will enable Karolinska Development to leverage the progress it has made executing its investment strategy with the aim of creating additional value for all share/bond holders.



Karolinska Development's portfolio now compromises nine therapeutics and medtech companies. Six of them are presented on the following pages.



Project APR-246

Primary indication
Ovarian cancer

Development Phase Phase IIa

Holding in company\*
Karolinska Development 1%\*\*
KDev Investments 17%

KDev Investments 17%
Other investors
Versant Ventures (US),

5AM Ventures (US), HealthCap (Sweden) Sectoral Asset Management (Canada), KCIF Co-Investment Fund KB

Origin Karolinska Institutet

### More information



- \* Fully-diluted ownership based on current investment plans.
- \*\* Includes indirect holdings through KCIF Co-Investment Fund

### Aprea Therapeutics AB



## A unique approach to treating broad range of cancers

Aprea Therapeutics (Stockholm, Sweden and Boston, USA) is a biotech company focusing on discovery and development of novel anticancer compounds targeting the tumor suppressor protein p53. De-activation of p53 results in uncontrolled growth of the cell leading to cancer. Mutations of the p53 gene occur in around 50% of tumors and restoring its normal function represents a very attractive approach for treating a broad range of cancers including those resistant to cancer chemotherapeutics.

Aprea's exciting lead anti-cancer drug candidate APR-246, is a first-in-class compound that reactivates the tumor suppressor protein p53, inducing programmed cell death in many human cancer cells.

APR-246 is currently undergoing a Phase Ib/II clinical study (the PiSARRO study) investigating its safety and efficacy in combination with chemotherapy in second-line treatment of patients with high grade serous ovarian cancer. Aprea has presented efficacy and safety data from the Phase Ib part of PiSARRO at key clinical congresses including the European Society for Medical Oncology (ESMO) annual meeting in October, and the American Society of Clinical Oncology (ASCO) meeting in June. The results showed that APR-246 combined with standard chemotherapy is generally well tolerated and showed robust signals of efficacy.

Aprea has now advanced APR-246 into the Phase II portion of the PiSARRO study, which aims to enroll up to 250 relapsed high-grade serous ovarian cancer patients in Europe and the US. Patients will be randomized between carboplatin and pegylated liposomal doxorubicin with or without APR-246; the primary endpoint for the study is progression-free survival.

#### The market

The market potential in ovarian cancer is substantial. There are around 225,000 women living with ovarian cancer in the seven major markets, with 67,000 new patients diagnosed each year. Of those diagnosed annually, approximately 20,000 have stage III-IV, recurrent disease with mutated p53. This is the primary target population for APR-246. The overall ovarian cancer pharmaceutical market is expected by analysts to grow by more than 13% annually to 2020, reaching a total market value of USD 2.3 billion.

#### Recent progress

- Promising efficacy and safety data from Phase Ib part of PiSARRO presented at ESMO (Oct 2016) confirming earlier results presented at ASCO (Jun 2016).
- First patients enrolled into Phase II part of the PiSARRO study (Oct 2016).
- Christian S. Schade appointed as President and Chief Executive Officer (Jun 2016).
- SEK 437 million raised from leading international life science investors (Mar 2016).

- Complete recruitment into the Phase II part of the PiSARRO study.
- Results of Phase II part of PiSARRO study expected 2018.



#### **Project**

Sevuparin

#### Primary indication Sickle cell disease (SCD)

### Development Phase

Phase II

### Holding in company\*

KDev Investments 74%

#### Other investors

The Foundation for Baltic and East European Studies, Praktikerinvest

#### Origin

Karolinska Institutet, Uppsala Univesity

### More information

modustx.com

\*Fully-diluted ownership based on current investment plans

### Modus Therapeutics AB



### Targeting relief for sickle cell disease patients

Modus Therapeutics (formerly Dilaforette; Stockholm, Sweden) is developing sevuparin, an innovative, disease-modifying drug which has potential to become the best-in-class treatment for sickle cell disease (SCD).

Sevuparin's anti-adhesive mechanism means it has the potential to prevent and resolve the microvascular obstructions experienced by SCD patients. These obstructions cause the severe pain experienced by patients during Vaso-Occlusive Crises (VOCs) and result in high morbidity through organ damage as well the risk of premature death.

Modus is conducting a Phase II study of sevapurin in hospitalized SCD patients experiencing VOC, the results of which are expected in 2018.

The trial is targeting 150 evaluable patients who will have been randomized to receive either an intravenous infusion of sevuparin or placebo on top of standard pain medication. This proof-of-concept study is designed to demonstrate reduced time to resolution of VOC, defined as freedom from parenteral opioid use and readiness for discharge from hospital. Secondary end-points include pharmacokinetics and safety. The study is taking place in Europe and the Middle East under a co-development deal with Ergomed, which will co-invest a proportion of its revenues from the clinical and regulatory activities of this trial in return for an equity stake in Modus.

Modus is also aiming to develop a presentation of sevuparin that could be self-administered by SCD patients in a timely manner to prevent VOCs developing.

#### The market

SCD is an orphan disease with approximately 100,000 patients in the US and 35,000 patients in Europe. In addition to this, there is a large patient pool in the Middle East, India, South America and Africa. The average number of VOCs per patient seeking hospital care is in the order of one VOC per year. The commercial impact of a SCD treatment that reduces hospital stay and the use of opioid analgesics is expected to be substantial. A label expansion to include also the preventive treatment would expand the market size significantly.

#### **Recent progress**

- Dilaforette announced name change to Modus Therapeutics (Oct 2016).
- Phase II study expanded to include adolescent SCD patients, sample size increased (Nov 2016).
- Posters strengthening the mechanism of action of sevuparin in treating SCD were presented at the European Hematology Association congress (Jun 2016) and at the 58<sup>th</sup> American Society of Hematology annual meeting in San Diego (Dec 2016)
- Clinical collaboration agreement with Arabian Gulf University (Bahrain) for Phase II clinical development of sevuparin for SCD (Feb 2016).

- Complete recruitment into Phase II proof-of-concept trial.
- Results from Phase II trial expected in 2018.



Project
GR-3027-GABA modulator

Primary indication Hepatic encephalopathy

**Development Phase** Phase Ib/IIa

Holding in company\* Karolinska Development 67%

Other investors
Norrlandsfonden
Fort knox förvaring AB
Partnerinvest

**Origin** Umeå University

More information

umecrine cognition.com

\* Fully-diluted ownership based on current investment plans.

### **Umecrine Cognition AB**



### Unique approach to hepatic encephalopathy treatment

Umecrine Cognition (Solna, Sweden) is developing a drug against hepatic encephalopathy (HE), which is a serious neuropsychiatric and neurocognitive complication in acute and chronic liver disease. The disorder has detrimental effects on health related quality of life as a consequence of diverse and debilitating symptoms. An increase in the inhibitory GABA (a neurotransmitter) system in the CNS is a plausible main driver for the clinical signs and symptoms.

Neuroactive steroids are key drivers of this increased GABA signaling, causing cognitive impairment. This makes neurosteroid-antagonists, as developed by Umecrine Cognition, a credible therapeutic class to explore for novel treatments in HE.

Umecrine cognition's exciting drug candidate GR-3027 is a first-in-class drug to treat acute life-threatening HE and long-term maintenance in minimal HE caused by endogenous GABA-steroids.

GR3027 is currently in the first part of a combined phase Ib/IIA clinical study that will investigate the safety and efficacy of the compound in treating HE.

#### The market

HE is a severe disorder with a large unmet need. In total, liver cirrhosis affects up to 1% of US and EU populations. Between 125,000 and 200,000 patients with cirrhosis in the US are hospitalized due to complications of HE. Once HE develops, mortality reaches 22-35% after five years. HE is also associated with large societal and individual costs. The total cost for hospitalizations with HE in the US is estimated to around USD 2 billion.

#### Recent progress

- SEK 60 million raised from syndicate of local investors (Mar & Nov 2016).
- Start of Phase Ia clinical study (H1 2016).
- Bruce Scharschmidt, a key opinion leader in the field of HE, joins the Board of Directors (Jul 2016).
- Positive Phase 1a top line data with GR3027 demonstrate safety, tolerability, and CNS target engagement (Nov 2016)
- Initiated Phase Ib of the combined Phase Ib/IIa proof-of-concept study (Jan 2017).

- Complete recruitment into Phase 1b clinical trial.
- Phase lb/lla study results expected in H1 2018.



## **Project** Tafoxiparin

Primary indication
Protracted labor

Development Phase Phase II

Holding in company\* KDev Investments 35%

#### Other investors

The Foundation for Baltic and East European Studies Praktikerinvest Rosetta Capital Lee's Pharma

#### Origin Karolinska Institutet

# More information Dilafor.com

\* Fully-diluted ownership based on current investment plans.

### Dilafor AB



### Reducing complications with childbirth

Dilafor (Stockholm, Sweden) is a drug development company focusing on the development of tafoxiparin for obstetric indications. The company's primary goal with tafoxiparin is to decrease the incidence of slow progress of labor both after induction of labor and after spontaneous onset of labor. Tafoxiparin has shown in a Phase II clinical trial encouraging evidence that it can decrease the proportion of women with labor more than 12 hours. A Phase IIb dose-finding study is underway.

Protracted labor (i.e. labor that lasts more than 12 hours) is the main cause of emergency surgical deliveries, such as caesarian section. The condition is often associated with complications for both mother and child. These complications lead to short and long term consequences for the mother and the newborn in addition to substantial health care costs.

The Phase IIb study aims to test tafoxiparin/placebo in addition to standard care (oxytocin infusion) in term-pregnant first-time mothers that, after spontaneous onset of labor, require labor augmentation due to primary slow progress or labor arrest. The target is to enroll 360 pregnant women into the study in Europe.

Dilafor has outlicensed tafoxiparin for development and commercialization in the Chinese market to Lee's Pharmaceuticals.

#### The market

It has been estimated that up to 40% of pregnant women run into complication during childbirth in the form of protracted labor, where pharmaceutical therapy is relevant. This number represents the primary target population for Tafoxiparin, which indicate a substantial market potential. Existing pharmacological therapies that improve uterine contractions are usually insufficient, as they are not working well enough in up to 50% of cases. Consequently, there is strong interest in better treatments such as Tafoxiparin, which has "first-in-class" potential.

#### Recent progress

- Initiated 360-patient Phase IIb dose-finding study with tafoxiparin in Europe (Jan 2017).
- Raised SEK 51 million (USD 5.9 million) from new and existing investors. New investors include Lee's Healthcare Industry Fund, Rosetta Capital IV and Pila AB (Sep 2016).
- US patent granted for tafoxiparin providing key IP protection in the US until at least Apr 2033, with the possibility of up to five years' additional patent term extension (Dec 2016).

- Complete recruitment into Phase IIb dose-finding trial.
- Results from Phase IIb trial expected 2018.



#### **Project**

OSSDSIGN® Cranial and OSSDSIGN® Facial

### **Primary indication**

Cranial implants

#### **Development Phase** Marketed

Holding in company\* Karolinska Development 28%\*\*

#### Other investors

SEB Venture Capital Fouriertransform

Karolinska University Hospital, Uppsala University

#### More information ossdsign.com



- \* Fully-diluted ownership based on current investment plans
- \*\* Includes indirect holdings through KCIF Co-Investment Fund

### OssDsign AB



## Commercializing the best craniofacial implants

OssDsign (Uppsala, Sweden) is an innovator, designer and manufacturer of implants and material technology for bone regeneration. Its lead products - OSSDSIGN® Cranial and OSSDSIGN® Facial - are already being sold in Germany, the UK and the Nordic region, as well as selected non-European markets including Singapore and Israel. The Company is preparing for its first product launch in the US, which is anticipated during the first guarter of 2017, and is also undertaking regulatory and commercial activities in

OssDsign's commercial strategy is focused on building sales of its innovative products through a combination of its internal sales organization and distribution partnerships, and the Company is well-funded to support this strategy.

OssDsign's personalized bone regeneration technology provides improved healing properties that are clinically proven to enhance patient outcomes. By combining a regenerative ceramic material reinforced with titanium, with tailored patient-specific designs enabled by state-of-the-art computer-aided design, 3D printing and moulding techniques, the technology platform aims to contribute to the permanent healing of a range of bone defects. Enhanced healing means a better implant solution for patients and cost savings for hospitals.

#### The market

The market for material products in orthopedics was estimated at EUR 1.5 billion in 2013. The market for OssDsign's lead product in cranioplasty alone is expected to amount to approximately EUR 100 million in 2017. OssDsign pursues a focused business strategy on a well-defined patient population. The advantages are that the targeted procedures are carried out in a limited number of easily identifiable hospitals around the world. The indications are relatively price insensitive and on many markets easy to access from a regulatory perspective.

#### Recent progress

- Agreement with Matador Medical for US distribution of OSSDSIGN® Cranial (Feb 2017).
- 510(k) clearance granted by US FDA to market OSSDSIGN® Cranial in the US (Jan 2017).
- European distributor network expanded with partnerships signed in five countries (Jan 2017).
- Preliminary data presented at the European Congress of Neurosurgery highlighted benefits of OSSDSIGN® Cranial implants for cranioplasty (Sep 2016).
- Simon Cartmell appointed Chairman of the Board (Apr 2016).
- CE mark received for Cranioplug, an innovative device for cranial fixation (Jan 2016).

- Second wave of launch of OSSDSIGN® Cranial and OSSDSIGN® Facial on new EU markets and selected markets outside of Europe.
- Launch of OSSDSIGN® Cranial in the US.



Project

HAnano Surface

Primary indication Implant surface

**Development Phase** Marketed

Holding in company\* KDev Investments 32%

Other investors
ALMI Invest
K-Svets Venture

Chalmers Ventures

Origin

Chalmers University of

More information

Promimic.com

Technology

\*Fully-diluted ownership based on current investment plans

### Promimic AB



### Coatings to enhance the properties of medical implants

Promimic (Gothenburg, Sweden) is a biomaterials company that develops and markets a unique coating for medical implants called HA<sup>nano</sup> Surface, which increases their integration into bone and anchoring strength.

The HA<sup>nano</sup> Surface is nanometer thin, which helps preserve the micro-structure of the implant and reduces the risk of cracks in the coating. Furthermore, the coating improves the hydrophilicity of the implant, which increases the possibility for bone cells to attach to the surface. The HA<sup>nano</sup> Surface has been evaluated in both *in vitro* and *in vivo* studies, which have shown that it can reduce healing times. The coating process is easy to implement in the industrial scale production of implants.

Promimic has established a sales operation in the US and series of development and commercial partnerships, including Sistema de Implante Nacional (S.I.N), a leading provider of dental implants in Brazil, which launched the first product using Promimic's technology in that market in January 2016. Promimic also has signed an agreement with Amendia Inc. (US) focused on the development of HA<sup>nano</sup> Surface technology for use with its spinal implants.

A manufacturing facility for HA<sup>nano</sup> coated implants to supply the US and China markets has also been established by the Company's partner, Danco Anodizing.

#### The market

The implant industry is a large, high-growth market which delivers high profit margins. The competition amongst implant manufacturers is fierce and each market segment is dominated by 4-8 global companies. The strategies of many of these companies rely on in-licensing new technologies in order to differentiate their products and strengthen their market position. Promimic has a business model designed to meet these needs. It is centered on out-licensing its HA<sup>nano</sup> Surface technology to leading implant manufacturers so that they can incorporate it into their products.

#### Recent progress

- Raised SEK 23.8 million from new and existing investors to finance the establishment of Promimic Inc., its commercial operations in the US (Sep 2016).
- Magnus Larsson appointed CEO (Jan 2017) replacing Ulf Brogren, who relocates to the US to lead Promimic Inc. as Head of Sales.
- S.I.N. launched HA<sup>nano</sup> coated implants in Brazil in Jan 2016 and sales development during 2016 has exceeded expectations.
- Promimic and Danco Anodizing entered partnership where Danco will invest in a US production line (Mar 2016), which was completed in Oct 2016.
- Promimic elected Tord Lendau as Chairman of the Board of Directors, and Håkan Krook and Patrik Sjöstrand as Non-Executive Directors (October 2016) (Oct 2016).

#### **Expected milestones**

 Further product launches and license agreements with major manufacturers expected during 2017

## Financial Development - Investment Entity

The Investment Entity refers to the Parent Company (Karolinska Development AB) and all subsidiaries, joint ventures, associated companies and other long-term securities holdings which are all recognized at fair value. Amounts in parenthesis refer to corresponding period in the prior year unless otherwise stated.

#### Financial development in summary

SEKm	2016	2015	2016	2015
	Oct-Dec	Oct-Dec	Full-year	Full-year
Condensed income statement				
Result of change in Portfolio Fair Value in portfolio companies	-6.3	-99.7	-147.0	-976.5
Net profit/loss	-23.0	-121.6	-216.8	-1,054.7
Balance sheet information				
Cash, cash equivalents and short-term investments			248.1	297.2
Share information				
Earnings per share, weighted average, before and after				
dilution (SEK)	-0.4	-2.3	-4.1	-19.8
Net asset value per share (SEK) (Note 1)			0.7	4.7
Equity per share (SEK) (Note 1)			0.6	4.7
Share price, last trading day in the reporting period (SEK)			6.0	9.6
Portfolio information				
Investments in portfolio companies	4.8	15.7	28.9	130.8
Of which investments not affecting cash flow	0.5	0.6	1.9	11.5
Fair value of portfolio holdings			149.4	267.7

#### Results fourth quarter 2016

Revenue in fourth quarter amounted to SEK 3.7 million – an increase of SEK 3.2 million compared to same period in 2015. SEK 3.3 million of the Revenue was dividend from the portfolio company BioArctic.

As part of the restructuring of Karolinska Development the number of employees has been reduced during 2015. During January – December 2016 this has resulted in Personal Costs being reduced with 45% from SEK 31.2 million in 2015 to SEK 17.3 million in 2016. In the fourth quarter, Personal Costs were SEK 4.8 million – a SEK 5.0 million reduction compared to same period in 2015.

Adjusted for Result of Change in Portfolio Fair Value Operating Loss in fourth quarter decreased with 51% from SEK -11.8 million in fourth quarter in 2015 to SEK -5.8 million in fourth quarter in 2016. January – December 2016 Operating Loss adjusted for Result of Change in Portfolio Fair Value amounted to SEK -27.1 million – a decrease of 38% compared to SEK -43.8 million in same 2015.

During fourth quarter Portfolio Fair Value of Inhalation Science Sweden was reduced resulting in Result of Change in Portfolio Fair Value being SEK -6.3 million.

The above made Operating Loss during the fourth quarter decrease by 93% to SEK -12.1 compared to SEK -111.4 in same period in 2015. January – December Operating Loss amounted to SEK -174.0 million – mainly because of the reduction in Portfolio Fair Value in Akinion and Clanotech.

Financial Costs amounted to SEK -10.9 million during the fourth quarter compared to SEK -10.2 million in same period 2015. Interest on convertible bond amounted to SEK -11.3 million during the fourth quarter compared to SEK -10.0 million for same period in 2015. The SEK 0.4 million in difference between SEK -10.9 million in Financial Costs and SEK -11.3 million in Interest on the convertible bond was positive interest from loans provided to portfolio companies.

The result for the fourth quarter increased with 81% and amounted to SEK -23.0 million compared to a result of SEK -121.6 million in same period in 2015. The main reason for the difference was the reduction in Fair Value of the portfolio companies made in 2015 as part of the portfolio clean-up.

#### Investments in portfolio companies fourth quarter 2016

Part of Karolinska Development's investment focus has been to attract external specialized life science investors to its portfolio companies, and during the fourth quarter SEK 35.6 million was invested by external investors. In the same period Karolinska Development invested SEK 4.8 million. The investments amounted to:

- Umecrine Cognition SEK 4.3 million
- Interest on loans to portfolio companies SEK 0.5 million

Of the SEK 4.8 million invested by Karolinska Development during the fourth quarter, SEK 4.3 million was cash investments and SEK 0.5 million was non-cash investments.

A key element in the restructuring of Karolinska Development was securing financing of the portfolio companies to next development stage from external specialized life science investors. During January – December 2016 SEK 554.8 million was raised from external investors (of which SEK 338.7 million was invested during the period) and SEK 55.1 million was raised from Karolinska Development (of which SEK 28.9 million was invested during the period).

#### Value development fourth quarter 2016

During the fourth quarter, Fair Value of the portfolio directly invested in by Karolinska Development increased by SEK 6.2 million to SEK 143.7 million. The part of the portfolio invested indirectly by KDev Investments decreased with SEK 11.5 million to SEK 261.6 million. Total Portfolio Fair Value was SEK 405.2 million and the change in Total Portfolio Fair Value amounted to SEK -5.2 million.

Due to the SEK 11.5 million decrease in the KDev Investments portfolio, the potential distribution to Rosetta Capital decreased by SEK 3.8 million and potential distribution to Rosetta Capital was reduced to SEK 255.8 million. By that Net Portfolio Fair Value decreased by SEK 1.4 million and ended at SEK 149.4 million.

With a decrease of SEK 1.4 million in Net Portfolio Fair Value and SEK 4.8 million invested by Karolinska Development, the Result of Change in Portfolio Fair Value in the Profit and Loss Statement amounted to SEK -6.3 million (SEK -1.4 million and SEK -4.8 million).

#### Financial position (comparative figures refer to 31 December 2015)

The Investment Entity's equity to total assets ratio was 7% (40%) on 31 December 2016 and equity amounted to SEK 29.8 million (SEK 247.9 million). Cash, cash equivalents and short-term investments in the Investment Entity amounted to SEK 248.1 million (SEK 297.2 million), of which SEK 30.4 million is provisionally allocated for anticipated follow-on investments in the KDev Investments portfolio. Total assets amounted to SEK 438.3 million (SEK 614.5 million).

## Financial Development - Parent Company

The Parent Company refers to Karolinska Development AB.

During the period, January - December 2016, the Parent Company's operating loss amounted to SEK -175.5 million (SEK -839.3 million), a change of SEK 663.8 million compared with the same period in 2015. Impairment losses during the same period amounted to SEK -148.4 million (SEK -795.5 million) and were recognized in the holdings in KDev Investments AB SEK -147.6 million, KCIF Co-Investment Fund KB SEK 0.7 million and share of result in KCIF Co-Investment Fund KB SEK -1.5 million. The impairment losses in the KDev investments portfolio are mainly due to write offs on shares in portfolio companies Akinion Pharmaceutical AB and ClanoTech AB. Equity at the end of December 2016 amounted to SEK 14,3 million (SEK 234,4 million).

### Information on Risks and Uncertainties

#### **Parent Company and Investment Entity**

#### Valuation risks

Companies active in pharmaceutical development and medical technology at an early phase are, by their very nature, difficult to value, as lead times are very long and development risks are high. Due to the uncertainty in these assessments and the subjectivity in the inputs, the estimated value of the portfolio may deviate substantially from future generated value. This is largely due to sensitivities in the valuation calculations to movement of expected milestone or exit dates, costs of trials and similar assumptions, which are not necessarily accounted for in arriving at an actual deal value in negotiations with partners. Financing strategy decisions can have an effect on valuations.

#### Project development risks

Risks and uncertainties are primarily associated with investments in portfolio companies and the development of projects in these companies. The operations of the therapeutic portfolio companies consist of the development of early stage pharmaceutical projects. By their very nature such operations are distinguished by very high risk and uncertainty in terms of results. The medtech portfolio is considered having less risk and uncertainty than the therapeutic portfolio companies.

#### Financial risks

Karolinska Development needs to strengthening its equity position, thereby reducing its overall financial risk profile and ensure the requirements regarding the size of the equity in the Swedish Companies Act (Aktiebolagslagen). Therefore, the board has called for an Extraordinary General Meeting (EGM) for approval of the board's decision on a new issue of B-shares directed to the convertible holders offering the convertible holders to "set-off" their claims as payment for new B-shares.

#### Future financing needs

Development of the portfolio companies' research projects will require capital contributions by their investors in order to capitalize on the value potential. The portfolio companies have no guarantees that required capital will be obtained to finance their projects on favorable terms, or that such capital may be obtained at all.

Karolinska Development maintains a strategy to invest in the portfolio companies in syndicate with other investors. If portfolio companies are not successful in attracting other investors, Karolinska Development may choose to invest alone. If Karolinska Development chooses not to invest in the portfolio companies, investments may be made solely by other investors, which may have a negative impact on the valuations of portfolio companies.

Portfolio companies may fail to achieve milestones or meet development milestones according to plan. In such cases, investors may decide to discontinue investing in a project. If so, the portfolio companies may have to limit their operations. Karolinska Development's shareholdings may also be diluted by other investors, and other investors may refrain from co–investing on equal terms.

Investments in existing portfolio companies during 2017 are expected to stay in the same level as previous year, as a consequence of several companies being fully financed until next value inflection point and due to Karolinska Development's strategy of investing in syndication with other investors. Several companies are expected to enter license agreements with partners, receive non-dilutive grants such as EU contributions, and third party investments are expected to increase.

Karolinska Development is continuously exploring the opportunity to invest in new portfolio companies.

Other than the above, no new risk areas have been identified since 31 December 2015. For a detailed description of risks and uncertainties, see the annual report 2015.

The Board of Directors proposes that no dividend will be paid for financial year 2016.

This report has not been reviewed by the Company's auditors.

Solna, 28 februari 2017

Jim Van heusden CEO

### Dates for Publication of Financial Information

Annual Report 2016 19 April 2017

Interim Report January-March 2017 16 May 2017

Annual General Meeting 24 May 2017

Interim Report January-June 2017 29 August 2017

Interim Report January-September 2017 28 November 2017

Karolinska Development is required by law to publish the information in this interim report. The information was published on 28 February 2016.

This interim report, together with additional information, is available on Karolinska Development's website: www.karolinskadevelopment.com

Note: This report is a translation of the Swedish interim report. In case of any discrepancies, the Swedish version shall prevail.

## **Financial Statements**

#### Condensed income statement for the Investment Entity

SEK 000	Note	2016 Oct-Dec	2015 Oct-Dec	2016 Full-year	2015 Full-year
Dividend <sup>1</sup>					
Dividend		3,333	0	3,333	0
Other revenue		377	508	2,027	2,942
Revenue		3,710	508	5,360	2,942
Other expenses		-5,200	-2,409	-15,415	-15,363
Personnel costs		-4,757	-9,759	-17,344	-31,167
Depreciation of tangible non-current assets		0	-53	-106	-212
Result of change in fair value of shares in portfolio companies	2	-6,265	-99,682	-146,988	-976,488
Result from sale of shares in portfolio companies		444	-	444	-
Operating profit/loss		-12,068	-111,395	-174,049	-1,020,288
Financial net		-10,944	-10,199	-42,783	-34,385
Profit/loss before tax		-23,012	-121,594	-216,832	-1,054,673
Taxes		-	-	-	-
NET PROFIT/LOSS FOR THE PERIOD		-23,012	-121,594	-216,832	-1,054,673

#### Condensed statement of comprehensive income for the Investment Entity

SEK 000	Note	2016 Oct-Dec	2015 Oct-Dec	2016 Full-year	2015 Full-year
Net/profit loss for the period		-23,012	-121,594	-216,832	-1,054,673
Total comprehensive income/loss for the period		-23,012	-121,594	-216,832	-1,054,673

#### **Earnings per share for the Investment Entity**

SEK	Note	2016 Oct-Dec	2015 Oct-Dec	2016 Full-year	2015 Full-year
Earnings per share, weighted average, before and after dilution		-0.43	-2.29	-4.08	-19.84
Number of shares, weighted average		53,220,713	53,184,132	53,210,223	53,151,328

<sup>&</sup>lt;sup>1</sup> Dividend from BioArctic

### Condensed balance sheet for the Investment Entity

SEK 000 N	lote	31 Dec 2016	31 Dec 2015
ACCETO			
ASSETS			
Non-current assets			106
Tangible non-current assets		-	106
Shares in portfolio companies at fair value through profit or loss	2	149,408	267,651
Loans receivable from portfolio companies	2	957	914
Other financial assets		38.113	38,113
Total non-current assets		188,478	306,784
Current assets			
Receivables from portfolio companies		229	3,549
Other current receivables		660	5,995
Prepaid expenses and accrued income		806	897
Short-term investments, at fair value through profit or loss		237,545	277,646
Cash and cash equivalents		10,602	19,589
Total current assets		249,842	307,676
TOTAL ASSETS		438,320	614,460
Equity			
Share capital		26,732	26,725
Share premium		1,874,236	1,874,236
Retained earnings		-1,871,153	-1,653,080
Total equity		29,815	247,881
Long-term liabilities			
Convertible loan	3	394,438	349,205
Other financial liabilities		4,798	5,439
Total long-term liabilities		399,236	354,644
Current liabilities			
Accounts payable		1,460	1,444
Liabilities to portfolio companies		-	513
Other current liabilities		960	4,425
Accrued expenses and prepaid income		6,849	5,553
Total current liabilities		9,269	11,935
Total liabilities		408,505	366,579
TOTAL EQUITY AND LIABILITIES		438,320	614,460

### Condensed statement of changes in the Investment Entity's equity

SEK 000	Equity attributable to Investment Entity's shareholders					
	Share	Share premium	Retained	Tota		
	capital		earnings			
Opening equity at 1 Jan 2016	26,725	1,874,236	-1,653,080	247,881		
Net profit/loss for the period			-216,832	-216,832		
Total comprehensive income for						
the period			-216,832	-216,832		
Effect of incentive programs			-1,241	-1,241		
Share issue	7			7		
Closing equity at 31 Dec 2016	26,732	1,874,236	-1,871,153	29,815		
Opening equity at 1 Jan 2015 (restated)	26,692	1,828,844	-598,724	1,256,812		
Net profit/loss for the period		1,0-0,0	-1,054,673	-1,054,673		
Total comprehensive income for						
the period			-1,054,673			
the period			-1,004,073	-1,054,673		
Convertible loan - equity part		49,528	-1,004,010			
		49,528 -4,136	-1,004,010	49,528		
Convertible loan - equity part		•	317	49,528 -4,136		
Convertible loan - equity part Issue costs	33	•		-1,054,673 49,528 -4,136 317 33		

#### Condensed statement of cash flows for the Investment Entity

SEK 000	Note	2016 Full-year	2019 Full-yea
Operating activities			
Operating profit/loss		-174,049	-1,020,288
Adjustments for items not affecting cash flow		400	0.4
Depreciation	0	106	21:
Result of change in Portfolio Fair Value Other items	2	146,988 -1,371	976,48 17
Proceeds from short-term investments		-1,371	73
Interest paid/received		-193	12
Cash flow from operating activities before changes in working capital		U	12.
and operating investments		-28,519	-42,55
Cash flow from changes in working capital			
Increase (-)/Decrease (+) in operating receivables		7,851	2,55
Increase (+)/Decrease (+) in operating federables		-2,665	-18,34
increase (+)/Decrease (-) in operating habilities		-2,005	-10,34
Operating investments			
Acquisitions of shares in portfolio companies		-26,987	-119,29
Proceeds from sale of short-term investments <sup>1</sup>		41,326	
Investments in short-term investments <sup>1</sup>		-	-147,38
Cash flow from operating activities		-8,994	-325,02
Financing activities			
Share issue		7	3
Convertible debentures issue		-	364,00
Issue costs		-	-32,30
Cash flow from financing activities		7	331,72
Cash flow for the period		-8,987	6,70
Cash and cash equivalents at the beginning of the year		19,589	12,88
-ac. and tac. equitations at the beginning of the jour		10,602	19,58

CASH AND CASH EQUIVALENTS AT THE END OF THE PERIOD	10,602	19,589
Short-term investments, market value at closing date	237,545	277,646
CASH, CASH EQUIVALENTS AND SHORT-TERM INVESTMENTS AT		
THE END OF THE PERIOD	248,147	297,235

<sup>1</sup>Surplus liquidity in the Investment Entity is invested in interest-bearing instruments and is recognized as short-term investments with a maturity exceeding three months. These investments are consequently not reported as cash and cash equivalents and are therefore included in the statement of cash flows from operating activities. The supplemental disclosure is presented to provide a total overview of the Investment Entity's available fund including cash, cash equivalents and shortterm investments described here.

#### **Condensed income statement for the Parent Company**

SEK 000 Note	2016 Oct-Dec	2015 Oct-Dec	2016 Full-year	2015 Full-year
Dividend	3,333	-	3,333	-
Other revenue	377	508	2,027	2,942
Revenue	3,710	508	5,360	2,942
Other expenses	-5,200	-2,409	-15,415	-15,363
Personnel costs	-4,757	-9,759	-17,344	-31,167
Depreciation of tangible non- current assets	0	-53	-106	-212
Impairment losses on shares in subsidiaries, joint ventures, associated companies and other long-term securities holdings	-7,768	-102,003	-148,440	-795,470
Result from sale of shares in portfolio companies	444	<u>-</u>	444	-
Operating profit/loss	-13,571	-113,716	-175,501	-839,270
Financial net	-10,945	-10,199	-43,425	-44,233
NET PROFIT/LOSS FOR THE PERIOD	-24,516	-123,915	-218,926	-883,503

#### Condensed statement of comprehensive income for the Parent Company

SEK 000 Note	2016 Oct-Dec	2015 Oct-Dec	2016 Full-year	2015 Full-year
Net profit/loss for the period	-24,516	-123,915	-218,926	-883,503
Total comprehensive income/loss for the period	-24,516	-123,915	-218,926	-883,503

#### **Condensed balance sheet for the Parent Company**

SEK 000 No	ote	31 Dec 2016	31 Dec 2015
ASSETS			
Non-current assets			
Tangible non-current assets		-	106
Shares in subsidiaries, joint ventures, associated companies			
and other long term-securities holdings		107,610	229,513
Loans receivable from portfolio companies		28,734	27,523
Other financial assets		33,010	33,386
Total non-current assets		169,354	290,528
Current assets			
Receivables from portfolio companies		229	3,549
Other current receivables		660	5,995
Prepaid expenses and accrued income		3,448	2,500
Short-term investments		237,545	277,646
Cash and cash equivalents		10,602	19,589
Total current assets		252,484	309,279
TOTAL ASSETS		421,838	599,807
Restricted equity Share capital		26,732	26,725
Share capital		26,732	26,725
Unrestricted equity		4 004 040	4 004 040
Share premium reserve		1,884,310	1,884,310
Accumulated losses		-1,677,789	-793,045
Net profit/loss for the period		-218,926	-883,503
Total equity		14,327	234,487
Long-term liabilities			
Convertible loan	3	394,438	349,205
Pension obligations		3,804	4,180
Total long-term liabilities		398,242	353,385
Current liabilities			
Accounts payable		1,461	1,444
Liabilities to portfolio companies		-	513
Other current liabilities		959	4,425
Accrued expenses and prepaid income		6,849	5,553
Total current liabilities		9,269	11,935
Total liabilities		407,511	365,320

#### Condensed statement of changes in equity for the Parent Company

SEK 000	Note		nrestricted equit		
	Restricted equity				
	Share capital	Share premium reserve	Accumulated losses	Net profit/loss for the period	Total equity
Opening equity at Jan 1 201	6 26,725	1,884,310	-793,045	-883,503	234,487
Appropriation of loss			-883,503	883,503	
Net profit/loss for the period				-218,926	-218,926
Total	26,725	1,884,310	-1,676,548	-218,926	15,561
Effect of incentive programs			-1,241		-1,241
Share issue	7				7
Closing equity at 31 Dec 201	6 26,732	1,884,310	-1,677,789	-218,926	14,327

Opening equity at Jan 1 2015	26,692	1,838,918	-502,588	-290,774	1,072,248
Appropriation of loss			-290,774	290,774	
Net profit/loss for the period				-883,503	-883,503
Total	26,692	1,838,918	-793,362	-883,503	188,745
Convertible loan - equity part		49,528			49,528
Issue costs		-4,136			-4,136
Effect of incentive programs			317		317
Share issue	33				33
Closing equity at 31 Dec 2015	26,725	1,884,310	-793,045	-883,503	234,487

### Notes to the Financial Statements

### NOTE 1 Accounting policies

This report has been prepared in accordance with the International Accounting Standard (IAS) 34 Interim Financial Reporting and the Annual Accounts Act. The accounting policies applied to the Investment Entity and the Parent Company correspond, unless otherwise stated below, to the accounting policies and valuation methods used in the preparation of the most recent annual report.

#### Information on the Parent Company

Karolinska Development AB (publ) ("Karolinska Development," "Investment Entity" or the "Company") obtains funds from several independent investors/shareholders by issuing shares and interest-bearing instruments. The Company invests the proceeds in portfolio companies that develop medical innovations, and whose sole purpose is to generate a return through capital appreciation and investment income. These temporary investments, which are not investment entities, are designated "portfolio companies" below. The Company, with Corporate Identity Number 556707-5048, is a limited liability company with its registered office in Solna, Sweden. Karolinska Development AB aims to create value for investors, patients and researchers by investing in portfolio companies that develop products that can be sold. The business model is to select the most commercially attractive medical innovations, develop innovations to the stage where the greatest return on investment can be achieved and commercialize innovations through the sale of portfolio companies or outlicensing of products. Investments are made directly in the portfolio companies and via KDev Investments AB with Corporate Identity Number 556880-1608. Future deal flow will be sourced via an amended agreement with Karolinska Institutet Innovations AB, through an extended network of contracts at research institutions across the Nordic region, and through relationships with other specialist life sciences investors.

#### Going concern

Karolinska Development needs to strengthening its equity position, thereby reducing its overall financial risk profile and ensure the requirements regarding the size of the equity in the Swedish Companies Act (Aktiebolagslagen). Therefore, the board has called for an Extraordinary General Meeting (EGM) for approval of the board's decision on a new issue of B-shares directed to the convertible holders offering the convertible holders to "set-off" their claims as payment for new B-shares. If the EGM does not approve the board's decision or no or only convertible holders representing a minor part of the convertible debt are accepting the offer there is a risk that Karolinska Development will not continue to meet the requirements regarding the size of the equity. The Board of Directors has considered these facts and conditions and decided to prepare the interim condensed consolidated financial statements of the Company as of December 31, 2016, based on a going concern assumption.

#### Changes in accounting principles and information's

No changes in accounting principles and information as of this reporting period.

#### New and revised accounting principles 2016

No new or revised IFRS standards or recommendations from IFRS Interpretations Committee has had impact on the Investment Entity.

#### **Definitions**

**Portfolio companies**: Companies where Karolinska Development has made investments (subsidiaries, joint ventures, associated companies and other long-term securities holdings) which are active in pharmaceuticals, medtech, theranostics and formulation technology.

**Fair value**: The NASDAQ Stockholm regulations for issuers require companies listed on NASDAQ Stockholm to apply the International Financial Reporting Standards, IFRS, in their consolidated financial statements. The application of the standards allows groups of an investment company nature to apply so-called fair value in the calculation of the carrying amount of certain assets. These calculations are made on the basis of established principles and are not included in the opening accounts of the Group's legal entity, nor do they affect cash flows.

Karolinska Development applies the accounting principles of fair value according to the International Private Equity and Venture Capital Valuation Guidelines and adheres to the guidance of IFRS 13 Fair Value Measurement. Based on the valuation criteria provided by these rules, an assessment is made of each company to determine a valuation method. This takes into account whether the companies have recently been

financed or involved with a transaction that includes an independent third party. If there is no valuation available based on a similar transaction, risk adjusted net present value (rNPV) calculations are made of the portfolio companies whose projects are suitable for this type of calculation. In other cases, Karolinska Development's total investment is used as the best estimation of fair value. In one other case, the valuation at the time of the last capital contribution is used.

The part of the Fair Value that is related to the value of Karolinska Development's portfolio companies is named Portfolio Fair Value or Fair Value of the portfolio. The calculation of the Portfolio Fair Value is based on IFRS 13 standards of deciding and reporting fair value and the International Private Equity and Venture Capital Valuation Guidelines (IPEV Valuation Guidelines) decided by the IPEV board that represent the current best practice, on the valuation of private equity investments.

The Portfolio Fair Value is divided into Total Portfolio Fair Value and Net Portfolio Fair Value.

**Total Portfolio Fair Value**: The aggregated proceeds that would be received by Karolinska Development and KDev Investments if the shares in their portfolio companies were sold in an orderly transaction between market participants at the measurement date.

**Net Portfolio Fair Value** (after potential distribution to Rosetta Capital) is the net aggregated proceeds that Karolinska Development will receive <u>after</u> KDev Investments' distribution of proceeds to Rosetta Capital (calculated as Total Portfolio Fair Value minus Potential Distribution to Rosetta Capital).

**Net asset value per share**: Fair value of the total portfolio (SEK 149 million), loans receivable from portfolio companies (SEK 1 million), short-term investments (SEK 238 million), cash and cash equivalents (SEK 11 million), and financial assets less interest-bearing liabilities (SEK 38 million minus SEK 399 million) in relation to the number of shares outstanding (53 220 713) on the closing date (31 December 2016).

Equity per share: Equity on the closing date in relation to the number of shares outstanding on the closing date.

Interim period: The period from the beginning of the financial year through the closing date.

Reporting period: Current quarter.

#### NOTE 2 Fair value

The table below shows financial instruments measured at fair value based on the classification in the fair value hierarchy. The various levels are defined as follows:

Level 1- Fair value determined on the basis of observed (unadjusted) quoted prices in an active market for identical assets and liabilities

Level 2- Fair value determined based on inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly

Level 3- Fair value determined based on valuation models where significant inputs are based on non-observable data

#### Fair value as of 31 December 2016

SEK 000	Level 1	Level 2	Level 3	Total
Financial assets				
Shares in portfolio companies, at fair value through profit or loss	<u>-</u>	_	149,408	149,408
Loans receivable from portfolio companies	-	957	, -	957
Other financial assets	-	-	38,113	38,113
Receivables from portfolio companies	-	229	-	229
Cash, cash equivalents and short-term investments	248,147	_	<u>-</u>	248,147
Total	248,147	1,186	187,521	436,854
Financial liabilities				
Other financial liabilities	-	-	4,798	4,798
Accounts payable	-	1,460	-	1,460
Liabilities to portfolio companies	-	-	-	0
Total	-	1,460	4,798	6,258

#### Fair value as of 31 December 2015

SEK 000	Level 1	Level 2	Level 3	Total
Financial assets				
Shares in portfolio companies, at fair value through profit or loss	_	<u>-</u>	267,651	267,651
Loans receivable from portfolio companies	-	914	-	914
Other financial assets	-	_	38,113	38,113
Receivables from portfolio companies	-	3,549	-	3,549
Cash, cash equivalents and short-term investments	297,235	-	-	297,235
Total	297,235	4,463	305,764	607,462
Financial liabilities				
Other financial liabilities	-	-	5,439	5,439
Accounts payable	-	1,444	-	1,444
Liabilities to portfolio companies	=	513	=	513
Total	-	1,957	5,439	7,396

#### Fair value (level 3) as of 31 December 2016

SEK 000	Shares in portfolio companies	Other financial assets	Other financial liabilities
At beginning of the year	267,651	38,113	5,439
Transfers to and from level 3 (loans receivable from portfolio companies)	-	-	-
Acquisitions	28,797	-	-
Disposals	-	-	-
Gains and losses recognized through profit or loss	-146,988	-	-641
Closing balance 31 Dec 2016	149,460	38,113	4,798
Total unrealized gains and losses for the period in profit or			
loss	-146,988	-	-641
Gains and losses in profit or loss for the period for assets and liabilities included in the closing balance			
<b>,</b>	-146,988	-	-641

#### Fair value (level 3) as of 31 December 2015

SEK 000	Shares in portfolio companies	Other financial assets	Other financial liabilities
At beginning of the year	1,113,454	38,113	11,686
Transfers to and from level 3 (loans receivable from portfolio companies)	0	-	-
Acquisitions	130,835	-	_
Disposals	-150	-	-
Gains and losses recognized through profit or loss	-976,488	-	-6,247
Closing balance 31 Dec 2015	267,651	38,113	5,439
Total unrealized gains and losses for the period in profit or			
loss	-976,488	-	-6,247
Gains and losses in profit or loss for the period for assets and liabilities included in the closing balance	-976,488	-	-6,247

The Investment Entity recognizes transfers between levels in the fair value hierarchy on the date when an event or changes occur that give rise to the transfer.

#### Impact of Portfolio Fair Value

In the table below, "Total Portfolio Fair Value" is as defined in Note 1.

#### Impact on Portfolio Fair Value of the agreement with Rosetta Capital

"Potential distribution to Rosetta Capital" is the amount that KDev Investments according to the investment agreement between Karolinska Development and Rosetta Capital is obligated to distribute to Rosetta Capital from the proceeds received by KDev Investments (KDev Investments Fair Value). The amount includes repayment of SEK 33 million that Rosetta Capital currently has invested in KDev Investments' portfolio companies and the distribution of dividends from Rosetta Capital's common and preference shares. The distribution to Rosetta Capital will only happen when KDev Investments distribute dividends. KDev Investments will only distribute dividends after all eventual payables and outstanding debt has been repaid.

If Rosetta Capital has not received 2.5 times the amount invested in KDev Investments by Rosetta Capital by 7 March 2018, then Rosetta Capital may require within 60 days that Karolinska Development acquires Rosetta's shares in KDev Investments. The price payable for the KDev Investments shares is the fair market value of the shares, although capped at 10 % of the market capitalization of Karolinska Development at the time of the purchase, Karolinska Development can decide whether to pay the purchase price in cash or in the form of Karolinska Development shares. With the market capitalization of Karolinska Development at the end of the fourth quarter 2016 being SEK 312 million the price payable for the KDev Investments shares is capped to SEK 31 million.

"Net Portfolio Fair Value is as defined in Note 1.

# Expanded Portfolio Fair Value calculations taking the portfolio valuation and potential distribution to Rosetta Capital in consideration

MSEK	2016-12-31	2015-12-31
Karolinska Development Portfolio Fair Value	143	134
KDev Investments Portfolio Fair Value	262	458
Total Portfolio Fair Value	405	592
Potential distribution to Rosetta Capital of fair value of KDev Investments	256	324
Net Portfolio Fair Value (after potential distribution to Rosetta Capital)	149	268

<sup>\*</sup> SEK 33 million repayment of investments in KDev Investments made by Rosetta Capital and SEK 223 million distribution of dividends to preference shares and common shares.

#### Information on fair value measurement in level 3

The valuation of the company's portfolio is based on the International Private Equity and Venture Capital Valuation Guidelines (IPEV) and IFRS 13 Fair Value Measurement. Based on the valuation criteria provided by these rules, an assessment is made of each company to determine a valuation method. This takes into account whether the companies have recently been financed or involved with a transaction that includes an independent third party. If there is no valuation available based on a similar transaction, discounted cash flow models (DCF) may be used. DCFs of the Underlying Business considers all of the cash flows of a portfolio company that are then discounted with an appropriate rate and also risk adjusted to take the developments risks in pharmaceutical development into consideration. The revenue streams are approximated from epidemiological data on the intended therapeutic indication, and a number of assumptions such as for example pricing per patient and year, market share and market exclusivity (from IPR and regulatory market protection). As described in the IPEV Valuation Guidelines the inputs into the DCF models are constructed with a high level of subjectivity. Hence, this method is only suitable for late stage assets, i.e. either pharmaceutical companies with lead projects in late stage (Phase III) development or technology projects with an established market presence where the revenues can be projected with a higher degree of confidence than in products in earlier stages of development, As of December 31, 2016, there are currently no portfolio companies valued by DCF.

Companies with an established sales revenue stream may be valued by sales multiples. The multiples should be derived from current market-based multiples with comparable companies. As with valuation with DCF, this method require that the portfolio company is mature in its market presence and that the sales forecasts can be made with sufficient certainty. Furthermore, as this method only considers revenue streams, the IPEV Valuation Guidelines stipulates that non-operating assets or liabilities need to be taken into account when applying this method. As of December 31, 2016, there are currently no portfolio companies valued by multiples.

Early stage companies, defined as pharmaceutical assets prior to Phase III development and technology assets prior to establishing targeted and sustainable sales revenues, that have recently not been financed by

a transaction involving a third party investor (as defined in 2,2) are valued by the price of recent investment corresponding to the last post-money valuation completed for that company. Companies in such early stages of development typically show a relatively flat value increase through the financing rounds as the company completed its preclinical and early clinical milestones. It is therefore not expected to see any significant value uplift during this period and the post-money valuation, despite not being validated by an external investor, is considered a good approximation of the Portfolio Fair Value.

Such situations occur when Karolinska Development alone or with other investors that have previously also participated in preceding investment rounds reinvest in portfolio companies. Should a new investor join an investment round, the valuation method will fall under a higher valuation priority (described in the top of Note 2), although the actual metric – post-money valuation is the same as if only existing owners would participate.

Should Karolinska Development opt out of an investment round with no intention to participate at later rounds the price of recent investment (without Karolinska Development) may still be a valid valuation method, granting that these circumstances lead to disproportionate post-money valuation because of the loss of negotiation power over the pricing (and Karolinska Development's ownership may be drastically diluted). However, as the unwillingness to invest from Karolinska Development also likely mirror a lower perceived value compared to previous post-money valuations, a lowering of value is often a good indication of Portfolio Fair Value in such cases.

As the share price of the internal financing rounds are decided by the existing investors, caution is taken to ensure that the share price is not artificially inflated. At each quarterly Portfolio Fair Value assessment the postmoney valuation by internal investment rounds are benchmarked against portfolio company progress (met or failed milestones for example), comparable values for peer companies, bids from external investors (e.g. term sheets, LOIs) and other applicable valuation methods to ensure that the post-money valuation is at an appropriate level to be considered Portfolio Fair Value.

The cautious approach is particularly true if an investment round with existing owners succeeds an investment rounds that included a then third party investor. An uplift in Portfolio Fair Value may be merited if e.g. milestones have been met during the time between investments but high increases may not be considered in the Portfolio Fair Value. To mitigate, the amount invested into the portfolio company since the post-money valuation from the transaction involving third party investors should be added, while additional uplifts in post-money valuation may not be included in Portfolio Fair Value until the value is validated by a third party investor yet again.

Net asset value, defined as a portfolio company's assets minus its liabilities, is used for portfolio companies without current operations. This typically occurs in companies considered financial assets as a consequence of discontinued development projects or withdrawn products. In essence these companies are valued by its liquidation value.

#### NOTE 3 Convertible loan

Karolinska Development has issued convertible debentures, so called compound financial instruments, in which the holder has right to convert into shares, the number of shares to be issued are not affected by changes in fair value of the shares.

The debt portion of the compound financial instrument is initially recognized at fair value for a similar debt without a conversion right into shares. The equity portion is initially recognized as the difference between the total fair value of compound financial instrument and the fair value of the debt portion. Directly attributable transaction costs are allocated to the debt respectively equity portion based on their initial recognized values.

Post-acquisition the debt portion of the compound financial instrument is valued to amortized costs based on the effective interest method. The equity portion of the compound financial instrument is not revalued post-acquisition, except at conversion or redemption.

The Investment Entity issued convertible debentures with a nominal amount of SEK 387 million on 2 January 2015 which have a nominal interest rate of 8 percent. The convertible debentures will fall due for payment on 31 December 2019 at the nominal amount of SEK 586 million (provided that accrued interest is interest bearing), the convertibles grant a right to convert into shares at a conversion rate of 22 SEK per series B share. The value of the debt and equity part (conversion right) was determined on the date of issuance.

The convertible debentures are presented in the balance sheet as shown in the below table.

SEK 000	31 Dec 2016	31 Dec 2015
Nominal amount of convertible debentures issued on 2		
January 2015	386,859	386,859
Issue costs	-28,171	-28,171
Equity portion	-49,528	-49,528
Debt at issuance date 2 January 2015	309,160	309,160
Accrued interest costs	85,278	40,045
Paid interest	-	-
TOTAL	394,438	349,205

#### NOTE 4 Unconsolidated subsidiaries

Karolinska Development is an investment entity according to IFRS 10. Subsidiaries are not consolidated in the Investment Entity's financial statements. The table below indicates all unconsolidated subsidiaries. Ownership interests include indirect ownership through portfolio companies. The ownership interest corresponds to formal voting rights through participating interests.

		Total holding		
Name	Registerad office	31 Dec 2016	31 Dec 2015	
Avaris AB (dormant)	Huddinge	0.00%	94.87%	
KCIF Fund Management AB	Solna	37.50%	37.50%	
KD Incentive AB	Solna	100.00%	100.00%	
KDev Oncology AB	Solna	0.00%	100.00%	

#### Influence over the portfolio companies

In addition to the above named subsidiaries, Karolinska Development holds majority interests, though not controlling interests, in KDev Investments AB, Modus Therapuetics Holding AB and Umecrine Cognition AB.

Karolinska Development's ownership interests in these portfolio companies ranges from 59% up to 87%. Karolinska Development has entered into shareholder agreements with other shareholders regarding these companies. The shareholder agreements ensure other owners influence. Therefore Karolinska Development is not considered to have controlling interest, even if its ownership interest formally exceeds 50% and it is concluded that in these situations the holdings should be accounted for as investments in joint ventures.

### NOTE 5 Pledged assets

SEK 000	31 Dec 2016	31 Dec 2015
Pledged assets	3,804	4,180
Total	3,804	4,180

### NOT 6 Related party transactions

Karolinska Development AB has entered into an agreement with a company related to the Chairman of the Board, OrfaCare Consulting GmbH, regarding consultations by the Chairman of the Board, Bo Jesper Hansen. The consultancy agreement covers other kind of consultancy services than what follows byhis position as Chairman of the company. The agreement is valid from 1 March 2015, after extension, until the date of the Company's Annual General Meeting 2017. The consultancy fee is market based and amounted during the period January – December 2016 to SEK 1.3 million (SEK 0.9 million same period 2015), of which SEK 0.3 million (SEK 0.3 million) during the fourth quarter 2016.