



# Key Consolidated Financial Figures, IFRS

(all figures in EUR K unless otherwise noted)	2017	2016
Profit and loss statement		
	5.011	4.263
Revenues	5,811	4,262
Research and development expenses  General administrative and selling expenses	-17,853	-23,408
	-3,828	-5,129
Net result	-12,093	-20,118
Personnel expenses included therein	-4,166	-5,375
Number of shares outstanding (weighted average, basic)	59,118,686	53,245,632
Number of shares outstanding (weighted average, diluted)	59,558,627	53,491,803
Earnings per share in EUR (basic)	-0.20	-0.38
Earnings per share in EUR (diluted)	-0.20	-0.38
Balance sheet		
Intangible assets	2,415	2,688
Cash and cash equivalents	24,839	30,111
Equity	25,229	24,943
Current liabilities	6,656	13,040
Balance sheet total	31,885	37,983
Cash flow		
Cash flow from operating activities	-17,720	-11,586
Cash flow from investing activities	-25	-192
Cash flow from financing activities	12,494	9,212
Employees		
Group employees (average)	33	36

# **PAION AR # 2017**

Annual Report of PAION AG



## Dr. Wolfgang Söhngen, Chief Executive Officer

- Graduated physician, Diploma in Pharmaceutical Medicine (DGPharMed) and Master of Business Communication
- Founder of PAION Deutschland GmbH (2000) and PAION AG (2004)
- Over 30 years experience in drug development and strategic planning at globally operating pharmaceutical companies
- Responsible inter alia for Licensing, Business Development, Fundraising and Production



## Abdelghani Omari, Chief Financial Officer

- Degree in Business Administration
- Has been involved in the repositioning of PAION AG and was responsible for and accompanied various capital market transactions and licensing agreements
- More than 17 years of experience in finance, before joining PAION he worked in audit and consulting at KPMG for several years
- Responsible inter alia for Finance and Accounting, Controlling, Taxes,
   Legal and Compliance, Human Resources and IT



## Dr. Jürgen Beck, Chief Development Officer

- Graduated physician, diploma in business administration
- Over 25 years of experience in the European pharma/biotech business,
   with positions held in various drug development projects
- Responsible inter alia for product development, in particular for the remimazolam development program in procedural sedation in the U.S. and for the EU Phase III program in general anesthesia



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## **About PAION AG**

PAION AG is a publicly listed specialty pharmaceutical company developing and aiming to commercialize innovative drugs to be used in out-patient and hospital-based sedation, anesthesia and critical care services. PAION's lead compound is remimazolam, an intravenous, ultra-short-acting and controllable benzodiazepine sedative/anesthetic drug candidate which is in the final stage of clinical development for use in procedural sedation in the U.S. Currently, PAION is mainly focusing its business and financial resources on successfully completing its development program in procedural sedation in the U.S. Outside the U.S., PAION has so far focused on the development of remimazolam in the indication general anesthesia. A full clinical development program for general anesthesia was completed in Japan. In the EU, PAION is currently planning to continue the clinical development program by starting a Phase III trial in the second half of 2018. Development of remimazolam in the indication intensive care unit (ICU) sedation is also part of the longer term life-cycle plan for remimazolam.

PAION is headquartered in Aachen (Germany) with a further site in Cambridge (United Kingdom).

PAION's vision is to become an acknowledged "PAIONeer" in sedation and anesthesia.

PAION is listed at the Frankfurt Stock Exchange (Prime Standard Regulated Market, Stock Symbol PA8, ISIN DE000A0B65S3).

# 2017 at a glance

### **February**

PAION AG announces successful completion of capital increase with subscription rights with gross proceeds of EUR 5.0 million

### March

- PAION reports positive headline data in U.S. clinical safety trial of remimazolam in high-risk patients undergoing colonoscopy
- PAION successfully completes patient recruitment in U.S.
   Phase III study with remimazolam for procedural sedation during bronchoscopy

### May

Annual General Meeting approves all agenda items and elects
 Dr. Dr. Irina Antonijevic and Dr. Chris Tanner to the Supervisory Board

### June

 PAION reports positive headline data in U.S. Phase III trial with remimazolam for procedural sedation during bronchoscopy

### July

- PAION AG raises EUR 8.0 million in private placement

### **August**

- R-Pharm starts remimazolam Phase III trial in Russia

## September

 European Patent Office grants formulation patent for remimazolam in the EU

### October

- Japan Patent Office grants dosing patent for remimazolam in Japan
- PAION hosts remimazolam symposium at Japan Society for Clinical Anesthesia Annual Meeting in Japan

#### **November**

 FDA informs PAION that it considers current human abuse liability program with remimazolam in the U.S. as sufficient; no second intranasal study required

### December

- Dr. Jürgen Beck appointed as Chief Development Officer of PAION AG with effect from 01 January 2018
- PAION grants exclusive license to Mundipharma for development and commercialization of remimazolam in Japan

## Letter to Shareholders



Dr. Wolfgang Söhngen Chief Executive Officer of PAION AG

## Dear Shareholders and Friends of PAION.

2017 was a very successful year for us. We achieved all major clinical development goals and announced positive Phase III results from U.S. trials with remimazolam. We were also very pleased to see the substantial progress made by our commercialization and development partners in several territories and were excited to end the year with closing a partnership for remimazolam in Japan. In addition, we strengthened our patent portfolio and completed two successful financings. Our key goals for 2018 are the completion and delivery of data and documentation to Cosmo, our partner for the U.S., and the initiation of an EU Phase III study in general anesthesia. We also expect several of our partners to make key clinical and regulatory progress in their respective territories during the year.

### 2017 - Positive remimazolam Phase III results in the U.S.

In 2017, we mainly focused on the completion of the US Phase III remimazolam development program in procedural sedation. We are particularly proud of the outstanding Phase III results of the bronchoscopy study, which we published in June 2017. These confirmed the very good data from the colonoscopy study.

The trial was designed to evaluate the efficacy and safety of remimazolam compared to placebo (with midazolam rescue medication) in procedural sedation in patients undergoing bronchoscopy. The endpoints were achieved with high statistical significance.

The U.S. Phase III development program also included a safety study with remimazolam in high-risk colonoscopy patients (ASA III/IV). Again, this study provided excellent efficacy data and confirmed the good safety of remimazolam.

Based on the results of preclinical and Phase I studies, and in consultation with the FDA, PAION conducted additional Phase I studies to further assess the abuse potential of remimazolam. Two aspects were studied: if remimazolam could inappropriately be used as a knock-out cocktail in combination with alcohol and if it could be abused intranasally. In November 2017, the FDA informed PAION that it determines the abuse liability program conducted by PAION as sufficient to provide the necessary data regarding the abuse potential of remimazolam

in humans. PAION therefore assumes the clinical development program for remimazolam in procedural sedation in the U.S. as completed.

We are currently working intensely to complete and deliver the data packages and documentation from the extensive U.S. clinical development program to U.S. license partner Cosmo, who plans to submit for regulatory approval in the U.S. in the fourth quarter 2018/first quarter 2019. We believe that regulatory filing in the U.S. will positively affect the further regulatory filings in other territories.

### Reset in the EU

In consultation with key opinion leaders in general anesthesia, PAION has successfully conducted a Phase I trial which served as a means to define key elements and sample size calculation for the planned Phase III trial. Based on the results of this study, subsequent simulations and Scientific Advice obtained from the European authority EMA in January 2018 for defining the new European Phase III program, we currently assume that approximately 500 patients will be required for the EU Phase III study in general anesthesia.

The study design in general surgery is planned to be close to the successfully completed Phase III program in general anesthesia in Japan, but in sicker patients, where the medical need to reduce hypotensive events is greater. We currently plan to start the study in the second half of 2018.

### New partner in Japan

The license agreement with Mundipharma for remimazolam in Japan was a very important milestone for us, which we were able to conclude at the end of the year after an intensive partnering process. Mundipharma has obtained the exclusive licensing rights to develop and market remimazolam in Japan and will bear all cost for market authorization and distribution. PAION has received an upfront payment of EUR 1 million and is also entitled to receive additional payments totaling up to EUR 25 million depending on the achievement of certain regulatory and commercial milestones in the three indications procedural sedation, general anesthesia and Intensive Care Unit (ICU) sedation. We are also entitled to receive tiered royalties starting in the

low double-digits to over 20% of net sales, depending on sales levels and sales price (National Health Insurance (NHI) price), which will be determined by the Japanese government. Based on the positive pre-NDA meeting with the Japanese authority, we had started preparations for filing of remimazolam. Mundipharma has now taken over these tasks with our support and currently plans filing for market approval in Japan in 2018.

### **Progress of other license partners**

Our other licensing partners are also very active in clinical development and regulatory processes to prepare for the future filing in their respective territories.

In May 2017, our Canadian remimazolam license partner, Pendopharm, had a pre-NDS meeting with Health Canada for the indication conscious sedation. Health Canada stated in the meeting that the non-clinical and the clinical data package, including the human abuse liability data available at the time, were regarded as adequate for filing. Currently, we expect filing for market approval in Canada after the market approval dossier in the U.S. has been filed.

In August 2017, our Russian remimazolam license partner R-Pharm, announced the start of a Phase III trial in general anesthesia in Russia. Recruitment of the study was recently completed and R-Pharm currently plans to submit the regulatory filing end of 2018.

Hana Pharm, our South Korean remimazolam license partner, is currently conducting a Phase III Remimazolam study in general anesthesia in South Korea. The completion of the study is expected in 2018.

Our Chinese remimazolam license partner Yichang Humanwell is going to conduct a Phase II study with remimazolam in general anesthesia and a Phase III study with remimazolam in procedural sedation in China.

### **Outlook: PAION in 2018**

We expect an exciting year 2018. Our key goals for 2018 are the transfer of all documents to Cosmo in order to enable our U.S. license partner to submit the regulatory filing in the U.S. as early as possible preferably in 2018, as well as the launch of a new

EU phase III Study in general anesthesia. Our Japanese partner Mundipharma also plans to file for regulatory approval in 2018.

At present, we are working on the dossier preparation for the U.S. with our partner Cosmo and for Japan with our partner Mundipharma in parallel. In doing so, we use the synergies that arise from the various focuses of the respective indications. In the US, procedural sedation data are supplemented with general anesthesia safety data from Japan, and vice versa in Japan, data from general anesthesia studies are supplemented by U.S. safety data from procedural sedation. We also try to use synergies in production. Due to different sizes of the pharmaceutical formulation (20 mg and 50 mg) these can later be used in the different indications and territories by us or by our current and future partners.

The very good remimazolam data as well as our and our partners' profound market analysis strengthen our belief that we are developing a competitive product. In our view the pending regulatory filings and the prospect of attractive royalties are the basis for a market-oriented equity story of PAION AG. We rely on the confidence of our shareholders and attract the interest of new investors to seek and exploit mutually beneficial opportunities to further develop PAION and realize our vision of an own regional commercialization of remimazolam.

# Dear Shareholders, Dear PAION Friends and Dear Colleagues,

I would like to thank all shareholders for their interest in PAION and their great trust in us. My sincere thanks go to all our employees and our cooperation partners. With their great personal commitment, they made a significant contribution to the success and thus paved the way for a successful future.

Your Wolfgang Söhngen Chief Executive Officer

Biling.

## **Business Model**

Strategic focus to become a specialist in anesthesia and intensive care further continued

PAION is a specialty pharmaceutical company that focuses on the development and commercialization of innovative products for procedural sedation, general anesthesia and sedation in intensive care units (ICUs).

PAION is focusing its clinical development activities on remimazolam in order to achieve its vision of becoming an acknowledged "PAIONeer" in sedation and anesthesia.

### Lead substance remimazolam

Remimazolam is an ultra-short-acting intravenous benzodiaze-pine sedative/anesthetic that has already shown positive results in clinical Phase III trials. In the human body, remimazolam is rapidly metabolized to an inactive metabolite by tissue esterases and not metabolized by cytochrome-dependent hepatic pathways. Like other benzodiazepines, remimazolam can be reversed with flumazenil to rapidly terminate sedation and anesthesia if necessary. During clinical studies, remimazolam demonstrated efficacy and safety in over 1,700 volunteers and patients. Data so far indicate that remimazolam has a rapid onset and offset of action combined with a favorable cardio-respiratory safety profile.

Remimazolam is in the final stage of clinical development for procedural sedation in the U.S. Currently, an integrated overall analysis of all clinical studies with remimazolam is being conducted in preparation of Cosmo's filing for market approval. After completion of the development for procedural sedation, Cosmo will be responsible for any further development activities in the U.S. The U.S. license partner currently plans to file for market approval in procedural sedation in the fourth quarter 2018/first quarter 2019. A full clinical development program for general anesthesia was completed in Japan, and the remimazolam license partner for this region, Mundipharma, is planning filing for market approval in this indication in Japan in 2018. In Europe, it is planned to start a Phase III study in general anesthesia in the second half of 2018 which can be expected

to be the only necessary outstanding trial for filing for market approval in Europe based on the scientific advice obtained from the European Medicines Agency (EMA) in January 2018.

Based on the positive results of a Phase II study, ICU sedation beyond 24 hours is another possible attractive indication for further development in the EU by PAION as well as by partners in the licensed territories.

Remimazolam is partnered in the U.S., Canada, China, Russia (CIS), Turkey, the MENA region, South Korea and Japan with Cosmo, Pharmascience (Pendopharm), Yichang Humanwell, R-Pharm, TR-Pharm, Hana Pharm, and Mundipharma, respectively. For all other markets outside the EU, remimazolam is available for licensing.

### Market

### Overview

Procedural sedation is a technique of administering sedatives or dissociative agents, with or without analgesics, to induce a state that allows the patient to tolerate unpleasant procedures such as colonoscopy while maintaining cardiorespiratory function.

General anesthesia leads to loss of consciousness and loss of sensation of patients through the administration of anesthetics in combination with opioid analgesics. This allows medical procedures such as major surgery, that would otherwise be unbearable, to be carried out with minimal discomfort or added risk.

The number of surgical procedures worldwide continues to grow driven by population growth and other factors such as obesity, low physical activity levels, dietary habits, smoking, and alcohol but also the medical progress. Current estimates place the number of surgical procedures at more than 230 million per year; the majority in the areas of general, orthopaedic/trauma and obstetric/gynaecological surgery.

The market for sedation and anesthesia has been short on pharmaceutical development during the last decade and there remains room for innovation. Sedative and anesthetic safety is continuously reviewed as part of quality assessments and includes such elements as efficacy, unintended intraoperational awareness, respiratory depression, hemodynamic

stability, post-operative/procedure emergence and recovery, long-term effects of anesthesia and patient morbidity. In sedation, it is important to avoid any significant cardiorespiratory side effects and, at the same time, to ensure a high treatment efficiency. The relevant parameters for general anesthesia as well as for procedural sedation offer a considerable potential for innovations, which PAION intends to use with remimazolam.

### Procedural sedation market (U.S. lead indication)

Based on external sources (Symphony Health Solutions, Centers for Disease Control and Prevention) and own projections, PAION estimates that approximately 43 million procedures using procedural sedation took place in the U.S. in 2013, predominantly outside the hospital setting.

The growth of the procedural sedation market in the U.S. has been driven for many years by the increase in medical interventions requiring procedural sedation, such as colonoscopies, as well as an increase in general demand for preventive screenings. According to iData Research, which examines historical trends and creates procedure forecasts in the U.S. drawing from an extensive collection of national- and state-level procedure databases, 26.7 million colonoscopy and endoscopy claims were reported in 2015 in the U.S., and the number is expected to grow at an average rate of 2.6% annually through 2020. PAION estimates that 75% of the colonoscopies and endoscopies claimed were conducted in an out-patient setting.

Regular endoscopic screening for people aged 50 or older is recommended and covered by all major health insurance plans, including those under the Centers for Medicare and Medicaid Services ("CMS"), a U.S. federal agency that administers Medicare (the national social insurance program), since effective prevention is considered to reduce the likelihood of incidence of illnesses such as cancer, thereby reducing the suffering of patients and related financial burden to be borne by the payors. Statistics show that the rate at which people are diagnosed with colon cancer in the U.S. has dropped by 30% between 2005 and 2015 for those aged 50 years and older, partly due to more people getting recommended screening tests. Colorectal cancer is the third most diagnosed cancer and the third leading cause of cancer death in the U.S. Despite the decrease of colorectal cancer death rates as a result of early screening and detection, it was reported in 2010 that only 59% of people

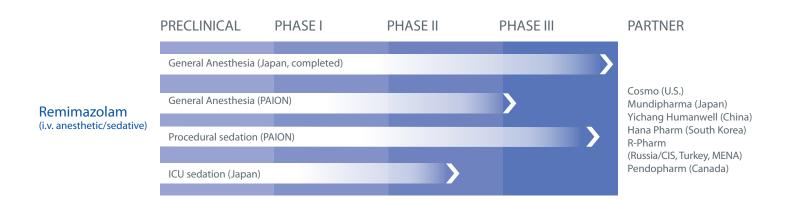
aged 50 or older, for whom screening is recommended, reported having received colorectal cancer testing consistent with current guidelines. The market for endoscopies in gastroenterology represents the most lucrative market segment for remimazolam in procedural sedation with approximately 20 million procedures per year in the U.S.

Currently, the most widely used products in procedural sedation are propofol and midazolam – both generic. PAION estimates that these two drugs each have a market share of approximately 50% in terms of volume of procedures performed in the out-patient market for colonoscopies in the U.S. The propofol label mandates the presence of an anesthesia professional throughout the procedure due to propofol's potential for respiratory- and cardio-depressive effects, which results in additional cost. For midazolam, these side effects are less pronounced and have a different relevance, since an undesirably deep sedation can be reversed with flumazenil. Midazolam has a slower onset and a longer duration of action which can impact patient throughput and overall efficiency.

In the U.S. increased enrollment and screenings are expected to result in a performance-based payment system that will seek to better align payments with high quality of care measures. This would imply that cost-efficient medicines with clinical value will be used more extensively and that continued premium will be placed on innovative medicines with strong clinical profile. Thus, PAION believes that concerns related to the overall cost of procedures, driven by the need for anesthesia professionals monitoring during procedures using agents such as propofol, will impact the choice of drug products for procedural sedation. Costs related to anesthesia services in gastrointestinal endoscopy procedures alone were estimated at USD 1.3 billion in 2009. Accordingly, PAION expects reimbursement regimes under national and commercial healthcare systems, such as Medicare, which differentiate the amounts reimbursed to physicians and/or patients depending on whether an anesthesia professional's service is used, may also positively impact the demand for products that do not require monitoring by an anesthesia professional.

PAION believes that remimazolam, subject to FDA approval with a safety labeling comparable to that of midazolam, could benefit from the pending changes in payment policies. Provided that it could be administered under the

### Portfolio Overview



supervision of a proceduralist, remimazolam would be able to offer a competitive alternative to midazolam. This is based on its enhanced efficiency profile compared to midazolam.

## General Anesthesia (Japan + EU lead indication)

Based on publicly available European procedure statistics and market research, PAION estimates that in the EU, approximately 29 million procedures requiring general anesthesia are performed each year. Of these, approximately 10 million are performed for high-risk patients (American Society of Anesthesiologists ("ASA") classifications III or higher) who are particularly prone to hemodynamic instability. Approx. 55% of all anesthesias are balanced anesthesia (a combination of intravenous agents for induction and volatile gases for maintenance), approx. 20% are total intravenous anesthesias ("TIVA") using propofol, and the remaining approx. 25% include regional anesthesia (for example epidural administration). Based on PAION's market research in the EU, the current standard-of-care drugs for general anesthesia are propofol (especially for induction) and narcotic gases; mostly used in conjunction with intravenous opioids.

Patient demographics in the EU will presumably continue to evolve driven by the aging population. PAION anticipates an increasing number and complexity of medical interventions requiring induction and maintenance of anesthesia in the EU in the future also driven by an ongoing ageing of the population. General anesthesia is more frequently offered to elderly patients than in the past, therefore the choice of a tailored anesthesia is made depending on the type of surgery, the underlying disease, and an assessment of the general physical health of the patient, including co-morbidities.

Accordingly, PAION believes that in the EU the demand for safer agents with low respiratory and cardio-depressive effects will increase over the coming years, creating opportunities for anesthetics with an enhanced safety profile such as remimazolam, even at higher prices compared to existing generic drugs. PAION also expects similar developments for the U.S. and other important international markets, subject to further market research.

### Intensive care unit (ICU) sedation

Plans for further development of remimazolam for use in ICU sedation in the future are based on PAIONs expectation that the market for ICU sedation will present an attractive business opportunity. Based on available information from 2012 published in Critical Care Medicine which estimates average days of care in ICUs per year in the U.S., and journal articles published in the Intensive Care Medicine in 2012, which records, among others, the volume of ICU admissions per year and the number of total adult beds in various countries in the EU, PAION estimates that there are approximately 14 million ICU patient days requiring ICU sedation in the U.S. and EU combined per year. PAION expects this number to increase in the years to come, driven by demand from the aging population in both regions. PAION believes that such development, in turn, will foster demand for safer agents such as remimazolam, given the fact that elderly patients are much more likely to suffer from systemic health problems.

Internationally renowned anesthesiologists have repeatedly confirmed to PAION that ICU sedation might bear the biggest market potential of all remimazolam indications. However, development would be associated with the highest risk of side effects given the treatment of severely ill patients. For this reason, initially development in general anesthesia has priority for PAION. Development for ICU sedation requires additional funds.

Another field of high clinical need is pediatric use, which is a development requirement for both the EU and U.S. after the respective first approval. For pediatric development in the EU, further funds will be required.

### Cooperations

Remimazolam is partnered in the U.S., Canada, China, Russia (CIS), Turkey, the MENA region, South Korea and Japan with Cosmo, Pharmascience (Pendopharm), Yichang Humanwell, R-Pharm, TR-Pharm, Hana Pharm and Mundipharma, respectively. For all other markets outside the EU, remimazolam is available for licensing.

For detailed information on partnering, please refer to page 38 et seq.

# Report of the Supervisory Board



Dr. Jörg Spiekerkötter Chairman of the Supervisory Board of PAION AG

## Dear Shareholders.

during the 2017 fiscal year, the Supervisory Board performed its duties pursuant to the law, the company's articles of association and the by-laws and, in fulfilment of its advisory and supervisory function, closely followed the business conduct of the Management Board. The Supervisory Board was directly involved in all decisions of major importance to the company and the group. In the course of fulfilling its duties, the Supervisory Board received regular, prompt and comprehensive written and verbal reports from the Management Board on PAION AG's corporate planning, the state and development of the company and the group as well as all significant business transactions.

The Supervisory Board carefully examined, discussed and voted on the decisions or measures of the Management Board that, pursuant to the law, the articles of association or the by-laws of the Management Board, require its approval as well as other decisions of fundamental importance. In addition to receiving its reports, the Chairman of the Supervisory Board maintained continued contact with the Management Board. The Chairman kept himself informed of the current business development, the liquidity situation, the progress of the development activities with remimazolam and the possibilities of its optimal commercialization as well as other essential business transactions.

### **Changes in the Supervisory Board**

On 17 May 2017 the Annual General Meeting elected Dr. Dr. Irina Antonijevic and Dr. Chris Tanner to the Supervisory Board, effective 12 June 2017, increasing the Board to five members.

### **Changes in the Management Board**

Dr. Jürgen Raths, Chief Operating Officer (COO) and member of the Management Board, left the company in March 2017.

Dr. Jürgen Beck was appointed as member of the Management Board and Chief Development Officer (CDO) with effect from 1 January 2018.

# Meetings of the Supervisory Board and focus of deliberations

The Supervisory Board held a total of eight board meetings throughout the 2017 fiscal year. The members attended six of these in person, while two meetings were conducted as joint conference calls. All board meetings were attended by all board members.

The Supervisory Board established an Audit Committee. Dr. Jörg Spiekerkötter, Mr John Dawson and Dr. Chris Tanner are members of this committee. Mr John Dawson was appointed chair of the committee and fulfils all requirements of section 100(5) of the German Stock Corporation Act (AktG).

The Supervisory Board established an HR and Nomination Committee. Dr. Jörg Spiekerkötter, Dr. Karin Dorrepaal and Dr. Chris Tanner are members of this committee. Dr. Karin Dorrepaal was appointed chair of the committee.

The Supervisory Board established a Research and Development Committee. Dr. Jörg Spiekerkötter, Dr. Karin Dorrepaal and Dr. Dr. Irina Antonijevic are members of this committee. Dr. Dr. Irina Antonijevic was appointed chair of the committee.

No further committees were established.

The Supervisory Board focused on the following topics during the 2017 fiscal year:

- The strategic positioning of the PAION Group
- The funding of the PAION Group
- The Phase III development programs of remimazolam in the U.S. and Europe
- The possibilities of an optimal commercialization of remimazolam, either with a partner or through own commercialization in certain territories
- The composition of the Management Board and the staffing of PAION Group
- Partnering discussions in Japan and the conclusion of a license agreement with Mundipharma

Adjustments to the 2017 corporate budget and the corporate budget planning for 2018 as developed by the Management Board were examined in detail and approved by the Supervisory Board. Based on mid- and long-term corporate planning as well as scenario comparisons, the strategic orientation was

discussed, reviewed and adjusted. Special attention was also paid to both the risk situation and risk management of the company.

The Management Board kept the Supervisory Board regularly informed of the net assets, financial position and results of operations of the PAION group. The basis for this were the timely presented monthly finance reports, quarterly statements, the half-year and annual financial reports as well as variance analyses with regard to the planning.

The Supervisory Board respectively its Audit Committee discussed quarterly statements and the half-year financial report with the Management Board before publication.

No conflicts of interest involving the members of the Supervisory Board, as set out in number 5.5 of the German Corporate Governance Code, arose in the 2017 fiscal year.

The audit committee held four meetings in the fiscal year 2017 and focused on the following subjects:

- The accounting of the company and the PAION Group
- Material accounting issues
- The audit tender for the 2017 audit of financial statements and consolidated financial statements of PAION AG
- The award of the audit engagement to the auditor and the determination of the audit focus
- The monitoring of the accounting process, the effectiveness of the risk management system and the internal control system

The meetings of the Audit Committee were attended by all its members.

The HR and Nomination Committee held two meetings in the 2017 fiscal year and focused on the composition of the Management Board and the staffing of PAION Group. The meetings of the Committee were attended by all its members.

The Research and Development Committee held two meetings in the 2017 fiscal year and focused on the Phase III development programs of remimazolam in the U.S. and Europe. The meetings of the Committee were attended by all its members.

### **Corporate Governance**

The concept of corporate governance stands for transparent business management that also aims to create long-term value. The Supervisory Board subscribes to the principles of the German Corporate Governance Code. In December 2017, the Supervisory Board and the Management Board jointly released an updated Declaration of Conformity in accordance with section 161 of the German Stock Corporation Act which was subsequently rendered available on the company's website at http://www.paion.com/media-and-investors/corporate-governance/declaration-of-conformity/. At the time of declaration in December 2017 PAION AG complied with all recommendations of the Government Commission German Corporate Governance Code in its version dated 7 February 2017. Information on corporate governance at PAION AG can be found in the joint declaration on Corporate Governance by the Supervisory Board and the Management Board. The declaration can be found in the annual report and is publicly available on the company's website at http://www.paion.com/media-and-investors/ corporate-governance/declaration-on-corporate-governance/.

### Financial statements and consolidated financial statements

Ernst & Young GmbH Wirtschaftsprüfungsgesellschaft, branch office Cologne, ("Ernst & Young") was appointed auditor and group auditor for the financial year 2017 by the Annual General Meeting on 17 May 2017 and subsequently mandated by the Supervisory Board. In accordance with number 7.2.1 of the German Corporate Governance Code, the independence of Ernst & Young was confirmed to us in writing prior to the Annual General Meeting. Ernst & Young has audited the Financial Statements and Consolidated Financial Statements of PAION AG prepared by the Management Board, the Management Report and the Group Management Report for the financial year 2017 and furnished them with an unqualified auditor's opinion. The Group Financial Statements were drawn up in accordance with section 315e of the German Commercial Code (HGB) on the basis of the International Financial Reporting Standards (IFRS).

All members of the Supervisory Board received the financial statements as well as the audit reports from the auditor well in advance of the Supervisory Board Meeting on 21 March

2018, in which the Financial Statements were discussed. They studied these documents in detail in preparation for this meeting. During the meeting, the Supervisory Board discussed and examined the Financial Statements and Consolidated Financial Statements of PAION AG, the Management Report and the Group Management Report. The assessments made by the Management Board in the Management Report and the Group Management Report were consistent both with those previously communicated in its reports to the Supervisory Board and own assessments of the Supervisory Board. The auditor also took part in this meeting. He reported on the audit, especially that no major weaknesses in the internal control system and risk management system with respect to the accounting process existed, commented on the focal points of the audit and was available to answer questions and provide supplementary information to the Supervisory Board.

The Supervisory Board approves the audit reports on the Financial Statements and Consolidated Financial Statements as well as on the Management Report and the Group Management Report. The Supervisory Board does not raise any objections and approves the Financial Statements and Group Financial Statements prepared by the Management Board. The Financial Statements are therefore adopted.

The Supervisory Board would like to thank the members of the Management Board and all employees for their great commitment and their achievements during the 2017 fiscal year.

Aachen, March 2018

For the Supervisory Board

Spiler loth

Dr. Jörg Spiekerkötter

Chairman

# Corporate Governance Report

## **Declaration on Corporate Governance**

The Declaration on Corporate Governance (Section 289f German Commercial Code) comprises the declaration of compliance, information on corporate governance practices and a description of the Management Board and Supervisory Board procedures. Our aim is to present PAION's corporate governance principles as clearly and concisely as possible. You will find the complete declaration on our webpage under http://www.paion.com/media-and-investors/corporate-governance/declaration-on-corporate-governance.

## Corporate Governance Report

The Supervisory Board and the Management Board of PAION AG are both committed to the principles of responsible management and governance aimed at sustainable value creation and set great store by these principles in their actions. In ensuring good and transparent corporate governance, the Supervisory Board and the Management Board of PAION AG are guided by the statutory provisions as well as the suggestions and recommendations of the Government Commission of the German Corporate Governance Code. The suggestions and recommendations laid down in the German Corporate Governance Code are based on internationally and nationally recognized standards of good and responsible business management.

In December 2017, the Supervisory Board and the Management Board released their annual Declaration of Compliance following the recommendations of the Government Commission of the German Corporate Governance Code in accordance with section 161 of the German Stock Corporation Act. The declaration is provided permanently on the company website (http://www.paion.com/media-and-investors/corporate-governance/declaration-of-conformity) alongside now outdated Declarations of Compliance from previous years. PAION complies with all recommendations of the latest version of the German Corporate Governance Code dated 07 February 2017.

## **Code of Conduct**

PAION AG has developed into a renowned and respected company focused on the clinical development of drugs in anesthesia

for which there is a high unmet medical need. As a listed clinical drug development and research company, PAION carries a major responsibility towards many stakeholders. Doctors and patients alike must be able to rely on our ability to develop safe and effective products. Business partners, shareholders and investors must also be able to place trust on us that all our activities and relationships both with business partners and governmental authorities remain within the framework and principles of integrity in business relationships as recorded in our corporate "Code of Conduct". Please visit http://www.paion.com/media-and-investors/corporate-governance/code-of-conduct for more information about the Code of Conduct at PAION.

Information on Company management and supervision In accordance with the provisions of the German Stock Corporation Act, PAION AG maintains a dual management and supervision structure formed by two bodies, the Management Board and the Supervisory Board. The Management Board consists of three members, who collectively bear all responsibility and are accountable for the company's good management. The Supervisory Board, comprising five members, appoints, supervises and advises the Management Board and is directly involved in decisions that are of fundamental importance to the company. In overseeing and directing the composition of the Management Board, the Supervisory Board pays attention to the principle of diversity, specifically the representation of women. Moreover, the Supervisory Board has determined that these goals are supposed to be considered for recommendations for the election of Supervisory Board members to the Annual General Meeting. The strategic objectives of the company are developed by the Management Board but coordinated with the Supervisory Board.

The Management Board and the Supervisory Board work together closely for the sole benefit of the company and its stakeholders. The Supervisory Board determined objectives regarding its composition outlining that at a size of five members, at least two members shall be independent. The age limit for Supervisory Board members is 75 years and the tenure is limited to an aggregate total of fifteen years. Furthermore, the Supervisory Board resolved that at least one of its members must be female. During financial year 2017 all members were

independent and younger than 75 years. The Chairman of the Supervisory Board coordinates its work and chairs its meetings. The Chairman of the Supervisory Board maintains regular contact with the Management Board. In the By-Laws developed for the Management Board, the Supervisory Board laid down the duties of the Management Board. This includes the provision of information and reports, the allocation of duties, and further defines the necessary levels of cooperation within the Management Board including the processes and business transactions requiring approval by the Supervisory Board. The Supervisory Board established an Audit Committee currently chaired by John Dawson, an independent member of the Supervisory Board with specific knowledge and experience in the application of accounting principles and the auditing of financial statements. The Supervisory Board established an HR & Nomination Committee chaired by Dr. Karin Dorrepaal, an independent member of the Supervisory Board, and the Supervisory Board established an R&D Committee currently chaired by Dr. Dr. Irina Antonijevic, an independent member of the Supervisory Board. Duties and tasks of the Supervisory Board and its committees are also regulated by specific rules of procedure. Further details concerning the work of the Supervisory Board can be found in the Report of the Supervisory Board. PAION AG has taken out a D&O insurance policy for the members of the Management Board and the Supervisory Board. This insurance policy provides partial coverage for the Management Board and the Supervisory Board in accordance with legal requirements, and specifically the German Corporate Governance Code. Insurance coverage is not provided in the event of fraudulent actions, omissions or deliberate breaches of duty.

Conflicts of interest of the Management or Supervisory Board members must be disclosed immediately to the Supervisory Board.

No conflicts of interest involving the members of the Supervisory Board, as set out in subsection 5.5 of the German Corporate Governance Code, were reported in the 2017 financial year.

Three members of the Management Board were appointed as managing directors of PAION Deutschland GmbH. Two Management Board members were appointed managing

directors of PAION Holdings UK Ltd including its subsidiaries. Further mandates held by members of the Management Board and Supervisory Board are listed in the notes to the Consolidated Financial Statements.

# Equal participation of Men and Women in executive positions

The Supervisory Board and the Management Board actively support the company in achieving an adequate representation of women in executive positions.

The Supervisory Board had determined a target of 30% to be achieved for the representation of women by 30 June 2017 in accordance with Section 111(5) Stock Corporation Act (AktG). This was based on the internal requirement that at least one member of the Supervisory Board shall be female. In the meantime the Supervisory Board was extended from three to five members by resolution of the Annual General Meeting held on 17 May 2017. On 30 June 2017 two of the five Supervisory Board members were female. The target was achieved. By resolution dated June 2017 the Supervisory Board determined to maintain the target of at least one female appointee to the Supervisory Board. Consequently a target of 20% was defined for the reporting period commencing on 01 July 2017. The agreed deadline for reporting is 30 June 2022.

At the end of the first reporting period on 30 June 2017 the Management Board of PAION AG was comprised of two members – Dr. Wolfgang Söhngen (CEO) and Abdelghani Omari (CFO). There were no women represented on the Management Board. Given existing contractual obligations, the Supervisory Board had determined, in accordance with Section 111(5) Stock Corporation Act (AktG), that no female representation was mandated for the Management Board of PAION AG until expiration of the reporting period on 30 June 2017. The target stood as achieved. Effective 01 January 2018 Dr. Jürgen Beck (CDO) was appointed to the Management Board increasing the number of appointees from two to three. By resolution dated June 2017 the Supervisory Board determined that owed to the specific circumstances of the company no representation of women on the Management Board of PAION AG was mandated until the end of the new reporting period on 30 June 2019.

At the close of the first reporting period on 30 June 2017 the representation of women within the first and second management levels below the Management Board of the PAION Group was calculated at 17.65%. In August 2015, the Management Board had defined a target of 20% for the representation of women within the first and second management levels in accordance with Section 76(4) Stock Corporation Act (AktG). Despite the fact that the level of female representation on 30 June 2017 was determined above the level of 13.3% on 31 December 2015 the target of 20% was not achieved. The reasons are primarily to be found in the change of staffing levels within the second management level due to the specific strategic alignment of the company and further in the promotion of key staff from the second to the first level. Notwithstanding, the Management Board is of the opinion that the company is on the right track in increasing the representation of women in the first and second management levels below the Management Board. Consequently it was decided to maintain the current target of 20% for the new reporting period which started on 01 July 2017 and will end on 31 December 2019.

# Compliance as a key management duty of the Management Board

Compliance, in the sense of measures designed to ensure adherence to statutory provisions and internal company policies including observance of these measures, represents a key obligation in the PAION group. Pursuant to Section 91(2) of the German Stock Corporation Act, the Management Board is obliged to implement effective measures – namely a monitoring system – to enable the early identification of any developments that may threaten the survival of the company. The German Corporate Governance Code stipulates the Management Board's responsibility for the implementation of a suitable risk management and control system.

The Management Board of a joint stock corporation is jointly and severally liable for the fulfillment of its organizational duties, especially risk management and risk control. The Management Board must define an organizational structure for the company ensuring that its operations comply with legal requirements. Any infringement of rights and legally protected

interests of third parties must reasonably be excluded. A Management Board is only eligible for exemption from liability if it provides evidence of compliance with its organizational obligations.

One of the organizational obligations for the Management Board is represented by the formal assignment of business responsibilities defining the individual areas of responsibility for its members. This plan forms an integral part of the rules of engagement for the Management Board and must be approved by the Supervisory Board. In addition, regular meetings and consultations ensure that the members of the Management Board are well informed of any important developments. In case of any deficits and/or irregularities, the Management Board must collectively implement suitable countermeasures.

The Management Board must not delegate management tasks to lower levels of the organization. This excludes the vast majority of common operational tasks. The Management Board further delegated specific tasks to subordinate executives and expert members of staff in the Legal, Investor & Public Relations as well as Finance departments forming part of its efforts to comply with capital market statutes. These tasks and responsibilities are defined in the individual job descriptions. The members of staff that perform tasks related to compliance within capital market statutes are subject to ongoing monitoring and training.

All staff and members of the Management and Supervisory Board across the entire PAION Group of companies receive regular communications raising awareness of compliance with relevant financial market regulations. This includes, for example, the handling of sensitive confidential information, specifically insider information.

### Transparency and communication

Good corporate governance is distinguished by open, transparent and up-to-date communications. PAION AG ensures this by post-ing ad-hoc reports on the company's website and by forwarding without delay all relevant information for publication to the relevant service providers (Business Register, Deutsche Börse, Federal Gazette, Europe-wide publication).

All inside information according to Section 17 MAR, Directors' dealings notifications according to Section 19 MAR, press releases, voting right notifications (Section 40 WpHG), financial reports, information on the Annual General Meeting as well as information on the company's corporate governance principles can be accessed by the public on the company's website (http://www.paion.com). The website also features a financial calendar that provides information on the publication dates of the financial publications as well as an event calendar detailing upcoming presentations by the company. For all events and discus-sions, PAION AG ensures that no investor receives material information in a favorable manner and that the equal treatment of all shareholders is ensured. Information such as inside information announcements, press releases, quarterly releases, half-year reports and annual reports are also made available in English.

PAION AG reports regularly and promptly on the development of its business as well as the net assets, financial position and operational results for the entire group. The Annual Financial Report is published within 90 days from the end of the respective financial year.

Further information about transparency and communications can be found in the Investor Relations section of the Annual Report.

### Shareholders and Annual General Meeting

The shareholders of PAION AG are entitled to exercise their rights at the Annual General Meeting. Each share entitles the holder to one vote. The shareholders have the possibility to exercise their voting rights themselves or of appointing a proxy in writing. PAION AG implemented facilitating measures for the shareholders to exercise their voting rights by appointing a representative assisting in the exercise of shareholders' voting rights in accordance with their instructions. All reports and documents required to be made available for inspection in connection with the Annual General Meeting are also posted on the PAION webpage (http://www.paion.com/media-and-investors/annual-general-meeting/).

### Auditing of the financial statements

The consolidated financial statements of PAION AG are drawn up by the Management Board in accordance with the International Financial Reporting Standards. Following vote at the Annual General Meeting, Ernst & Young GmbH Wirtschaftsprüfungsgesell-schaft, branch office (Zweigniederlassung) Cologne, ("Ernst & Young") was commissioned by the Supervisory Board to audit the annual and consolidated financial statements of PAION AG. It was agreed upon between the Supervisory Board and Ernst & Young that the auditor would report to the Chairman of the Supervisory Board or to the Chairman of the Audit Committee, without delay all findings and events essential for the fulfilment of the duties of the Supervisory Board that were discovered during the audit. Fur-thermore, the auditor is required to inform the Supervisory Board and the Audit Committee, or to include a note in the auditor's report, if he discovers any facts during the audit that are not consistent with the Declaration of Compliance issued by the Management Board and the Supervisory Board in accordance with section 161 of the German Stock Corporation Act. In regard to the audit of the consolidated financial statements and the audit and adoption of the financial statements by the Supervisory Board we refer to the report of the Supervisory Board

## Risk management

Good corporate governance involves the responsible handling of risks by the company. Details of the risk management system im-plemented by the PAION group of companies are outlined in the Group Management Report. Please refer to the section "Report on risks and opportunities".

## Remuneration of the Management Board

The remuneration of the members of the Management Board Members is determined by the Supervisory Board. Regular reviews are conducted. The remuneration is comprised of a fixed component, a variable bonus, long-term performance-related remuneration components in the form of stock options, as well as contributions in terms of company car remuneration, insurance premiums and pension schemes.

In accordance with the statutory provisions, the remuneration of each individual member of the Management Board is disclosed in the Group Management Report under the section "Remuneration Report – Management Board". Moreover, this section includes explanations of the kind and structure of the remuneration of the Management Board as well as details on commitments in case of the termination of the contract of Management Board members. Reference is made to the detailed statements in the Group Management Report, which forms an integral part of this Corporate Governance Report.

### Remuneration of the Supervisory Board

The remuneration of the Supervisory Board is laid down in the Articles Of Association of PAION AG. Members of the Supervisory Board receive a basic remuneration and attendance fees in addition to the reimbursement of their expenses. Performancerelated remuneration for the members of the Supervisory Board is currently not envisaged. The basic annual remuneration amounts to EUR 20,000 and the attendance fee to EUR 1,000. Meetings that are held in the form of conference calls are not taken into consid-eration in the calculation of the attendance fee. The Chairman of the Supervisory Board receives double and the vice-Chairman one and a half times the basic remuneration and attendance fee. The attendance fee is paid for a maximum of five meetings per year. The remuneration paid to each individual member of the Supervisory Board is presented in the Group Management Report in the section "Remuneration Report -Supervisory Board". Reference is made to the detailed statements in the Group Management Report, which at the same time form an integral part of this Corporate Governance Report. The members of the Supervisory Board did not receive any remuneration or compensation for services rendered individually, in particular consultancy and agency services, in the financial year 2017.

Share transactions by and shareholdings of the members of the Management Board and the Supervisory Board

In accordance with Section 19 of the Market Abuse Regulation, members of the Management Board, the Supervisory Board and persons associated with them are required to disclose the selling or buying of PAION AG shares if the value of the combined transactions reaches or exceeds EUR 5,000 in any calendar year. These transactions are published by PAION AG immediately on the company's website and notified to the Federal Financial Supervisory Authority. In the fiscal year 2017, notifiable transactions were reported by Dr. Wolfgang Söhngen on 17 February 2017 and on 07 March 2017.

As of 31 December 2017, Dr. Wolfgang Söhngen held 1.06 % (648,546 voting rights) of the shares in PAION AG. This equity interest includes 0.01 % (6,425 voting rights) of the shares in PAION AG held by Dres. Söhngen Beteiligungs GmbH, in which Dr. Wolfgang Söhngen holds 50 %. The other members of the Management and Supervisory Board did not own any shares in PAION AG as of 31 December 2017.

### Share-based incentive systems

PAION AG introduced the Stock Option Plans 2008, 2010, 2014 and 2016 as remuneration components with long-term incentives and risk characteristics. The Stock Option Plans allow for stock options to be granted to members of the Management Board as well as employees. The precise structure of these plans as well as the options issued to date within the framework of these plans are presented in the notes to the Consolidated Financial Statements in section "Other Disclosures" under "Stock Option Plans". Furthermore, the explanations in the Group Management Report in the section "Remuneration Report - Management Board" contain statements on the value of the options granted to the members of the Management Board. Reference is made to the statements in the notes to the Consolidated Financial Statements and the Group Management Report, which at the same time form an integral part of this Corporate Governance Report.

## Aachen, March 2018

## The Management Board of PAION AG

Dr. Wolfgang Söhngen Abdelghani Omari

Dr. Jürgen Beck

## The Supervisory Board of PAION AG

Dr. Jörg Spiekerkötter John Dawson

Dr. Karin Dorrepaal Dr. Dr. Irina Antonijevic

Dr. Chris Tanner

# Declaration of Conformity with German Corporate Governance Code

Pursuant to section 161 of the German Stock Corporation Act (AktG), the Management Board and the Supervisory Board of PAION AG have an obligation to declare annually that the company has complied and is complying with the recommendations of the latest version of the "Government Commission on the German Corporate Governance Code" (the "Code") published by the Federal Ministry of Justice in the official section of the Federal Gazette, or which of the recommendations have not been or are not being applied and why.

Pursuant to section 161 of the German Stock Corporation Act, the Management Board and the Supervisory Board of PAION AG declare: Since the last declaration of conformity in December 2016, PAION AG complied with all recommendations of the Code in the version dated 05 May 2015, with the following exception that subsisted until 19 June 2017:

## Formation of committees (clause 5.3.3)

The Code recommends that the Supervisory Board shall form a Nomination Committee, composed exclusively of shareholder representatives, which proposes suitable candidates to the Supervisory Board for its recommendations to the General Meeting. The Supervisory Board of PAION AG previously consisted of three members. The nomination of candidates was carried out by the whole Supervisory Board, so that the Supervisory Board had refrained from forming a Nomination Committee.

Since 12 June 2017 the Supervisory Board consists of five members. Following resolution dated 19 June 2017 the Supervisory Board of PAION AG formed a Nomination Committee in fulfilment of the recommendation of number 5.3.3 of the Code.

On 07 February 2017 the "Government Commission on the German Corporate Governance Code" agreed on a revised version of the Code that was published in the Federal Gazette on 24 April 2017. PAION AG complies and continues to comply, with exception of aforementioned non-compliance with the recommendation for the formation of a Nomination Committee under number 5.3.3 of the Code that subsisted until 19 June 2017, with all recommendations of the revised 2017 Code.

Aachen, December 2017

### **Supervisory Board of PAION AG**

The Supervisory Board of PAION AG
Dr. Jörg Spiekerkötter, Chairman of the Supervisory Board

### The Management Board of PAION AG

Dr. Wolfgang Söhngen, Chairman of the Management Board Abdelghani Omari, Member of the Management Board

## **Investor Relations**

## **Investor Relations**

Our vision is to become an acknowledged "PAIONeer" in sedation and anesthesia helping to advance patient care. In respect to corporate communications, we place great emphasis on transparent, comprehensive and timely communication. Information on significant developments within the company is made available immediately and simultaneously to all stakeholders.

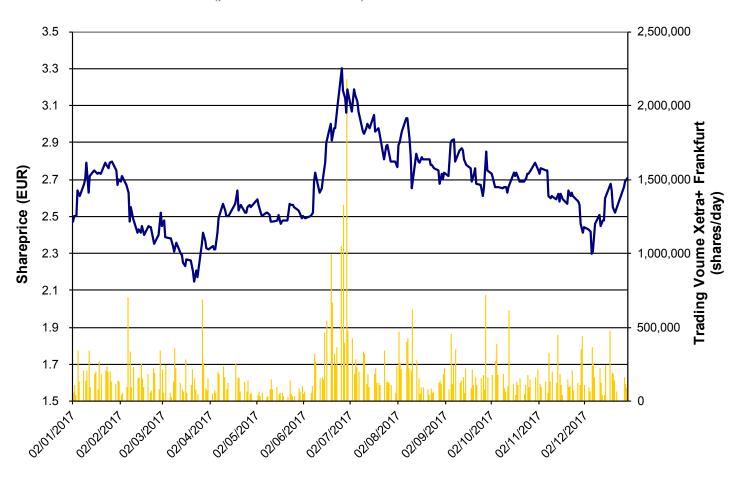
PAION is listed in the Prime Standard segment of the Frankfurt Stock Exchange and therefore also fulfills extended disclosure requirements in addition to the ad-hoc disclosure obligations.

## Performance of PAION shares in 2017

PAION shares opened 2017 with a Xetra price of EUR 2.45. The highest price was reached on 26 June 2017 at EUR 3.30 as a result of very positive Phase III data in the U.S. bronchoscopy trial, while the low was EUR 2.15 on 22 March 2017 (both Xetra). The closing price on 29 December 2017 was EUR 2.71 (Xetra). This represents a premium of approx. 11% compared to the closing price of 30 December 2016 (EUR 2.45; Xetra). This means that PAION has been able to increase its share price in each year since 2014 compared to the previous year.

The market capitalization of PAION AG at the end of the financial year amounted to EUR 166 million (31 December 2016: EUR 137 million). Thereby PAION increased its market capitalization for the sixth consecutive year since 2011.

## Xetra Stock Performance in 2017 (price and volume in EUR)



## Annual General Meeting and analyst conference

At the Annual General Meeting, held in Aachen on 17 May 2017, we welcomed about 100 shareholders and guests. The shareholders present owned 25% of PAION's shares (previous year: 16%). All proposals were approved with a large majority.

As in previous years, PAION AG used the German Equity Capital Forum on 27 November 2017 to host its annual analyst conference which made a great impression.

## Analyst coverage

The following analysts regularly publish reports on PAION:

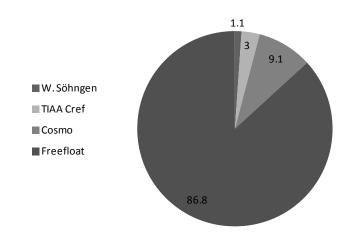
- Igor Kim (ODDO BHF)
- Dennis Hulme (Edison Investment Research)
- Simon Scholes (First Berlin)

Selected analyst reports are available under the investor relations section of the PAION website (http://www.paion.com/media-and-investors/information-on-shares/analysts/).

### Shareholder structure

PAION is characterized by a very high free float of approximately 87%. Cosmo Pharmaceuticals N.V., Amsterdam, Netherlands, is the largest single shareholder, owning 9.09% of PAION shares, pursuant to the available notifications (30 June 2016).

The current share capital amounts to EUR 61,120,046.



## Do you have any questions about PAION?

Please contact our investor and public relations team:

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# Group management report for fiscal year 2017

## Fundamental information of PAION AG and the PAION Group

## I. Business model of PAION AG and PAION Group

PAION AG is a publicly listed specialty pharmaceutical company developing and aiming to commercialize innovative drugs to be used in out-patient and hospital-based sedation, anesthesia and critical care services. PAION AG is a holding company exclusively providing management and other services to its subsidiaries. These services primarily focus on the development of the group strategy, administrative tasks, including accounting, legal, human resources, public relations, and controlling. In addition, PAION AG supports the financing of its subsidiaries' ongoing business activities, while the Group companies provide each other with development-related services. The activities of the PAION Group (hereinafter also referred to as PAION) are mainly determined by the development operations of the subsidiaries, particularly PAION UK Ltd, which are presented below.

PAION's portfolio exclusively comprises the drug candidate remimazolam. The product candidates M6G and GGF2 are not in active development and are therefore no significant value drivers in the portfolio of PAION group. M6G is licensed to Yichang Humanwell for the Chinese market. GGF2 is licensed to Acorda Therapeutics, Inc. (Acorda).

For remimazolam which is already in the final stage of clinical development in two of the three indications explained in more detail in the following, PAION has license partners in the U.S., China, South Korea, Canada, Russia/CIS, Turkey, the MENA region and Japan.

Fiscal year 2017 was marked by the concentration of PAION on the continuation of the development of remimazolam, in particular the completion of the U.S. Phase III development, as well as the preparations of an EU Phase III study and a market approval dossier in Japan.

## 2. Internal management system of PAION AG and PAION Group

Financial performance indicators are liquidity (cash and cash equivalents from the balance sheet and cash flows from the cash flow statement), equity, revenues, research and development expenses, general administrative and selling expenses, and the number of employees. The financial management system of PAION and the PAION Group is based on monthly reports on a cost centre and cost unit basis that also show deviations from budget of the financial performance indicators. Significant deviations are updated in the short- and long-term corporate planning. Moreover, the planned development progress is checked against the planned budget. By simulating different scenarios, the planning tool used for this purpose enables management to identify and assess opportunities and risks at an early stage and determine their influence on the future development of the group, particularly with regard to the key financial performance indicator liquidity.

The non-financial performance indicators essential for PAION's business activity mainly arise from the development and commercial activities. The clinical, non-clinical, regulatory and production development activities are characterized by the involvement of external service providers. The management of the development activities is based on using detailed project plans that

contain defined work packages associated with specified reporting and information obligations. In this regard, the data generated in the course of the development of remimazolam in respect to positioning in comparison to competing products, the development progress as well as the relevant data for an aimed approval in respect to safety and efficacy are of specific interest. The results are continuously processed in the internal project teams and reported to the Management Board.

Commercial and licensing activities aim at the subsequent commercialization of remimazolam by PAION (in the EU) or partners. The progress of these activities is being documented and discussed continuously. PAION has already signed several regional license agreements. The cooperation partners operate independently in their respective license territory. However, the cooperation agreements require the partners to exchange relevant information. Development in the U.S. has been conducted by PAION and will be handed over to U.S. license partner Cosmo Pharmaceuticals (Cosmo) after the development program agreed with the U.S. regulatory authority FDA (Food and Drug Administration) including subsequent reports and necessary analyses has been completed. Cosmo will then be responsible for all further activities in the U.S.

The central coordination of the information flow worldwide between the license partners is managed by PAION. All activities are monitored and are being reviewed and reported to the Management Board continuously.

## 3. Research and Development

The business of PAION is driven mainly by the research and development activities which are described in detail in Section 2. "Presentation of the course of business and development activities".

### Report on economic position

- 1. Macroeconomic and sector-specific environment
- a. Macroeconomic development

German economy has continued its growth also in 2017 with an increase of the gross domestic product (GDP) of 2.2% that even exceeded prior year's growth of 1.9%. Particularly investments with an increase of 3.6% but also consumption with an increase of 1.9% essentially pushed growth. <sup>1</sup>

<sup>1</sup> Federal Statistical Office: WISTA 1/2018 – Bruttoinlandsprodukt 2017.

An upswing has also manifested in the EU and globally <sup>2</sup> and seems to persist in 2018. EU GDP increased by 2.5% in 2017 and growth on a comparable level is expected for 2018 as well.<sup>3</sup> World GDP should have grown by approx. 3.7% in 2017; an increase of about 3.9% is anticipated for 2018.<sup>4</sup> For Germany, an increase of economic output of about 2.5% particularly pushed by private consumption is expected for 2018.<sup>5</sup>

Uncertainty especially prevails in regard to a potential so-called Brexit and international protective tendencies but does not seem to have curbed economy so far. Instead, the ECB's continuing expansive monetary policy allows for continuous growth in the EU. <sup>6</sup> Moreover, the U.S. tax reform has a stimulating effect on economy growth also beyond U.S. borders. <sup>7</sup> After a considerable increase of 2.3% in 2017, U.S. GDP is expected to grow by 2.7% in 2018 essentially pushed by the passed tax reform. <sup>8</sup>

In spite of positive growth forecasts in the short term, in the mid-term the outlook is curbed by geopolitical tensions, political uncertainty particularly in important emerging markets and still existing international protective tendencies which could be reflected in changes to the North American Free Trade Agreement currently in negotiation or conditions of the Brexit for instance. <sup>9</sup>

Stock markets also reflect the positive economic development in 2017. The DAX increased by 12.5% in comparison to the prior year's end closing value; the EUROSTOXX 50 showed at least a plus of 6.5%. In the U.S., the high increase of the Dow Jones amounting to 25.1% reflects a significant impact of the decrease of corporation tax enacted in course of the U.S. tax reform on valuation.

## b. Development of the pharmaceutical and biotechnology industry

The pharmaceutical and biotechnology industry continues to be marked by increasing costs for pharmaceutical development, lower income from formerly high-selling products and persisting price pressure not only stemming from increased competition by faster and more drug approvals for instance but also resulting from health reforms and law changes. <sup>10</sup> Average development costs of a new drug increased by approx. 29% in 2017 only. <sup>11</sup> Worldwide transaction volume in the pharmaceutical industry decreased by 44% in 2017 from a total of USD 201 billion in the previous year which should apparently be attributable to uncertainty in regard to the eventual design of the U.S. tax reform and potential new laws in the context of the U.S. health reform to a significant extent. <sup>12</sup>

- <sup>2</sup> German Institute for Economic Research: DIW Konjunkturbarometer Januar 2018: Deutsche Konjunktur im Höhenflug, press release dated 31 January 2018.
- <sup>3</sup> Commerzbank Research: Economic and Market Monitor Chart Book February 2018.
- <sup>4</sup> International Monetary Fund: World Economic Outlook Update, 22 January 2018.
- <sup>5</sup> Commerzbank Research: Economic and Market Monitor Chart Book February 2018.
- <sup>6</sup> Commerzbank Research: Economic and Market Monitor Chart Book February 2018.
- <sup>7</sup> International Monetary Fund: World Economic Outlook Update, 22 January 2018.
- <sup>8</sup> Commerzbank Research: Economic and Market Monitor Chart Book February 2018.
- International Monetary Fund: World Economic Outlook Update, 22 January 2018.
- Ernst & Young: Increased competition from new entrants, new sources of capital to lift life sciences M&A in 2018, San Francisco, 08 January 2018; PwC Health Research Institute: Top health industry issues of 2018 A year of resilience amid uncertainty, 2017; Deloitte: 2018 global life sciences outlook Innovating life sciences in the fourth industrial revolution: Embrace, build, grow, 2018.
- <sup>11</sup> Deloitte Centre for Health Solutions: A new future for R&D? Measuring the return from pharmaceutical innovation 2017, 2018.
- <sup>12</sup> Ernst & Young: 2018 M&A Firepower Report: Life Sciences Deals and Data, 2018.

Compared to the previous year, the financing environment for the pharmaceutical and biotechnology industry has improved in 2017 after a low in the first quarter. In Europe, financing volume increased to EUR 5.1 billion by approx. 54% compared to the prior year; funds raised through IPOs increased by 47% to EUR 0.8 billion. <sup>13</sup> In the U.S., funds raised through IPOs roughly doubled compared to the previous year. <sup>14</sup> The financing volume of biotech companies reached an all-time high of EUR 0.66 billion in Germany. <sup>15</sup> This development is also reflected in the valuation of pharmaceutical companies: While the DAXsubsector Biotechnology Index increased by a total of 15.5% in 2017 compared to the prior year's end closing value, the NASDAQ Biotechnology Index even showed a plus of 21.1% in 2017.

The significant competitive drivers are expected to also persist in 2018 and to further increase consolidation pressure. But not only intensifying competition and continuously increasing challenges, for instance in regard to regulatory requirements, digitalization or individualization of therapies, also the availability of significant amounts of funds due to the tax cut on repatriation of income held outside the U.S. enacted in course of the U.S. tax reform, could increase the global acquisition and transaction volumes in the pharmaceutical industry worldwide. <sup>16</sup> For this reason and under consideration of the general economic upswing, the positive financing environment is expected to persist in 2018. <sup>17</sup>

### 2. Presentation of the course of business and development activities

The development portfolio of PAION Group essentially comprises the lead compound remimazolam with its three indications procedural sedation, general anesthesia and ICU sedation.

### Remimazolam

Remimazolam is an ultra-short-acting intravenous benzodiazepine sedative/anesthetic that has already shown positive results in clinical Phase III trials. In the human body, remimazolam is rapidly metabolized to an inactive metabolite by tissue esterases and not metabolized by cyto-chrome-dependent hepatic pathways. Like other benzodiazepines, remimazolam can be reversed with flumazenil to rapidly terminate sedation and anesthesia if necessary. During clinical studies, remimazolam demonstrated efficacy and safety in over 1,700 volunteers and patients. Data so far indicate that remimazolam has a rapid onset and offset of action combined with a favorable cardio-respiratory safety profile.

<sup>&</sup>lt;sup>13</sup> Biocom AG: European biotech stocks with strong growth, press release dated 12 January 2018.

 $<sup>^{\</sup>rm 14}$  BioPharma Dive: Biotech IPOs show no signs of slowing down in 2018, 18 December 2017.

<sup>&</sup>lt;sup>15</sup> BIO Deutschland: Trends in der deutschen Biotechnologie-Branche 2018, 24 January 2018.

Ernst & Young: Increased competition from new entrants, new sources of capital to lift life sciences M&A in 2018, San Francisco, 08 January 2018; PwC Health Research Institute: Top health industry issues of 2018 – A year of resilience amid uncertainty, 2017; Rx Securities: Sector Note Biotechnology, 02 January 2018.

<sup>&</sup>lt;sup>17</sup> BioPharma Dive: Biotech IPOs show no signs of slowing down in 2018, 18 December 2017; Rx Securities: Sector Note Biotechnology, 02 January 2018.

Remimazolam is in the final stage of clinical development for procedural sedation in the U.S. Currently, an integrated overall analysis of all clinical studies with remimazolam is being conducted in preparation of Cosmo's filing for market approval. After completion of the development for procedural sedation, Cosmo will be responsible for any further development activities in the U.S. The U.S. license partner currently plans to file for market approval in procedural sedation in the fourth quarter 2018/first quarter 2019. A full clinical development program for general anesthesia was completed in Japan, and the remimazolam license partner for this region, Mundipharma, is planning filing for market approval in this indication in Japan in 2018. In Europe, it is planned to start a Phase III study in general anesthesia in the second half of 2018 which can be expected to be the only necessary outstanding trial for filing for market approval in Europe based on the scientific advice obtained from the European Medicines Agency (EMA) in January 2018.

Based on the positive results of a Phase II study, ICU sedation beyond 24 hours is another possible attractive indication for further development in the EU by PAION as well as by partners in the licensed territories.

Remimazolam is partnered in the U.S., Canada, China, Russia (CIS), Turkey, the MENA region, South Korea and Japan with Cosmo, Pharmascience (Pendopharm), Yichang Humanwell, R-Pharm, TR-Pharm, Hana Pharm, and Mundipharma, respectively. For all other markets outside the EU, remimazolam is available for licensing.

### **Procedural Sedation (U.S. lead indication)**

Based on external sources (Symphony Health Solutions, Centers for Disease Control and Prevention) and own projections, PAION estimates that approximately 43 million procedures using procedural sedation took place in the U.S. in 2013, predominantly outside the hospital setting.

The growth of the procedural sedation market in the U.S. has been driven for many years by the increase in medical interventions requiring procedural sedation, such as colonoscopies, as well as an increase in general demand for preventive screenings. According to iData Research, which examines historical trends and creates procedure forecasts in the U.S. drawing from an extensive collection of national- and state-level procedure databases, 26.7 million colonoscopy and endoscopy claims were reported in 2015 in the U.S., and the number is expected to grow at an average rate of 2.6% annually through 2020. PAION estimates that 75% of the colonoscopies and endoscopies claimed were conducted in an out-patient setting.

Regular endoscopic screening for people aged 50 or older is recommended and covered by all major health insurance plans, including those under the Centers for Medicare and Medicaid Services ("CMS"), a U.S. federal agency that administers Medicare (the national social insurance program), since effective prevention is considered to reduce the likelihood of incidence of illnesses such as cancer, thereby reducing the suffering of patients and related financial burden to be borne by the payors. Statistics show that the rate at which people are diagnosed with colon cancer in the U.S. has dropped by 30% between 2005 and 2015 for those aged 50 years and older, partly due to more people getting recommended screening tests. Colorectal cancer is the third most diagnosed

cancer and the third leading cause of cancer death in the U.S. Despite the decrease of colorectal cancer death rates as a result of early screening and detection, it was reported in 2010 that only 59% of people aged 50 or older, for whom screening is recommended, reported having received colorectal cancer testing consistent with current guidelines. The market for endoscopies in gastroenterology represents the most lucrative market segment for remimazolam in procedural sedation with approximately 20 million procedures per year in the U.S.

Currently, the most widely used products in procedural sedation are propofol and midazolam – both generic. PAION estimates that these two drugs each have a market share of approximately 50% in terms of volume of procedures performed in the out-patient market for colonoscopies in the U.S. The propofol label mandates the presence of an anesthesia professional throughout the procedure due to propofol's potential for respiratory- and cardio-depressive effects, which results in additional cost. For midazolam, these side effects are less pronounced and have a different relevance, since an undesirably deep sedation can be reversed with flumazenil. Midazolam has a slower onset and a longer duration of action which can impact patient throughput and overall efficiency.

In the U.S. increased enrollment and screenings are expected to result in a performance-based payment system that will seek to better align payments with high quality of care measures. This would imply that cost-efficient medicines with clinical value will be used more extensively and that continued premium will be placed on innovative medicines with strong clinical profile. Thus, PAION believes that concerns related to the overall cost of procedures, driven by the need for anesthesia professionals monitoring during procedures using agents such as propofol, will impact the choice of drug products for procedural sedation. Costs related to anesthesia services in gastrointestinal endoscopy procedures alone were estimated at USD 1.3 billion in 2009. Accordingly, PAION expects reimbursement regimes under national and commercial healthcare systems, such as Medicare, which differentiate the amounts reimbursed to physicians and/or patients depending on whether an anesthesia professional's service is used, may also positively impact the demand for products that do not require monitoring by an anesthesia professional.

PAION believes that remimazolam, subject to FDA approval with a safety labeling comparable to that of midazolam, could benefit from the pending changes in payment policies. Provided that it could be administered under the supervision of a proceduralist, remimazolam would be able to offer a competitive alternative to midazolam. This is based on its enhanced efficiency profile compared to midazolam.

### General Anesthesia (Japan + EU lead indication)

Based on publicly available European procedure statistics and market research, PAION estimates that in the EU, approximately 29 million procedures requiring general anesthesia are performed each year. Of these, approximately 10 million are performed for high-risk patients (American Society of Anesthesiologists ("ASA") classifications III or higher) who are particularly prone to hemodynamic instability. Approx. 55% of all anesthesias are balanced anesthesia (a combination of intravenous agents for induction and volatile gases for maintenance), approx. 20% are total intravenous anesthesias ("TIVA") using propofol, and the remaining approx. 25% include regional

anesthesia (for example epidural administration). Based on PAION's market research in the EU, the current standard-of-care drugs for general anesthesia are propofol (especially for induction) and narcotic gases; mostly used in conjunction with intravenous opioids.

Patient demographics in the EU will presumably continue to evolve driven by the aging population. PAION anticipates an increasing number and complexity of medical interventions requiring induction and maintenance of anesthesia in the EU in the future also driven by an ongoing ageing of the population. General anesthesia is more frequently offered to elderly patients than in the past, therefore the choice of a tailored anesthesia is made depending on the type of surgery, the underlying disease, and an assessment of the general physical health of the patient, including co-morbidities.

Accordingly, PAION believes that in the EU the demand for safer agents with low respiratory and cardio-depressive effects will increase over the coming years, creating opportunities for anesthetics with an enhanced safety profile such as remimazolam, even at higher prices compared to existing generic drugs. PAION also expects similar developments for the U.S. and other important international markets, subject to further market research.

### Intensive care unit (ICU) sedation

Plans for further development of remimazolam for use in ICU sedation in the future are based on PAIONs expectation that the market for ICU sedation will present an attractive business opportunity. Based on available information from 2012 published in Critical Care Medicine which estimates average days of care in ICUs per year in the U.S., and journal articles published in the Intensive Care Medicine in 2012, which records, among others, the volume of ICU admissions per year and the number of total adult beds in various countries in the EU, PAION estimates that there are approximately 14 million ICU patient days requiring ICU sedation in the U.S. and EU combined per year. PAION expects this number to increase in the years to come, driven by demand from the aging population in both regions. PAION believes that such development, in turn, will foster demand for safer agents such as remimazolam, given the fact that elderly patients are much more likely to suffer from systemic health problems.

Internationally renowned anesthesiologists have repeatedly confirmed to PAION that ICU sedation might bear the biggest market potential of all remimazolam indications. However, development would be associated with the highest risk of side effects given the treatment of severely ill patients. For this reason, initially development in general anesthesia has priority for PAION. Development for ICU sedation requires additional funds.

Another field of high clinical need is pediatric use, which is a development requirement for both the EU and U.S. after the respective first approval. For pediatric development in the EU, further funds will be required.

# **Clinical development**

Over 1,700 volunteers/patients treated with remimazolam		
Phase II and III studies	Phase I studies	
Procedural Sedation (U.S.) - completed		
Phase IIa Single bolus in upper GI endoscopy (100)	Phase I Single bolus in healthy volunteers (81)	
Phase IIb Multiple bolus in colonoscopy (161)	Phase Ib Multiple bolus in volunteers undergoing colonoscopy (51)	
Phase III in colonoscopy (461)	Phase I Renal Impairment (22)	
Phase III ASA III/IV in colonoscopy (79)	Phase I Thorough QT (54)	
Phase III in bronchoscopy (446)	Phase I Abuse Liability	
	• Intravenous administration (40)	
	Oral bioavailability (14)	
	Oral administration in combination with alcohol     (20)	
	• Intranasal administration (12)	
General Anesthesia	(Japan) - completed	
Phase II Induction and maintenance of anesthesia in general surgery (85)	Phase I Bolus in healthy volunteers (42)	
Phase II/III Induction and maintenance of anesthesia in general surgery (375)	Phase Ib Infusion in healthy volunteers (10)	
Phase III in ASA III or higher surgical patients (62)	Phase I Hepatic impairment (U.S.) (20)	
General And	esthesia (EU)	
Phase II in cardiac surgery patients (90)	Phase I PK/PD modeling study (EEG) in healthy volunteers (20)	
Phase III in cardiac surgery patients (23)**		
Phase III in general surgery (approx. 450–500)*		
ICU Sedat	ion (Japan)	
Phase II in ICU patients (49)**		
-		

Patient/volunteer numbers in brackets

- \*) Study not yet started
- \*\*) Discontinued studies, no safety concerns

### Procedural sedation (Lead indication U.S.)

Remimazolam currently is in preparation for the filing process in procedural sedation in the U.S. With a total of eight Phase I, two Phase II and three Phase III trials PAION deems the clinical development program for remimazolam in procedural sedation in the U.S. completed.

The first in-human trial explored a broad range of doses from no effect to loss of consciousness (not wanted for procedural sedation but indicative for induction of general anesthesia). Based on this trial, the next set of trials covered a colonoscopy study in healthy volunteers and a Phase IIa study in upper GI endoscopy. These studies confirmed the need for an approximately 50% dose reduction in combination with opioids (colonoscopy) and were the basis for the Phase IIb study in colonoscopy patients. In this study, a fixed dose regime consisting of starting dose and top-ups was tested with the lowest of the starting doses which was selected for use in the Phase III program.

In March 2015, the first U.S. Phase III study was started, the patient recruitment was completed in April 2016, and in June 2016, PAION announced that remimazolam met its primary efficacy endpoint. The Phase III trial enrolled 461 patients at 13 U.S. sites and was designed to evaluate the efficacy and safety of remimazolam compared to placebo (with midazolam rescue) in patients undergoing proceduralist-administered sedation for colonoscopy. In addition, the study had an open-label midazolam arm.

The primary outcome measure was a composite endpoint defined as: no need for rescue medication, completion of the procedure and no more than 5 doses within any 15-minute window. The primary endpoint was reached in 91.3% of the patients in the remimazolam arm and 1.7% in the placebo (including midazolam rescue) arm.

Important secondary endpoints in the remimazolam arm showed a median time from start of medication to start of procedure of 4.0 minutes (placebo 19.5 minutes) and a mean time from end of procedure to return to full alertness of 7.2 minutes (placebo 21.3 minutes). Additionally, time from last dose to "back to normal" as reported by patients on remimazolam was 331 minutes (placebo 572 minutes).

There were no treatment-emergent serious adverse events in the trial. Hypotension was 44.3% with remimazolam and 47.5% with placebo and accounted for most of the adverse events in all study arms. Hypoxia occurred in 1.0% of patients given remimazolam, 3.4% in the placebo arm.

On the Hopkins Verbal Learning Test administered five minutes after reaching the fully alert status, the total raw score, delayed recall, memory retention, and recognition discrimination scores were all better with remimazolam compared to placebo.

Patient satisfaction was similar in all arms of the study.

The open-label midazolam patients showed a median time from start of medication to start of procedure of 19.0 minutes and a mean time from end of procedure to return to full alertness of 15.7 minutes. Midazolam patients took 553 minutes to be back to normal.

In addition to the above study, the U.S. Phase III program includes a second confirmatory, prospective, double-blind, randomized, placebo-controlled multi-center trial with an open-label midazolam arm in 446 patients undergoing bronchoscopies.

In June 2015, the study was started, the patient recruitment was completed in March 2017, and in June 2017, PAION announced that the primary efficacy endpoint was met. The Phase III trial enrolled 446 patients at 15 U.S. sites and was designed to evaluate the efficacy and safety of remimazolam compared to placebo (with midazolam rescue medication) in procedural sedation in patients undergoing bronchoscopy.

The primary outcome measure was a composite endpoint defined as: no need for rescue medication, completion of the procedure and no more than 5 doses within any 15-minute window for remimazolam/placebo and no more than 3 doses within any 12-minute window for midazolam. The primary endpoint was reached in 82.5% of the patients treated in the remimazolam arm and 3.4% in the placebo arm (p-value of <0.0001). Important secondary endpoints included median time from start of medication to start of procedure (5.0 minutes in the remimazolam arm versus 17.0 minutes for placebo) and median time from end of procedure to return to full alertness (remimazolam 6.0 minutes versus placebo 14.0 minutes). Additionally, the patients' subjective impression of time from last dose to "back to normal" was a median of 404 minutes for remimazolam versus 935 minutes for placebo.

In the open-label midazolam arm, procedural success was achieved in 34.8% of patients. Midazolam patients showed a median time from start of medication to start of procedure of 16.0 minutes and a median time from end of procedure to return to full alertness of 12.0 minutes. Additionally, time from last dose to "back to normal" as reported by patients on midazolam was a median of 479 minutes.

As part of the U.S. development program, also a safety study in ASA III/IV patients undergoing colonoscopy (American Society of Anesthesiologists classification) was performed. In December 2016, successful completion of patient recruitment was announced, and in March 2017, PAION announced positive headline data from the U.S. clinical safety trial of remimazolam in ASA III/IV patients (American Society of Anesthesiologists classification) undergoing colonoscopy. The trial enrolled 79 patients and was designed to evaluate the efficacy and safety of remimazolam compared to placebo (with midazolam 'rescue' sedation) in patients undergoing proceduralist-supervised sedation for colonoscopy. This study also included an open-label arm in which midazolam was dosed according to U.S. label. The trial confirmed remimazolam's safety profile and tolerability shown in all previous studies in a more vulnerable patient population. Overall, remimazolam demonstrated good respiratory and cardiovascular stability as compared to placebo with midazolam rescue. No adverse events of concern were observed in either group. In addition, the efficacy and efficiency improvements were comparable to the two positive pivotal U.S. Phase III trials in colonoscopy and bronchoscopy patients. Success of the procedure (including no requirement for rescue medication and the application of not more than five doses in any 15-minute interval) was achieved in 84.4% of patients in the remimazolam arm and 0% in the placebo arm. Other relevant endpoints showed a median time from start of medication to start of procedure of 5.0 minutes for remimazolam (placebo: 18.5 minutes) and a median time from end of procedure to return to full alertness of 3.0 minutes (placebo: 5.0 minutes). By comparison, procedural success was achieved in 12.9% of the midazolam patients. Midazolam patients showed a median time from start of

medication to start of procedure of 19.0 minutes and a median time from end of procedure to return to full alertness of 7.0 minutes.

#### Summary of headline data of the three Phase III studies:

	Remimazolam	Placebo	Midazolam (Open Label)*
Primary endpoint achieved	82.5-91.3%	0.0-3.4%	12.9-34.8%
Time from start of medication	4.0-5.0 min	17-19.5 min	16.0-19.0 min
to start of procedure			
Time from end of procedure to	3.0-7.2 min	5.0-21.3 min	7.0–15.7 min
fully alert			
Time to back to normal	331–404 min	572-935 min	478.5–553 min

<sup>\*)</sup> not part of label claim

Based on the results of preclinical and Phase I studies and in consultation with the FDA, PAION conducted additional Phase I studies to further assess the abuse potential of remimazolam. Two aspects were being studied: if remimazolam could inappropriately be used as a knock-out cocktail in combination with alcohol and if it could be abused intranasally. In November 2017, the FDA informed PAION that it determines the abuse liability program conducted by PAION as sufficient to provide the necessary data regarding the abuse potential of remimazolam in humans. PAION therefore assumes the clinical development program for remimazolam in procedural sedation in the U.S. as completed.

#### General anesthesia (Lead indication in Japan + EU)

A total of four Phase I (Japan and EU), two Phase II (Japan and EU) and two Phase III (Japan) trials in general anesthesia have been completed. In the clinical program, specific attention was paid to hemodynamic stability, which addresses a current need in general anesthesia. Preclinical data had suggested and clinical data confirmed that a better hemodynamic stability can be reached with remimazolam than with propofol.

The Japanese program started with a comparative Phase I study building on PAION's first human trial and showed an identical pharmacokinetic and pharmacodynamic profile. The next step was a continuous infusion Phase I study to define induction and maintenance doses for anesthesia. The doses for induction and maintenance identified as safe and effective in the Phase II study subsequently conducted were then used in the Japanese Phase III studies, which confirmed remimazolam's efficacy and safety as a general anesthetic and its favorable hemodynamic profile compared to propofol.

A pre-NDA meeting (NDA = New Drug Application) with the Japanese Pharmaceuticals and Medical Devices Agency ("PMDA") took place in January 2016. The PMDA stated that the non-clinical and clinical data package of remimazolam were regarded as complete for filing in the indication "Induction and maintenance of general anesthesia" in Japan. The PMDA had already confirmed

earlier that both the raw materials produced by PAION in Europe as well as the finished formulation of remimazolam fulfill the requirements for filing in Japan. Based on the positive feedback by the Japanese authority, PAION has started preparations for a market approval dossier for remimazolam. In course of the license agreement for remimazolam in Japan entered into in December 2017, Mundipharma has now taken over these tasks with PAION's support.

In order to allow using the Japanese data for filing in the EU, the same induction and maintenance doses were used in the European Phase II trial performed in 2014, delivering further evidence for a potentially beneficial hemodynamic profile of remimazolam. The primary efficacy endpoint for general anesthesia was achieved in 98% of patients in the remimazolam dose groups and 96% in the propofol/sevoflurane group demonstrating an excellent efficacy rate across all treatment groups. As expected, the onset and offset of action profile was comparable between all treatment groups, showing that remimazolam indeed shares the fast-acting sedative profile of propofol.

One of the key targets of this trial was to assess the hemodynamic stability during cardiac surgery with remimazolam when compared to propofol/sevoflurane, both of which are known to cause cardiac depression. The study evaluated a substantial number of parameters to analyse these effects. Remimazolam confirmed the improved hemodynamic stability that had already been shown in the Ono Phase III study.

Based on these positive data, a multi-national, multi-center, randomized, single-blind, propofol-controlled, confirmatory Phase III study in patients undergoing major cardiac surgery was started in the EU in August 2015. Due to the complex study design in cardiac surgery, the trial faced recruitment challenges. Despite intensive efforts to enhance patient recruitment, the trial proved to be difficult to implement in practice. Therefore, in February 2016, PAION decided to discontinue the trial in order to avoid a long and expensive study with the existing design. No drug-related serious adverse events were observed.

In the meantime, PAION evaluated how to resume the clinical development of remimazolam in the EU. In consultation with key opinion leaders in general anesthesia, PAION has successfully conducted a Phase I trial which served as a means to define key elements and sample size calculation for the planned Phase III trial. Based on the results of this study, subsequent simulations and scientific advice obtained from the European authority EMA for defining the new European Phase III program, PAION currently assumes that approximately 450 to 500 patients will be required for the EU Phase III study in general anesthesia.

PAION plans a study design in general surgery close to the successfully completed Phase III program in general anesthesia in Japan, but in sicker patients, where the medical need to reduce hypotensive events is greater. PAION currently plans the study start in the second half of 2018.

#### **ICU** sedation

PAION's former partner in Japan, Ono, independently initiated a Phase II trial for sedation in intensive care units (ICUs). Higher than by Ono expected plasma concentrations of remimazolam were observed in isolated cases after long-term treatment as is known from similar substances, and Ono

discontinued this exploratory trial in 2013. Patients were sedated successfully and no significant unexpected adverse events were reported.

The observed phenomenon of elevated remimazolam plasma concentrations was subsequently thoroughly investigated using a series of preclinical tests and pharmacokinetic models. None of these experiments was able to reproduce the findings or provide a mechanistic explanation for the elevated plasma concentrations. Further analysis has revealed that such pharmacokinetic deviations are common for utilization of sedatives like midazolam and propofol on the ICU and the most likely explanation is the underlying serious condition of patients presenting on the ICU. Further development of the program "ICU sedation" is part of the future remimazolam development plan which could be addressed after availability of required funds.

#### **Partnerships**

PAION selectively seeks to enter into development and commercialization collaborations with partners with local expertise or with a specific therapeutic focus with respect to remimazolam. Such collaborations are an effective way of funding and advancing remimazolam's late-stage development and of assisting PAION with its commercialization in international markets where PAION does not intend to directly conduct sales and marketing activities. PAION expects that the existing collaboration partners will continue the development of remimazolam on the basis of data generated from our U.S., Japanese and European clinical development programs, and subsequently PAION may receive additional data and payments under the existing agreements in the medium to long term. PAION's ultimate goal is to participate in the worldwide commercialization of remimazolam. In order to exploit remimazolam's full potential, it is PAION's defined target to commercialize remimazolam on its own in the EU or certain markets in the EU immediately after a potential market approval. PAION is also well positioned to find further collaboration partners. Pharmaceutical companies have a growing need to add drugs to their pipeline that have already demonstrated proof of concept in advanced stages of clinical trials and also provide a commercially viable alternative in a global healthcare environment characterized by increasing cost consciousness.

Remimazolam is partnered in the U.S., Canada, China, Russia (CIS), Turkey, the MENA region, South Korea and Japan with Cosmo, Pharmascience (Pendopharm), Yichang Humanwell, R-Pharm, TR-Pharm, Hana Pharm, and Mundipharma, respectively. For all other markets outside the EU, remimazolam is available for licensing.

All license partners have activities ongoing to support future filings in their respective territories with a focus on clinical studies and regulatory interactions.

In May 2017, PAION's remimazolam license partner for Canada, Pendopharm, a division of Pharmascience Inc., together with PAION delegates, had a pre-NDS meeting with Health Canada for remimazolam for the indication conscious sedation. Health Canada is the agency responsible for approving drugs in Canada. During the meeting, the main questions raised for discussion following the preliminary assessment of remimazolam by Health Canada were clarified. Health Canada stated in the meeting that the non-clinical and the clinical data package, including the human abuse liability data available at the time, were regarded as adequate for filing. Currently, PAION expects filing for market approval in Canada after the market approval dossier in the U.S. has been filed.

PAION's Russian remimazolam license partner R-Pharm announced the start of a Phase III study with remimazolam in general anesthesia in Russia in August 2017. Completion of the study is expected still in the first half of 2018. Subsequently, R-Pharm plans filing for market approval which is currently planned end of 2018.

In December 2017, PAION entered into a remimazolam license agreement with Mundipharma in course of which PAION has granted Mundipharma an exclusive license for the development and commercialization of remimazolam in Japan.

Under the terms of the agreement, Mundipharma has the right and obligation to further develop remimazolam in all indications in Japan with PAION's support. Mundipharma will bear all cost for market authorization and distribution. PAION receives a EUR 1 million upfront payment. PAION is also entitled to receive additional payments totaling up to EUR 25 million depending on the achievement of certain regulatory and commercial milestones in the three indications procedural sedation, general anesthesia and Intensive Care Unit (ICU) sedation. PAION is also entitled to receive tiered royalties starting in the low double-digits to over 20% of net sales, depending on sales levels and sales price (National Health Insurance (NHI) price), which will be determined by the Japanese government.

Based on the positive pre-NDA meeting with the Japanese authority, PAION had started preparations for a market approval dossier for remimazolam. Mundipharma has now taken over these tasks with PAION's support. Mundipharma currently plans filing for market approval in Japan in 2018.

PAION's South Korean remimazolam license partner Hana Pharm is going to conduct a Phase III study with remimazolam in general anesthesia in South Korea. Completion of the study is expected in 2018.

PAION's Chinese remimazolam license partner Yichang Humanwell is going to conduct a Phase II study with remimazolam in general anesthesia and a Phase III study with remimazolam in procedural sedation in China.

Upfront and milestone payments					
	Total received	Maximum outstan-	Royalty rates		
Ono, Japan (2007) (terminated in 2015)	USD 8 m	None	None		
Yichang Humanwell, China (2012)	EUR 3 m	EUR 4 m	10%		
Hana Pharm, S. Korea (2013)	EUR 1 m	EUR 2 m	10%		
R-Pharm, CIS (2013)	EUR 1 m	EUR 3 m	Low double-digit		
(T)R-Pharm, Turkey (2013)	EUR 1 m	EUR 3 m	Low double-digit		
(T)R-Pharm, MENA (2014)	EUR 1.5 m	EUR 5.5 m	Low double-digit		
Pendopharm, Canada (2014)	EUR 0.4 m*	~ EUR 3.8 m	Tiered (starting at 15%)		
Cosmo, U.S. (2016)	EUR 20 m**	EUR 42.5 m	20-25%***		
Mundipharma, Japan (2017)	EUR 1 m****	EUR 25 m	Up to over 20%****		
Total	EUR 34.8 m	~ EUR 88.8 m			

- \*)
- This amount relates to the premium received in the course of the private placement in the amount of EUR 4 million in July 2014 which was disclosed as revenues in 2014.

  Comprising EUR 10 million received via private placement in June 2016 and via capital increase with subscription rights conducted in February 2017 as well as the received upfront payment in the amount of EUR 10 million. \*\*)
- Subject to adjustments under specific circumstances, but not below 15% of net sales. Received after the balance sheet date.
- Tiered royalties starting in the low double-digits to over 20%

#### 3. Net assets, financial position and results of operations

#### a. Results of operations

	2017 KEUR	2016 KEUR	Change in result KEUR
Revenues Gross profit	5,811 5,811	4,262 4,262	1,549 1,549
Research and development General administrative and selling Other income (expenses) Operating expenses	-17,853 -3,828 -2 -21,683	-23,408 -5,129 -807 -29,344	5,555 1,301 805 7,661
Operating result	-15,872	-25,082	9,210
Financial result	20	21	-1
Income taxes	3,759	4,943	-1,184
Net result	-12,093	-20,118	8,025

**Revenues** of KEUR 5,811 recognized in the reporting period resulted from the upfront payment of EUR 10 million received from Cosmo in 2016 in the amount of KEUR 5,749 and increased by KEUR 1,549 compared to the previous year. Revenue recognition of the received upfront payment was dependent on the progress of certain development components. Revenues from the remimazolam license agreement for Japan entered into with Mundipharma in the reporting period have been recognized in the amount of KEUR 37.

**Research and development expenses** amounted to KEUR 17,853 and particularly resulted from the U.S. clinical development program for remimazolam in procedural sedation. The decrease of KEUR 5,555 compared to the prior year is mainly due to lower costs for Phase III studies on the one hand and higher costs for Phase I studies on the other hand.

**General administrative and selling expenses** amounted to KEUR 3,828 and decreased by KEUR 1,301 compared to the previous year. Administrative expenses decreased by KEUR 734 to KEUR 3,079 and selling expenses decreased by KEUR 567 to KEUR 749. Higher general administrative expenses incurred in the prior-year period mainly resulted from the preparation of potential capital measures that were ultimately not conducted, while selling expenses recognized in the

prior-year period comprised essential costs related to the initiation and preparation of license agreements which have only been incurred to a lesser extent in the reporting period.

**Income taxes** of the fiscal year essentially relate to tax claims for reimbursement of parts of the research and development expenses from the British tax authorities. The change in comparison to the prior year is mainly associated with the decrease of the development expenses for remimazolam in the reporting period.

PAION closes fiscal year 2017 with a **net loss** of KEUR 12,093 after a net loss of KEUR 20,118 in the previous year.

#### b. Net Assets

	31 Dec. 2017 KEUR	31 Dec. 2016 KEUR	Change KEUR
Non-current assets	2,528	2,855	-327
Current assets	29,357	35,128	-5,771
Assets	31,885	37,983	-6,098
Equity	25,229	24,943	286
Current liabilities	6,656	13,040	-6,384
Equity and liabilities	31,885	37,983	-6,098

The **non-current assets** mainly comprise the book value of the development project remimazolam (KEUR 2,353; 31 December 2016: KEUR 2,626) resulting from the value allocated per purchase price allocation in the course of the CeNeS acquisition in 2008 reduced by scheduled amortization.

Compared to 31 December 2016, **current assets** decreased by KEUR 5,771 to KEUR 29,357 and comprised cash and cash equivalents, prepaid expenses and other assets as well as trade receivables as of 31 December 2017. Cash and cash equivalents decreased by KEUR 5,272 in the reporting period from KEUR 30,111 as of 31 December 2016 to KEUR 24,839 as of 31 December 2017. Prepaid expenses and other assets decreased from KEUR 5,017 as of prior year's balance sheet date by KEUR 536 to KEUR 4,481 per year-end. The decrease is substantially due to a KEUR 988 lower tax claim for reimbursement of parts of the research and development costs from the British tax authorities as compared to 31 December 2016 amounting to KEUR 3,749 per year-end, as well as higher prepayments for development services compared to prior year's balance sheet date. Trade receivables amounted to KEUR 37 as of 31 December 2017 and increased by KEUR 37 compared to prior year's balance sheet date.

The increase in **equity** by KEUR 286 compared to 31 December 2016 mainly results from the net loss of the year and the capital increases conducted in February and July of the reporting period. The equity ratio amounts to 79.1% as of 31 December 2017 (31 December 2016: 65.7%).

The decrease of **current liabilities** by KEUR 6,384 to KEUR 6,656 is primarily due to KEUR 5,755 lower deferred income compared to 31 December 2016. This mainly comprised the portion of the upfront payment of KEUR 10,000 received from Cosmo not recognized as revenue yet as of prior year's balance sheet date that was entirely recognized as revenue in the reporting period. Compared to 31 December 2016, trade payables decreased by KEUR 432 to KEUR 5,921 as of 31 December 2017.

#### c. Financial Position

Compared to 31 December 2016, **cash and cash equivalents** decreased by KEUR 5,272 to KEUR 24,839. The change in cash and cash equivalents stems from the following areas:

	2017 KEUR	2016 KEUR	Change KEUR
Cash flow from operating activities	-17,720	-11,586	-6,134
Cash flow from investing activities	-25	-192	167
Cash flow from financing activities	12,494	9,212	3,282
Effect of exchange rate changes	-21	-3	-18
Change in cash and cash equivalents	-5,272	-2,569	-2,703

The **cash flow from operating activities** primarily results from the net loss of the year in the amount of KEUR 12,093 corrected for the share of revenues that had no cash effect amounting to KEUR 5,792.

The **cash flow from financing activities** results from the gross proceeds from the conduct of the capital increase with subscriptions rights in February 2017 (KEUR 5,000) and the capital increase under exclusion of subscription rights in July 2017 (KEUR 8,034), the cost of funds related to these capital increases (KEUR 687) as well as the exercise of stock options (KEUR 147).

#### d. Overall appraisal

The net loss of EUR 12.1 million is within the forecast range of approx. EUR 12 million to approx. EUR 14 million projected for fiscal year 2017 in the previous year.

Recognized revenues also meet the amount of EUR 5.8 million forecasted per prior year.

Also, general administrative and selling expenses as well as tax income with EUR 3.8 million each are within the ranges forecasted per prior year of approx. EUR 3.5 million to approx. EUR 4 million each.

With EUR 17.9 million, research and development expenses are slightly below the forecast range of approx. EUR 18 million to approx. EUR 20 million projected for fiscal year 2017 in the previous year.

In total, results of operations, net assets and financial position have evolved as expected in the reporting period.

Since remimazolam is not yet marketed and therefore no sustainable revenue is generated, PAION continues to incur losses.

#### Headcount

In fiscal year 2017, PAION employed an average of 33 persons (previous year: 36 employees). Of these 33 employees, 23 worked in development and ten in administration and sales. PAION UK Group had an average headcount of five employees. As of 31 December 2017, the headcount was 34 (31 December 2016: 34).

#### Remuneration report

#### I. Management Board

The remuneration paid to Management Board members comprises fixed annual remuneration, a variable bonus, a long-term performance-based remuneration component in the form of stock options as well as other remuneration in terms of company car remuneration, insurance premiums and pension contributions. All stock options granted to Management Board members so far have a ten-year term. The variable bonus depends on the achievement of long-term and sustainable financial and strategic corporate goals which are determined by the Supervisory Board at the beginning of each fiscal year. The level of goal achievement and the related amount of the variable remuneration is assessed and determined by the Supervisory Board. Bonuses are not subject to a minimum but are limited to a maximum amount and are paid depending on individual goal achievement. Moreover, the Supervisory Board is entitled to grant special remuneration to individual members of the Management Board in exceptional cases based on dutiful discretion.

The compensation as Management Board member covers also the managing director function at the subsidiaries.

From the Stock Option Plan 2008 approved by the Annual General Meeting on 5 May 2008, a total of 391,650 stock options were granted to acting Management Board members at the time of the respective grant. The Supervisory Board determined the number of stock options to be allocated to the Management Board. The two- to four-year waiting period before stock options

can be exercised acts as a long-term incentive to increase the company's value. The exercise price of stock options granted to current members of the Management Board is EUR 1.26 or EUR 1.84 per stock option depending on the grant date and is based on the average price of the shares in a certain time period before the allocation in accordance with the terms of the stock option plan. As of 31 December 2017, the exercise hurdle was EUR 1.84 or EUR 2.57 depending on the grant date.

From the Stock Option Plan 2010 approved by the Annual General Meeting on 19 May 2010, a total of 324,000 stock options were granted to acting Management Board members at the time of the grant. The Supervisory Board determined the number of stock options to be allocated to the Management Board. The four-year waiting period before stock options can be exercised acts as a long-term incentive to increase the company's value. The exercise price of stock options granted to current Management Board members is EUR 2.01 per stock option and is based on the average price of the shares in a certain time period before the allocation in accordance with the terms of the stock option plan. As of 31 December 2017, the exercise hurdle was EUR 2.40.

From the Stock Option Plan 2014 approved by the Annual General Meeting on 21 May 2014, a total of 277,500 stock options were granted to acting Management Board members at the time of the grant. The Supervisory Board determined the number of stock options to be allocated to the Management Board. The four-year waiting period before stock options can be exercised acts as a long-term incentive to increase the company's value. The exercise price of stock options granted to current Management Board members is EUR 1.99 or EUR 2.30 per stock option, depending on the date of issue of the stock options, and is based on the average price of the shares in a certain time period before the allocation in accordance with the terms of the stock option plan. As of 31 December 2017, the exercise hurdle was EUR 2.14 or EUR 2.64, depending on the grant date.

The stock option agreements with the individual members of the Management Board limit the numbers of stock options which can be granted. With the exception of minimum increases in value, no restrictions have been imposed in respect of the performance of the stock options, which is directly linked to PAION's share price performance.

The remuneration of the individual Management Board members in fiscal year 2017 (according to German Corporate Governance Code) can be gathered from the following tables:

Benefits granted in EUR	Dr. Wolfgang Söhngen CEO				
Delients granted in EUK					
	2016	2017	2017 (Min)	2017 (Max)	
Fixed compensation*	275,000	275,000	275,000	275,000	
Other remuneration	48,471	45,592	45,592	45,592	
Total	323,471	320,592	320,592	320,592	
One-year variable compensation	175,000	175,000	0	175,000	
Multi-year variable compensation					
Stock Option Plan 2014 - Grant 2016 (Waiting period 2016 to 2020)**	56,610	0	-	-	
Total	555,081	495,592	320,592	495,592	
Service cost	0	0	0	0	
Total remuneration	555,081	495,592	320,592	495,592	

<sup>\*)</sup> Fixed compensation for Dr. Raths in the reporting period includes a compensation payment for the remaining contract term after his lead \*\*) Applicable fair value at the time of issuance, calculated using the Black/Scholes option pricing model

Allocation in EUR	Dr. Wolfgang Söhngen CEO		
	2016	2017	
Fixed compensation*	275,000	275,000	
Other remuneration	48,471	45,592	
Total	323,471	320,592	
One-year variable compensation	124,600	132,405	
Multi-year variable compensation	0	0	
Total	448,071	452,997	
Service cost	0 0		
Total remuneration	448,071	452,997	

<sup>\*)</sup> Fixed compensation for Dr. Raths in the reporting period includes a compensation payment for the remaining contract term after his lear

	Abdelghani Omari CFO				Dr. Jürge CC until 14 M	00		
	2016	2017	2017 (Min)	2017 (Max)	2016	2017	2017 (Min)	2017 (Max)
	165,000	175,833	175,833	175,833	315,000	215,650	215,650	215,650
	15,127	15,127	15,127	15,127	127	21	21	21
	180,127	190,961	190,961	190,961	315,127	215,671	215,671	215,671
	70,000	90,000	0	90,000	50,000	0	0	0
	56,610	0	-	-	0	0	-	-
	306,737	280,961	190,961	280,961	365,127	215,671	215,671	215,671
	0	0	0	0	0	0	0	0
	306,737	280,961	190,961	280,961	365,127	215,671	215,671	215,671
ve on 14 March 2017 (EUI	e on 14 March 2017 (EUR 163,150)							

	Abdelghani Omari CFO		Dr. Jürger CO until 14 Ma	0
	2016	2017	2016	2017
	165,000	175,833	315,000	215,650
	15,127	15,127	127	21
	180,127	190,961	315,127	215,671
	53,690	68,094	41,100	0
	0	0	0	0
	233,817	259,055	356,227	215,671
	0	0	0	0
	233,817	259,055	356,227	215,671
ve on 14 March 2017 (EUR	163,150)			

The "other remuneration" item contains company car remuneration, insurance premiums and pension contributions paid by PAION.

Management Board remuneration in fiscal year 2017 amounted to KEUR 928 in total (previous year: KEUR 1,151) and is composed as follows:

in EUR	2017	2016
Fixed remuneration	666,483	755,000
Other remuneration	60,741	63,725
Total non-performance based remuneration	727,224	818,725
Short-term variable remuneration	200,499	219,390
Total short-term remuneration	927,723	1,038,115
Long-term variable remuneration	0	113,220
Total long-term remuneration	0	113,220
Total remuneration	927,723	1,151,335

The decrease of total remuneration compared to the previous year mainly results from two factors: Short-term remuneration has decreased compared to the previous year due to the lower average number of Management Board members in fiscal year 2017. Moreover, in contrast to the previous year, no long-term variable remuneration in form of stock options was granted in the reporting period.

The Management Board members held the following stock options as of 31 December 2017:

Status of non-exercised stock options	as of 31 December 2017:	Dr. Wolfgang Söhngen	Abdelghani Omari
Stock options 2008	No.	98,067	0
Stock options 2008 - fair value*	EUR	163,909	-
Stock options 2010	No.	162,000	80,000
Stock options 2010 - fair value*	EUR	270,540	133,600
Stock options 2014	No.	111,000	111,000
Stock options 2014 - fair value*	EUR	119,325	119,325

<sup>\*)</sup> Applicable fair value at the time of issuance, calculated using the Black/Scholes option pricing model

In the event of a change of control and the termination of employment within a certain period after the change of control, the Management Board members are each entitled to contractual termination benefits, which correspond to an amount of two annual fixed basic remunerations. In the event of early termination of the employment relationship relating to any other circumstance than a change of control, potential termination benefits must not exceed the amount of two annual fixed basic remunerations and must not compensate more than the remaining time of the employment contract. The employment contracts of Management Board members do not provide for transitional benefits upon expiry.

The Supervisory Board is entitled to reduce the total compensation of the Management Board members to the appropriate level according to the applicable provisions under stock corporation law in case of a significant degradation of the company's position if the continuation of granting the compensation were inequitable for the company.

Pursuant to the terms of the Stock Option Plans 2008, 2010 and 2014, in the event of a change of control, for all stock options issued to Management Board members for which the waiting period has not expired yet at the date of the change of control, the entitlement to subscribe to shares is converted into an entitlement to a cash settlement based on the share price on the day the controlling acquisition comes into effect. The corresponding stock options lapse. The company may choose to grant listed shares in the acquiring company instead of the cash settlement.

#### 2. Supervisory Board

Supervisory Board remuneration comprises basic remuneration and per-meeting fees. The members of the Supervisory Board currently do not receive performance-based remuneration. The Chairman of the Supervisory Board receives twice the basic remuneration and per-meeting fee, his deputy receives one-and-a-half times these amounts. The per-meeting fee is paid for a maximum of five meetings per year. The members of the Supervisory Board received the following remuneration for their activities in fiscal year 2017:

	Basic remuneration EUR	Per-meeting fees EUR	Total EUR
Dr. Jörg Spiekerkötter	40,000	10,000	50,000
Dr. Karin Dorrepaal	30,000	7,500	37,500
John Dawson	20,000	5,000	25,000
Dr. Dr. Irina Antonijevic	11,056	3,000	14,056
Dr. Hans Christoph Tanner	11,056	3,000	14,056

Supervisory Board remuneration in fiscal year 2017 amounted to KEUR 141. In the previous year the remuneration amounted to KEUR 122. The increase stems from two opposing factors: On the one hand, the size of the Supervisory Board was extended by two members during the reporting period. On the other hand, per-meeting fees as well as the maximum number of qualifying meetings per year were reduced in the reporting period.

Disclosures pursuant to section 315 a (1) HGB and explanatory report

#### Composition of subscribed capital

As of 31 December 2017, PAION AG had a subscribed capital of EUR 61,120,046.00, divided into 61,120,046 no-par value shares, each representing a notional share in the share capital of EUR 1.00. The shares are issued to the bearer and are fully paid in. Shareholders are not entitled to demand share certificates for their shares under Art. 6 (2) of the Articles of Incorporation. All shares carry the same rights and duties. Each share carries the right to one vote at the Annual General Meeting and also forms the basis of the holder's share in profit. More information on the individual rights and duties of shareholders can be found in the German Stock Corporation Act (Aktiengesetz, AktG), in particular Sections 12, 53a et seqq., 118 et seqq. and 186.

#### Restrictions relating to voting rights or the transfer of shares

Pursuant to German legislation and the Articles of Incorporation of PAION AG, no restrictions are imposed on the voting rights or transferability of the shares. The Management Board of PAION AG is also not aware of any voting rights or share transfer restrictions at shareholder level.

#### Equity interests exceeding 10% of voting rights

The German Securities Trading Act (Wertpapierhandelsgesetz, WpHG) stipulates that any share-holder who achieves, exceeds or falls short of specific shares in the voting rights in the company through the purchase or sale of shares or by other means, must notify the company and the German Federal Financial Supervisory Authority (Bundesanstalt für Finanzdienstleistungsaufsicht, BaFin) accordingly. The lowest threshold for this reporting obligation is 3%. Direct or indirect shares in the company's capital that equaled or exceeded 10% of the voting rights as of 31 December 2017 were not reported to the company.

#### Shares with special rights conferring powers of control

The bearers of PAION AG shares have not been granted any special rights by the company, in particular with regard to powers of control.

### Type of control of voting rights when employees are shareholders and do not directly exercise their control rights

The share options issued to employees and members of the Management Board can be exercised once the defined waiting period has expired and the other conditions have been met by the

beneficiaries. Shares acquired in this way give the beneficiaries the same rights as other shareholders and are not subject to any voting rights control.

# Legal provisions and provisions of the Articles of Incorporation on the appointment and removal of members of the Management Board and amendments to the Articles of Incorporation

Members of the Management Board are appointed and removed in accordance with Sections 84 and 85 AktG and the supplementary provisions of the Supervisory Board's rules of procedure, which stipulate an age limit of 65 years for Management Board members. Pursuant to Section 84 AktG, members of the Management Board can be elected for a maximum of five years by the Supervisory Board. Re-appointments or extensions of the term of office for up to a maximum of five years at a time are permissible. Pursuant to Art. 8 (1) of the Articles of Incorporation, the Management Board must comprise at least one member. The Supervisory Board determines the number of members on the Management Board. Furthermore, pursuant to Section 84 (2) AktG and Art. 8 (2) of the Articles of Incorporation, the Supervisory Board may appoint a member of the Management Board as CEO.

Amendments to the Articles of Incorporation are effected in accordance with Sections 179 and 133 AktG in conjunction with Art. 27 of PAION AG's Articles of Incorporation. The shareholder resolution required for any amendment to the Articles of Incorporation can, under PAION AG's Articles of Incorporation, be adopted by a simple majority of the share capital represented at the adoption of the resolution, provided this is permitted by law.

#### Authority of the Management Board to issue or buy back shares

The Management Board is authorized to increase the share capital on or prior to 16 May 2022, with the consent of the Supervisory Board, on one or more occasions, by up to EUR 29,098,058.00 in total by issuing up to 29,098,058 new no-par value bearer shares in return for cash contributions or contributions in kind (Authorized Capital 2017). In the case of capital increases against contributions in kind, the Management Board may also exclude pre-emptive rights, subject to the Supervisory Board's consent. Shareholders must be granted pre-emptive rights if the capital is to be increased against payments in cash. The new shares may also be taken by one or more financial institutions on condition that they offer them to shareholders. The Management Board may, subject to the Supervisory Board's consent, exclude fractional shares from shareholders' pre-emptive rights. The Management Board is also authorized to exclude shareholders' pre-emptive rights, subject to the consent of the Supervisory Board, if the issue price of the new shares is not significantly less than the market price and the shares issued in return for cash contributions with pre-emptive rights excluded pursuant to Section 186 (3) Sentence 4 AktG do not exceed 10% of the share capital as of 17 May 2017 and the time of the exercise of the authorization. The Management Board is moreover authorized to exclude shareholders' pre-emptive rights, subject to the consent of the Supervisory Board, to the extent necessary to grant pre-emptive rights to holders of convertible bonds, participation rights or options as defined in Section 221 AktG. By resolution from 17 July 2017,

the Authorized Capital 2017 was used in the amount of EUR 2,824,515.00 and amounts to EUR 26,273,543.00 as of 31 December 2017.

Furthermore, subject to the consent of the Supervisory Board, the Management Board is authorized to issue on or before 16 May 2022, on one or more occasions, bearer or registered convertible bonds, warrant-linked bonds, profit participation rights and/or participating bonds (or combinations thereof; hereinafter collectively "Bonds") of up to an aggregate of EUR 125,000,000.00 with or without a limited maturity period and to grant the holders or beneficiaries of the Bonds conversion rights or options to new shares in PAION AG with a proportionate amount of the share capital of up to EUR 26,200,000.00 in total (Conditional Capital 2017). Conditional Capital 2017 has not yet been used. Furthermore, the company is authorized to issue 419,190 shares (Conditional Capital 2008 I), 720,000 shares (Conditional Capital 2010 I), 740,000 shares (Conditional Capital 2014) and 840,000 shares (Conditional Capital 2016) in connection with the Stock Option Plans 2008, 2010, 2014 and 2016.

### Material arrangements of the company dependent on a change in control in the event of a takeover bid

The company has not concluded material arrangements which are dependent on a change in control in the event of a takeover bid.

### Compensation agreements entered into by the company with members of the Management Board and employees in the event of a takeover bid

The terms of the Stock Option Plans 2008, 2010, 2014 and 2016 stipulate both for members of the Management Board and for employees that in case of a change of control, the waiting period for all options for which the waiting period has not expired yet at the date of the change of control, the entitlement to subscribe to shares is converted into an entitlement to a cash settlement based on the share price on the day the change of control comes into effect; the corresponding stock options lapse. The company may choose to grant listed shares in the acquiring company instead of the cash settlement.

For information on further existing compensation agreements with Management Board members, please refer to the comments in the section "Remuneration Report".

#### Statement on Corporate Governance pursuant to Section 289 f HGB

The Statement on Corporate Governance pursuant to Section 289 f HGB has been published on PAION AG's website (http://www.paion.com/media-and-investors/corporate-governance/declaration-on-corporate-governance/).

#### Report on risks and opportunities

#### I. Risk management

As a specialty pharma company, PAION is exposed to the segment and market risks that are typically associated with the development of pharmaceutical products. In accordance with the German Law on Control and Transparency in Business (Gesetz zur Kontrolle und Transparenz im Unternehmensbereich, KonTraG), PAION has implemented a group-wide comprehensive and effective risk management system which is integrated into the operating processes and flexibly adaptable to the changing environment. The task of the risk management system is to promote the conscious and responsible handling of risks, and to enable the early identification, monitoring, analysis, evaluation and management of future developments with inherent risks. Involving all management levels and project management in the process of strategic and business development creates a shared awareness of the critical success factors and related risks.

PAION's risk management system comprises an internal control system, an early warning system for the detection of risks and a controlling system. These three sub-systems interact directly with each other and also take on tasks from each of the other sub-systems.

The financial accounting and cost accounting software "Microsoft Dynamics NAV" and an enterprise planning tool in Excel customized for PAION form the basis for controlling. Monthly internal reporting is performed on a cost centre and cost unit basis, allowing deviations from the budget to be identified at an early stage. Short-, mid- and long-term corporate planning (cost centre planning, cost unit and project planning, budget income statement, budget balance sheet and budget cash flow statement) is conducted using the Excel-based planning tool. Using this planning tool, management and the controlling department are in a position to simulate various scenarios to identify, assess and determine the impact of opportunities and risks on the future development of the company, particularly with regard to the key financial performance indicator liquidity.

The implemented internal control system includes rules for the management of business activities as well as arrangements for monitoring compliance with these rules. The primary tasks of the internal control system include application of the dual control principle, determining which types of business transactions require approval, limiting the issuance of signing and banking authority, standardizing workflows using procedural instructions, monitoring compliance with process steps by using checklists and establishing measures for the protection of data and IT systems. Furthermore, PAION commissioned an auditing firm with carrying out the tasks of an internal audit department. Internal Audit works on the basis of a multi-year audit plan, which was developed by Internal Audit in collaboration with the Management Board based on a risk-oriented audit approach and materiality aspects. The internal auditors report promptly on the audit procedures carried out and any findings there from. In addition, PAION has appointed an internal Compliance Officer. The Compliance Officer monitors the compliance of the group-wide compliance policies and reports once a year on his activities and any findings there from. Both the audit plan and the reports

of Internal Audit as well as the report of the Compliance Officer are forwarded to the Supervisory Board for information and discussion.

PAION has implemented a matrix organisation which combines both project organisation and department organisation. Detailed reporting and information structures have been set up within these organisational structures to ensure the early identification and communication of risks. The individual projects are managed and monitored by project teams. The project teams regularly provide the individual department heads and management with reports – also in writing – on the current progress of projects and potential risks.

The risk management system is reviewed once per year and discussed with the Supervisory Board. The risk analysis is updated during the year and presented to the Supervisory Board. Special risks are communicated ad-hoc. A comprehensive risk inventory is conducted on a yearly basis. The internal control system is reviewed continuously with regard to the effectiveness of the controls and is adjusted if required. The risk management system and the internal control system are audited by Internal Audit in line with a multi-year audit plan.

### 2. Risk management and internal control system relevant for the financial reporting process

The risk management system and the internal control system also involve the financial reporting processes and aim to ensure compliance and reliability of the consolidated financial statements, the group management report and the released interim financial statements.

The risk management and internal control system relevant for the financial reporting process address the risk of significant misstatements in the annual and interim financial statements. Essential measures and controls in financial reporting are the clear assignment of responsibilities, the dual control principle, the segregation of duties, the use of an appropriate financial accounting system with a corresponding authorization concept as well as the use of checklists and work instructions. Furthermore separate and consolidated financial statements are prepared every month for internal purposes. The monthly, interim and annual financial statements are analyzed by means of the group-wide controlling with regard to plan/actual variances and implausibilities and inconsistencies in the accounting. The monthly finance report is forwarded to the Supervisory Board. The interim and annual financial statements are published and are discussed with the Supervisory Board prior to publication.

Significant issues in connection with the preparation of financial statements are discussed promptly with the audit committee. Furthermore, the audit committee determines additional audit topics and key audit procedures for the auditor.

In addition, the auditor is obligated to report to the Supervisory Board on risks and control deficiencies relevant for the financial reporting process as well as other deficiencies of the risk management system and the internal control system that he becomes aware of in the course of his audit.

#### 3. Significant risks

Within the framework of the risk early warning system, risks are initially assessed as gross risks in terms of potential damage levels and likelihoods of occurrence before taking into account any risk-mitigating measures. Net risks are assessed in terms of damage level and likelihood under consideration of implemented risk-reducing actions and are classified based on the resulting expected value. For the evaluation of potential risks, company-internal as well as known relevant external factors are taken into account based on their respective relevance. Applied categories for likelihoods of occurrence and damage levels as well as the classification of resulting net risks are illustrated in the following table:

	Damage Level				
Likelihood of occurrence	Very low < KEUR 100	Low KEUR 100 - KEUR 500	Moderate  KEUR 500 - EUR 1 mill.	High EUR 1 mill EUR 5 mill.	Very high > EUR 5 mill.
Highly probable > 90%	Very low risk	Moderate risk	Increased risk		
Very probable 60%-90%	Very low risk	Low risk	Increased risk	High risk	
Probable 30%-60%	Very low risk	Low risk	Moderate risk	High risk	High risk
Possible 15%-30%	Very low risk	Very low risk	Low risk	Increased risk	High risk
Unprobable < 15%	Very low risk	Very low risk	Low risk	Moderate risk	Increased risk

In the following, identified risks will be outlined together with respective implemented risk-reducing measures and classified according to the illustrated table above. The classification is based on net risks under consideration of risk-mitigating activities. Risks potentially posing a threat to the continued existence of the group are defined as risks with a potential damage level of more than EUR 5 million in case of occurrence. Risks potentially posing a threat to the continued existence of the group are separately denoted accordingly. Net risks with an assessment as "Very low risk" and "Low risk" are not depicted since these do not significantly influence the decisions of a reasonable addressee. In the course of the necessary aggregation of risks, some of the risks depicted in the following may comprise individual partial risks. In this case, the classification of the risk always relates to the highest of the underlying partial risks. Potential changes of risk classifications compared to the previous year are denoted accordingly. If risks disclosed in the prior year do not exist anymore or if risks are presented for the first time in the reporting period, this is not outlined separately.

#### a. Risks in connection with the development and commercialization of remimazolam

Due to the complete concentration of all resources on remimazolam, PAION is highly dependent on its successful development and subsequent commercialization.

#### aa) Development and approval risks

Before remimazolam can be approved and marketed, its safety and efficacy must be proven in appropriate and carefully monitored clinical and non-clinical studies. As is common practice in the pharmaceutical industry, Clinical Research Organizations (CROs) are assigned to conduct the studies. PAION performs monitoring and control functions which are in line with practice in the pharmaceutical industry. Despite supervision, there is a risk that an inadequate conduct of studies only becomes evident once the study data are available or after filing for market approval in the course of study site inspections conducted by the respective authorities requiring rework amendments and causing delays in the approval process. In order to reduce this risk, CROs are carefully being selected based on defined processes and criteria and are regularly audited. Moreover, the conduct of clinical studies in the respective study centers as well as generated study data are monitored and checked by independent third parties. This is an industry-specific high risk. In case of occurrence of this risk, the potential damage level could pose a threat to the continued existence of the group. Among the industry, nearly 40% of all Phase III projects do not directly lead to approval according to Tufts Center for the Study of Drug Development.<sup>18</sup>

In order to ensure a timely filing for approval of remimazolam in the U.S. after successful completion of the clinical studies in the reporting period, PAION cooperates with renowned regulatory service providers. PAION regularly evaluates the rendered services also taking into account external data for comparison but is not in a position to entirely assess the adequacy and compliance with regulatory requirements due to the highly specialized expertise of the service providers. In spite of the professional track record of the contracted service providers there is a risk that regulatory requirements are not met sufficiently leading to a delay of market approval. This is an increased risk. In case of occurrence, the potential damage level could pose a threat to the continued existence of the group. The risk classification decreased by one category compared to the previous year.

PAION plans the start of an EU Phase III study in general anesthesia in 2018. There is a risk that patients cannot be recruited fast enough or at all. The resulting delay, necessary amendment or discontinuation of the study would usually (e. g. in case of the initiation of a new study) lead to higher costs and delayed market approval. Insights from all clinical studies conducted so far particularly in regard to recruitment of certain patient populations are being taken into account for the study design in order to guarantee optimal patient recruitment. In the course of study monitoring, PAION analyzes potential alternative and prevention scenarios on a need basis in order to be able to initiate these in a timely manner in case of occurrence of this risk. This is a high risk. In

<sup>&</sup>lt;sup>18</sup> Tufts Center for the Study of Drug Development (2014): Briefing – Cost of Developing a New Drug.

case of occurrence, the potential damage level could pose a threat to the continued existence of the group.

The results of clinical and non-clinical studies are not predictable. There is always the danger that unexpected serious adverse events occur or that promising results achieved in prior studies may not be confirmed to the same degree in subsequent studies. Reasons for the latter could be the inadequacy of the drug candidate for the planned indication or the respective study designs. If this risk occurs, further development could be delayed considerably or development of the drug candidate may be discontinued altogether. These are typical development risks which can only be influenced to a minor extent. In regard to unexpected serious adverse events, thorough dose finding and careful monitoring of safety aspects of the studies are carried out, and with respect to the results of studies, potential dosage modifications and amendments to clinical trial protocols mitigate the risk as far as possible. Unexpected serious adverse events are an increased risk. In case of occurrence, the potential damage level could pose a threat to the continued existence of the group. Insufficient study outcomes are a moderate risk.

There is also a risk that authorities impose additional regulatory requirements exceeding the needs PAION originally planned for. Tightening of clinical thresholds for safety and efficacy evaluations, or changes in the way regulators evaluate clinical data could lead to cost increases or significant delays in the conduct also of ongoing studies or necessitate the initiation of additional studies in order to be able to file for market approval. Assessments of individual authorities might also differ. Data sets regarded as sufficient in one country might be deemed insufficient by an authority in a different country. This is a typical drug development risk that can only be influenced by PAION to a minor degree. However, in order to reduce the risk to the highest possible extent, PAION has obtained official scientific advice from the respective authorities in the EU and the U.S. Moreover, PAION consults regulatory experts. This is a high risk.

Moreover, there is a risk that product defects and deficiencies in the manufacturing process of remimazolam or certain incidents at PAION's contractual manufacturers entail regulatory consequences or insufficient supply volumes that lead to the interruption and/or delay of the studies. PAION's quality assurance maintains a close cooperation with PAION's contractual manufacturers and regularly conducts audits in order to ensure a constantly high quality of the manufacturing. This is an increased risk. In case of occurrence, the potential damage level could pose a threat to the continued existence of the group.

Additionally, authorities regularly conduct pre-approval inspections in terms of the manufacturing of drugs before granting respective market approval. There is a risk that quality deficiencies at PAION or PAION's contractual manufacturers are identified within the scope of such inspections which might lead to delays of market approval. In order to minimize this risk, PAION maintains a close cooperation with its contractual manufacturers and regularly conducts own audits in order to ensure a constantly high quality of the manufacturing. This is an increased risk.

Apart from market approval per se, particularly the exact conditions of the received label play an important role for successful commercial usability of remimazolam. Based on the properties of remimazolam shown so far, PAION aims for a remimazolam label in the U.S. comparable to

midazolam which is allowed to be applied by adequately trained proceduralists and nurses conditional on a certain safety set-up and continuous monitoring of relevant cardiac and respiratory parameters. There is a risk that remimazolam will not be granted this target label significantly reducing or entirely eliminating commercial usability in the U.S. In order to reduce this risk, PAION has addressed this aspect with the FDA under consideration of existing study data at that time and used according feedback for the design of the U.S. Phase III program. PAION has implemented a system to continuously monitor the relevant parameters in this regard. This is a high risk and the potential damage level could pose a threat to the continued existence of the group in case of occurrence.

#### bb) Commercialization risks

With a constantly progressing degree of the development status of remimazolam, potential commercialization is closing in as well and imposes several risks.

PAION has conducted comprehensive market research as a basis for assessing different market potentials. However, there is a risk that assumed prices or other assumptions such as expected market share underlying the business plan and thus remimazolam's full potential cannot be realized. This risk cannot be influenced. This is a high risk. In case of occurrence, the potential damage level could pose a threat to the continued existence of the group.

There is also a risk that PAION or PAION's license partners will not be able to sufficiently prepare the market for launch by means of pre-marketing and market access activities as for example communication with the scientific community, and will therefore not be able to sell the anticipated volumes of remimazolam at the market. In order to reduce this risk, PAION continues to work on the preparation of the relevant markets, including bringing in external consultants for communication with the scientific community. Moreover, there is regular information exchange with the U.S. license partner Cosmo. PAION is also evaluating the possibility of initially launching remimazolam in a different indication than planned as main indication in single countries in order to support later commercialization in the main indication in these markets. This is a high risk. In case of occurrence, the potential damage level could pose a threat to the continued existence of the group.

In order to be able to successfully commercialize remimazolam upon market approval, PAION's (for a possible own commercialization in the EU) and partners' distribution set-ups need to be fully established. There is a risk that this process will not have been finalized until market approval. In order to reduce this risk to the highest possible degree, PAION has analyzed potential distribution set-ups and there is a regular information exchange with the U.S. cooperation partner Cosmo. This is an increased risk. In case of occurrence, the potential damage level could pose a threat to the continued existence of the group.

The health care sector is exposed to governmental regulations of different degrees depending on the respective region, which are often subject to changes or tightening over time. There is a risk that the rules of access, reimbursement, promotion and distribution for pharmaceutical products will be changed significantly to the disfavor of the pharmaceutical industry. This risk cannot

be influenced by PAION. This is a high risk. In case of occurrence, the potential damage level could pose a threat to the continued existence of the group.

#### cc) Production and purchase risks

So far, relatively low quantities of remimazolam have been produced in course of the clinical trials. Up until commercialization, a further so-called scale-up process needs to be finalized. There is a risk that as a result of this process, remimazolam cannot be produced in sufficient quantities or at competitive costs for the market. This is a typical development risk that can only be influenced to a minor extent. However, in order to reduce this risk, PAION cooperates with established manufacturers and conducts a process validation before beginning commercialization in order to guarantee technical feasibility. This is an increased risk. In case of occurrence, the potential damage level could pose a threat to the continued existence of the group.

Moreover, (additional) requirements of the authorities or problems relating to process validation might delay production development and manufacturing of market material and thus lead to a delay of commercialization. This is also an inherent risk in drug development and can barely be influenced. Still, the contractual manufacturers PAION works with are experienced in the process validation of manufacture of pharmaceutical products and the adoption of additional regulatory requirements. This is a high risk. In case of occurrence, the potential damage level could pose a threat to the continued existence of the group.

Due to the still incomplete availability of stability data for remimazolam, there is a risk that for potential new or further studies, additional batches of the drug product need to be manufactured unless process validation has been finalized until then. This could lead to a delay of studies and incur additional costs. PAION is therefore working on a timely process validation in cooperation with experienced and renowned Contract Manufacturing Organizations (CMOs). This is a moderate risk.

Although PAION already cooperates with experienced and established contractual manufacturers, commercial supply agreements have not been finalized yet. There is a risk that a timely agreement cannot be reached leading to a delay of commercialization or higher costs. This is a high risk that PAION addresses by means of industry-typical precautions. In case of occurrence, the potential damage level could pose a threat to the continued existence of the group.

Medical ingredients are combined with certain other substances in order to have a sufficient shelf life, to be well applicable and to be specifically operative in the human organism among other things. In spite of a variety of tests, there is a risk that such a so-called pharmaceutical formulation does not remain stable in the long term and can thus not or only be used with reduced shelf life for products sold at the market. In order to reduce this risk to the highest possible extent, PAION continuously conducts tests and long-term stability studies before commercialization. This is a moderate risk.

There is a risk that large amounts of remimazolam get lost due to events like fire, theft, accidents or comparable incidents. PAION chooses all of its contractors along the supply chain

thoroughly and places great importance on high security requirements. Also, PAION has hedged against potential damages to a high degree by industry typical insurances. This is a moderate risk.

Based on the production risks depicted, there is a risk that (potential) supply obligations towards license partners cannot be fulfilled if production development has not been completed or commercial supply agreements and purchasing infrastructures are not in place yet. In cooperation with its contractual manufacturers, PAION would initiate the acceleration of validation procedures or the finalization of commercial supply agreements and the establishment of purchasing infrastructures if a shortage in that regard should become foreseeable. This is a high risk. The risk classification increased by one category compared to the previous year.

#### dd) Risks in relation to patents and other intellectual property

PAION's business operations are largely dependent on its ability to secure extensive patent protection and other intellectual property protection for the individual substances and to defend these against third parties without violating their rights. There can be no assurance that current or future patent applications will be granted or that any patents issued or licensed to PAION will be valid and sufficiently extensive to provide PAION and its license partners with adequate legal protection or any commercial advantage. PAION continuously collaborates with an experienced patent law firm to secure the protection of PAION's intellectual property and to identify and address potential threats at an early stage as well as to make sure to not infringe any other third parties' patents itself. This is an increased risk.

#### ee) Risks in relation to cooperations

In light of the progress of the development activities for remimazolam, increasingly bigger clinical studies are being conducted by license partners and important regulatory coordinations and meetings with the respective regulatory authorities are increasingly coming into focus for PAION's license partners. There is a risk that results from clinical studies or discussions with the authorities render the further development of remimazolam unattractive for existing license partners in their respective licensed region and that they terminate their license for this reason. In order to reduce this risk, PAION is in regular exchange with all license partners and engages in the evaluation of development plans in order to share the comprehensive set of experience in the clinical development of remimazolam and regulatory interactions in this regard to thus guarantee the successful conduct of clinical trials and compliance with the respective regional regulatory requirements. This is a high risk and the potential damage level could pose a threat to the continued existence of the group in case of occurrence.

Since PAION neither owns distribution structures nor aims at implementing these globally, potential commercialization of remimazolam can only be carried out by license partners in certain regions. Should license agreements not be concluded in time, a potential commercialization could only start delayed in spite of the potential availability of market approval. PAION has partnering discussions with potential licensees in order to allow for an immediate commercialization of remimazolam after potential market approval. This is an increased risk.

#### b. Finance risks

#### aa) Financing risks

PAION expects future payments from existing and possible future cooperation agreements as well as from tax credits to cover its short- and mid-term financing needs. However, PAION needs additional funding for further development in the EU after completion of the planned Phase III study in general anesthesia or commercialization of remimazolam. Funding requirements may also arise due to delays or cost increases in development. Milestone payments could be cancelled if targets agreed with the license partners are not met.

PAION's future ability to secure additional funding will depend on the success of its development, partner and partnering activities, the situation on the capital markets and other factors. If PAION is unable to raise financing at favorable terms or unable to raise financing at all, it could be forced to reduce its operating expenses by delaying, reducing or discontinuing the development of remimazolam or to enter into license agreements in the EU or certain markets in the EU although this might only allow for less value creation than an own commercialization.

PAION conducts short-, mid- and long-term planning of the financing requirements and updates it continuously in order to identify additional financing requirements in due time and to take measures accordingly. Moreover, PAION maintains regular contact to investors and (potential) pharma partners. This is a high risk. In case of occurrence, the potential damage level could pose a threat to the continued existence of the group.

#### bb) Currency risks

Some of PAION's contracts are based on foreign currencies, mainly on the U.S. dollar and the pound sterling to a lower degree. These primarily relate to the finalization of the development of remimazolam in the U.S. A strong rise of the U.S. dollar in respect to the euro could increase the costs for the development and market preparation of remimazolam. In order to reduce this risk, PAION does maintain foreign currency funds in U.S. dollars. Currency risks also arise from translating the foreign subsidiaries' separate financial statements from pound sterling into euros because the pound sterling is the functional currency of the UK subsidiaries.

Currency risks are systematically recorded and monitored based on short- and mid-term planning. With the consent of the Supervisory Board of PAION AG, the Management Board has drawn up clear rules governing the hedging instruments that may be used to limit currency risks. Hedging contracts are transacted or foreign currency funds are held under certain circumstances for foreign currency items, for which the amounts and due dates of cash flows are relatively certain. This is a moderate risk.

#### cc) Liquidity and default risks

PAION's cash and cash equivalents are held at different banks. There is a risk that PAION is not able to retrieve invested funds in case of a default of one or more of these banks. In order to minimize this risk, wherever applicable, only investments with the lowest possible risk safeguarded by deposit protection fund are made. This is an increased risk. In case of occurrence, the potential damage level could pose a threat to the continued existence of the group.

#### dd) Tax risks

PAION AG and its subsidiaries have considerable tax losses carried forward available. PAION assumes that based on the current German and British tax legislation, these losses can be carried forward indefinitely and offset against future earnings according to the relevant tax regulations (e. g. minimum taxation). If the usage of tax losses is partly or completely disallowed, for example due to changes in legislation, changes in capitalization or ownership structure as well as other events, higher income tax payments than expected would become due on the expected earnings if remimazolam is developed successfully. Dependent on the actual structure which has neither been decided nor can be anticipated yet, the consequences of a potential Brexit could also lead to tax payments on potential earnings expected in the future. These tax payments would correspondingly reduce liquidity.

Based on current tax legislation in Great Britain, PAION receives tax credits in connection with the development costs for remimazolam. The calculation of the refund claims is based on the calculation method agreed in previous years between PAION and the British tax authorities. Should the legislation change or should the tax authorities change the calculation method or not accept current methods anymore, the tax credits might be significantly lower than expected or might not be received at all in the future. Tax claims already recognized in the accounts could not be recoverable anymore in such a case and received tax credit payments not finally reviewed by the British tax authorities yet could become repayable.

PAION continuously monitors the relevant tax legislation and jurisdiction and consults external tax consultants for all material issues. Usability of tax losses carried forward is an increased risk. In case of occurrence, the potential damage level could pose a threat to the continued existence of the group. The reduction or cessation of tax credits from British tax authorities is a moderate risk.

#### ee) Risk of insolvency

There is a risk that one or several subsidiaries could go into insolvency. The occurrence of this risk would lead to substantial impairment losses on the equity investments in subsidiaries and the loans to subsidiaries. This would accordingly reduce the equity of PAION AG. Furthermore, if

expected payments from subsidiaries, e. g. loan repayments, are not made, this could lead to the insolvency of PAION.

For the purpose of monitoring the financial position, results of operations and cash flows of the operative subsidiaries, a monthly reporting with a balance sheet and profit and loss statement is conducted for these companies. The liquidity is monitored on a daily basis for each company. This is a high risk. In case of occurrence, the potential damage level could pose a threat to the continued existence of the group.

#### c. IT risks

As a globally acting group, PAION has implemented complex IT systems providing instantaneous exchange of data via stationary as well as mobile devices. There is a risk that external third parties gain unauthorized access and delete, corrupt or misuse confidential data to PAION's disadvantage or damage the IT infrastructure on purpose. This could be carried out via direct attacks, access via mobile devices or by bringing in malware which is then involuntarily installed or executed by users. PAION has implemented an integrated multiple-level security concept that reduces this risk to a high degree. This is an increased risk. In case of occurrence, the potential damage level could pose a threat to the continued existence of the group.

#### d. Legal and Compliance risks

PAION cooperates with a variety of external partners in different regions, exchanges confidential data on a regular basis and conducts clinical trials in various countries with different jurisdictions inducing several risks.

There is a risk that confidential information is being forwarded, published or misused. PAION has implemented internal guidelines for dealing with confidential information and only exchanges information with external third parties based on confidentiality agreements. All employment contracts contain clauses with confidentiality obligations. This is a moderate risk.

Conducting clinical studies always bears a liability risk, for example in case of unexpected physical damage for volunteers or patients. PAION generally purchases country-specific insurance policies for all clinical trials. This is a moderate risk.

#### e. Risks in relation to a potential "Brexit"

A potential exit of the United Kingdom from the European Union (so-called "Brexit") bears a variety of potential risks which can neither be comprehensively captured or specified in more detail qualitatively nor be defined temporally or quantitatively in regard to potential damage levels. At the time of creation of this report, it is neither certain if the notified exit date in March 2019 will actually be adhered to or if the exit will take place at all nor which potential interim regulation could become effective for which period following a possible exit. Basically, potential risks for PAION could stem

from the following areas nevertheless. This overview is however not necessarily exhaustive due to the given uncertainties. Also, potential risks cannot be reasonably categorized due to this fact.

Regulatory requirements for market approval of new drugs could potentially change rendering currently conducted or planned development programs inadequate for regulatory approval of remimazolam in the UK without amendments and consequentially additional costs and longer development times resulting thereof. In case of market approval, customs or other duties could restrict PAION's competitiveness in the UK or reduce potential proceeds based on the commercial structures within the PAION group at that time.

As remimazolam is a drug candidate of the English group company PAION UK Ltd and there is a variety of intercompany service provision within the group also between Germany and England, restrictions in that regard might occur preventing a reasonable and efficient exchange of services within the group. This could e.g. relate to organizational, logistical, tax, personnel and financial aspects.

Moreover, also apart from intragroup services, tax risks in particular could result from a potential Brexit.

#### 4. Market opportunities

PAION is focusing on the clinical development of drug candidates in anesthesia for which there is a substantial unmet medical need with the vision to participate in the commercialization.

Essentially, the anesthesia market is regarded as sufficiently supplied, and there have been no relevant innovations for decades. Nonetheless, remimazolam's properties either show safety or efficacy advantages in certain interventions providing attractive market opportunities. Demand for innovative anesthesia solutions is growing because of an aging population with an increasing number and complexity of surgical interventions for which existing products show certain safety deficiencies. PAION intends to make use of this fact. Most big pharma companies have withdrawn from actively promoting their product range in this therapeutic field. Market research has shown that the highest medical need in this field is provision of substances which have a superior safety profile. Furthermore, anesthetists often express the desire for a short-acting, safe and well controllable agent. PAION is responding to this medical need with the development of remimazolam.

After the successful completion of the Phase III program in the reporting period, remimazolam is in the final stage of clinical development in procedural sedation for minor medical interventions in the U.S. Iicense partner Cosmo plans to file for market approval in the fourth quarter 2018/ first quarter 2019. PAION's Chinese license partner Yichang Humanwell is going to conduct a Phase III study in procedural sedation. The development for general anesthesia in Japan is completed, and the Japanese license partner Mundipharma plans to file for market approval in 2018. PAION's Russian license partner R-Pharm is currently conducting a Phase III study in general anesthesia; the South Korean license partner Hana Pharm is going to conduct a Phase III study and the Chinese license partner Yichang Humanwell is going to conduct a Phase II study in this indication. PAION expects that only one Phase III trial will be required for market approval in general anesthesia in the EU which is

planned to be started in the second half of 2018. The third indication is ICU sedation, and a respective Phase II study was already started in Japan but not completed. PAION deems each of these three indications to have attractive sales potentials based on the respective regional conditions.

PAION benefits from the progress of the development of remimazolam in the U.S. and the development partners in China, South Korea, Canada, Russia/CIS, Turkey, the MENA region, and Japan financially in the form of milestone payments and royalties from launch onwards as well as in the form of additional development data. For the EU, an own commercialization is targeted. For all other regions, it is targeted to find license or distribution partners. In 2018, focus is on the U.S. and the EU: In the U.S., finalization of the clinical development program and handing over all data and documents to Cosmo is of priority in order to reach filing for market approval in procedural sedation in the U.S by Cosmo as soon as possible. For the EU, focus is on the start of a new Phase III study in general anesthesia.

Overall, PAION has the chance of receiving significant license income or income from a potential own commercialization of remimazolam. Based on the results of the market research activities performed so far, remimazolam is an excellent candidate for developing a commercial platform in anesthesia.

#### Overall evaluation of opportunities and risks

The successfully completed Phase III program with remimazolam in the U.S. in the reporting period was an important milestone on the pathway to market approval and has further reduced the risk of failure of the clinical development in procedural sedation although this can still not be completely ruled out until actual market approval. The capital increases conducted in the reporting period as well as the remimazolam license agreement for Japan entered into with Mundipharma enable PAION to start and conduct the planned EU Phase III study in general anesthesia without further financing exceeding expected tax credits and milestone payments from partners based on current planning. Thus, the risk situation has improved compared to the previous year.

It is anticipated that Cosmo will be in a position to file for market approval for remimazolam in procedural sedation in the U.S. in the fourth quarter 2018/first quarter 2019 and that PAION will be able to start the EU Phase III study in general anesthesia in the second half of 2018. Moreover, based on the development progress of the other partners, PAION expects that for the licensed regions potential further filings for market approval for remimazolam could take place in 2018. Taking these factors into account, the opportunity situation has improved in comparison to the previous year. Since remimazolam is not yet marketed and therefore no sustainable revenue is generated, PAION continues to incur losses.

#### Report on post-balance sheet date events

Dr. Jürgen Beck has been appointed member of the Management Board of PAION AG effective 1 January 2018.

There were no further significant events in the period between the reporting date, 31 December 2017, and the preparation of this report.

#### Report on expected developments

#### Outlook on development and commercialization

PAION's major goals for 2018 are the completion and transfer of all data and documents in the U.S. to Cosmo and the start of a new EU Phase III study in general anesthesia. In addition, PAION continues to work on production development for remimazolam.

For the U.S., PAION is focusing on the integrated analysis of all clinical studies with remimazolam, which is necessary for preparing and filing for market approval in the U.S. Before filing, a pre-NDA meeting with the FDA is usually held, which Cosmo currently plans shortly before filing for approval. The necessary coordination and preparatory work are currently being conducted together with Cosmo, U.S. key opinion leaders and regulatory experts. Filing for market approval is Cosmo's responsibility. Cosmo currently expects to file for approval in the fourth quarter 2018/first quarter 2019.

For the EU, PAION is working on the continuation of the clinical development program for remimazolam with a study design comparable to the successfully completed Phase III program in general anesthesia in Japan. After the scientific advice with the relevant European regulatory authority EMA in January 2018 which served to outline the new European Phase III program, the study start is planned in the second half of 2018.

PAION expects its other regional remimazolam partners to continue their development activities towards filing. PAION's partner Mundipharma plans to file for market approval in Japan in 2018. PAION's partner R-Pharm is currently conducting a Phase III study in Russia; recruitment is expected to be completed in the first half of 2018. Subsequently, R-Pharm plans to file for market approval currently anticipated for end of 2018. PAION's partner Yichang Humanwell will conduct two clinical studies with remimazolam in China; one Phase III study in procedural sedation and one Phase II study in general anesthesia. PAION's partner Hana Pharm is going to conduct a Phase III study with remimazolam in general anesthesia in South Korea. The partners Pharmascience, Hana Pharm and TR-Pharm plan to file for market approval in their respective territories based on the U.S. or Japanese dossier.

#### Financial outlook

PAION expects revenues of about EUR 3 million in 2018, thereof EUR 2 million in connection with the planned regulatory filing for remimazolam in Japan by Mundipharma. Moreover, approx. EUR 1 million are related to the upfront payment received from Mundipharma in January 2018 in course of the remimazolam license agreement for Japan.

Due to the ongoing investment in the development of remimazolam including the EU Phase III study, PAION expects research and development expenses to amount to approx. EUR 15 million and approx. EUR 17 million, depending on the progress of development. Income from tax credits on parts of research and development expenses from British tax authorities is expected to amount to approx. EUR 3 million. General administrative and selling expenses are expected to amount to between approx. EUR 3.5 million and approx. EUR 4 million. Net loss is expected to amount to between approx. EUR 12.5 million and approx. EUR 15 million in 2018. Should filing for market approval in Japan be delayed to 2019, revenues and net result would decrease by EUR 2 million. In case of regulatory filing in the U.S. in the fourth quarter 2018, revenues as well as net result would increase in 2018.

This outlook assumes that PAION and partner activities progress as expected. Otherwise, essential cost blocks would shift into 2019. Plans are also based on the current status of discussions with regulatory authorities. Additional requirements by regulatory authorities could lead to higher costs than planned and to delays in approvals.

Based on current plans, PAION believes that cash and cash equivalents of EUR 24.8 million as of 31 December 2017 enable PAION to complete all activities for preparation of the filing dossier in procedural sedation in the U.S. PAION expects to receive payments from its license partners, subject to the achievement of certain regulatory milestones, and, once remimazolam is approved, royalties on net sales. Should development, filing and approval go according to plan, PAION will not need additional funding to bring remimazolam to the U.S. market.

For the planned EU Phase III study, no further funding is required based on current planning allowing for the planned study start in the second half of 2018. Cash and cash equivalents, including expected tax credits from the British tax authorities on parts of research and development expenses and expected potential milestone payments in connection with filings for market approval in the U.S. and Japan, secure the conduct of the targeted Phase III study in the EU based on current cost planning. Overall, this ensures a cash reach into the second half of 2019. Until filing for market approval in the EU, further funds of approx. EUR 15 million are required based on current planning. This funding requirement may partly be covered by potential further milestone payments.

Aachen, Germany, 21 March 2018 PAION AG

Dr. Wolfgang Söhngen

Dr. Jülrgen Beck

Abdelghanj Omari

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## **Consolidated Financial Statements**

PAION AG

### Consolidated Balance Sheet as of 31 December 2017

ASSETS	Note	31 Dec. 2017 EUR	31 Dec. 2016 EUR
Non-current assets			
Intangible assets	1.	2,414,870.55	2,687,855.47
Equipment	2.	113,682.01	167,210.31
Other assets		13.95	14.04
		2,528,566,51	2,855,079,82
Current accets			
Current assets Trade receivables	3.	27 /22 15	0.00
Prepaid expenses and other assets	3. 4.	37,433.15	
Cash and cash equivalents	4. 5.	4,480,716.05 24,838,652.24	5,017,115.86 30,111,355.87
Cash and Cash equivalents	٥.	29,356,801.44	35,128,471.73
		29,330,601.44	33,120,471.73
Total assets		31,885,367.95	37,983,551.55

EQUITY AND LIABILITIES	Note	31 Dec. 2017 EUR	31 Dec. 2016 EUR
Equity	6.		
Share capital		61,120,046.00	55,757,094.00
Capital reserve		135,854,744.31	128,548,802.57
Translation reserve		-630,192.60	-340,777.37
Loss carryforward		-159,021,995.85	-138,904,359.04
Result for the period		-12,093,427.29	-20,117,636.81
		25,229,174.57	24,943,123.35
Current liabilities			
Trade payables	8.	5,920,968.99	6,352,616.12
Provisions	7.	390,855.94	554,962.54
Other current liabilities	9.	325,453.79	358,814.11
Current portion of deferred income	10.	18,914.66	5,774,035.43
		6,656,193.38	13,040,428.20
Total equity and liabilities		31,885,367.95	37,983,551.55
iotai equity and navinues		31,003,307.93	37,703,331.33

# Consolidated Statement of Comprehensive Income for Fiscal Year 2017

	Note	2017 EUR	2016 EUR
Revenues	11.	5,811,199.73	4,261,774.17
Cost of revenues		0.00	0.00
Gross profit		5,811,199.73	4,261,774.17
Research and development expenses		-17,853,505.83	-23,408,395.77
General administrative and selling expenses		-3,827,551.76	-5,128,622.06
Other income (expenses), net	12.	-2,355.95	-806,887.33
Operating expenses		-21,683,413.54	-29,343,905.16
Operating result		-15,872,213.81	-25,082,130.99
Financial income	13.	19,811.94	20,882.18
Financial result		19,811.94	20,882.18
Result for the period before taxes		-15,852,401.87	-25,061,248.81
Income taxes	14.	3,758,974.58	4,943,612.00
Result for the period		-12,093,427.29	-20,117,636.81
of which attributable to other shareholders		0.00	0.00
of which attributable to shareholders of PAION AG		-12,093,427.29	-20,117,636.81
Foreign currency translation of subsidiaries		-279,641.89	88,698.06
Total income and expense recognized directly in equity that will be			
reclassified to profit or loss when specific conditions are met		-279,641.89	88,698.06
Cumulative foreign currency translation reclassified to profit or loss due			
to changes in the scope of consolidation		-9,773.34	0.00
Other comprehensive income		-289,415.23	88,698.06
Total comprehensive income		-12,382,842.52	-20,028,938.75
of which attributable to other shareholders		0.00	0.00
of which attributable to shareholders of PAION AG		-12,382,842.52	-20,028,938.75
Earnings per share (basic)	15.	-0.20	-0.38
Earnings per share (diluted)	15.	-0.20	-0.38

# Consolidated Cash Flow Statement for Fiscal Year 2017

	2017 EUR	2016 EUR
Cash flows from operating activities:		
Net result for the period	-12,093,427.29	-20,117,636.81
Reconciliation of net profit (loss) for the period to cash flows from operating activities:		
Income taxes	-3,758,974.58	-4,943,612.00
Amortization/depreciation and non-cash changes of fixed assets	347,254.29	758,914.35
Loss/Profits from the disposal of non-current assets	4,240.19	-4,745.39
Interest expenses and interest income	-19,811.94	-20,882.18
Release of deferred income	-5,478,666.89	-4,135,952.68
Expenses from stock option plans	174,474.72	198,365.47
Changes in assets and liabilities which are not attributable to investing or financing activities:		
Trade receivables	-37,433.15	0.00
Prepaid expenses and other assets	-300,545.32	1,788,336.56
Trade payables	-431,647.13	-979,842.00
Provisions	-145,609.20	274,221.29
Other current liabilities	-33,360.32	54,039.16
Deferred income	-276,453.88	9,865,510.81
Non-cash exchange losses/gains	-267,717.27	128,405.38
	-22,317,677.77	-17,134,878.04
Tax payments	-19,696.15	0.00
Tax payments received	4,596,583.91	5,529,216.50
Interest received	20,346.50	19,324.50
Net cash used in operating activities	-17,720,443.51	-11,586,337.04
Cash flows from investing activities:	-24,981.17	-198,864.35
Cash paid for investments in intangible assets and equipment	0.00	6,722.69
Proceeds from Sale of Property, Plant and Equipment	-24,981.17	-192,141.66
Net cash used in investing activities	7	
Cash flows from financing activities:		
Capital increase	5,362,952.00	5,097,654.00
Contributions to the capital reserve	7,818,544.16	4,589,483.82
Payments in connection with raising capital	-687,077.14	-475,271.94
Net cash provided from financing activities	12,494,419.02	9,211,865.88
Change in cash and cash equivalents	-5,251,005.66	-2,566,612.82
Effect of exchange rate changes on cash	-21,697.97	-1,828.51
Cash and cash equivalents at beginning of the period	30,111,355.87	32,679,797.20
Cash and cash equivalents at end of the period	24,838,652.24	30,111,355.87
Composition of cash and cash equivalents at the end of the period:		
Cash and cash equivalents	24,838,652.24	30,111,355.87

# Consolidated Statement of Changes in Equity for Fiscal Year 2017

EUR	Share capital	Capital reserve	Translation reserve	Loss carryforward	Equity
31 December 2015	50,659,440.00	124,236,225.22	-429,475.43	-138,904,359.04	35,561,830.75
Total comprehensive income	0.00	0.00	88,698.06	-20,117,636.81	-20,028,938.75
Issue of shares	5,097,654.00	0.00	0.00	0.00	5,097,654.00
Contribution to the capital reserve	0.00	4,589,483.82	0.00	0.00	4,589,483.82
Cost of raising capital	0.00	-475,271.94	0.00	0.00	-475,271.94
Additional contribution to the capital					
reserve due to the issue of options	0.00	198,365.47	0.00	0.00	198,365.47
31 December 2016	55,757,094.00	128,548,802.57	-340,777.37	-159,021,995.85	24,943,123.35
Total comprehensive income	0.00	0.00	-279,641.89	-12,093,427.29	-12,373,069.18
Issue of shares	5,362,952.00	0.00	0.00	0.00	5,362,952.00
Contribution to the capital reserve	0.00	7,818,544.16	0.00	0.00	7,818,544.16
Cost of raising capital	0.00	-687,077.14	0.00	0.00	-687,077.14
Additional contribution to the capital					
reserve due to the issue of options	0.00	174,474.72	0.00	0.00	174,474.72
Effects from changes in the scope of					
consolidation	0.00	0.00	-9,773.34	0.00	-9,773.34
31 December 2017	61,120,046.00	135,854,744.31	-630,192.60	-171,115,423.14	25,229,174.57

# **Consolidated Notes**

PAION AG

# Notes to the consolidated financial statements for fiscal year 2017

### General disclosures

The consolidated financial statements comprise PAION AG as the parent company, registered at Martinstrasse 10-12, 52062 Aachen, Germany, and the following wholly-owned and fully consolidated subsidiaries:

- PAION Deutschland GmbH, Aachen/Germany
- PAION Holdings UK Ltd, Cambridge/UK
- PAION UK Ltd, Cambridge/UK
- TheraSci Limited, Cambridge/UK

PAION AG is a holding company that provides various services to the subsidiaries. The PAION Group specializes in developing and commercializing medical innovations for procedural sedation, anesthesia and critical care services.

PAION AG shares are admitted to trading on the Frankfurt Stock Exchange and are listed in the Prime Standard of the Regulated Market.

The formerly wholly-owned subsidiary PAION, Inc., Delaware/U.S. was dissolved during the fiscal year. In course of the deconsolidation, cumulated currency gains from the translation of balance sheet and income statement into EUR recognized in equity in the amount of KEUR 10 were reclassified to the income statement. There were no further effects of the deconsolidation on the group accounts.

The consolidated financial statements as of 31 December 2017 are scheduled for authorization and approval for publication by the Supervisory Board in its meeting on 21 March 2018.

## Basis of accounting

The consolidated financial statements have been prepared according to Section 315e of the German Commercial Code (Handelsgesetzbuch, HGB) in accordance with the International Financial Reporting Standards (IFRSs) as adopted by the European Union (EU), and the interpretations of the International Financial Reporting Interpretations Committee (IFRIC). PAION

applied all IFRSs that had been issued by the International Accounting Standards Board (IASB), London, UK, and were effective as of the balance sheet date of 31 December 2017, and which had been adopted by the European Commission for application in the EU at the time of preparing the consolidated financial statements. Assets and liabilities are recognized and measured using those standards that were mandatory as of 31 December 2017 according to IAS 1.

The following new and/or revised standards, amendments and interpretations were applied for the first time in the fiscal year. The application of these standards and interpretations did not necessitate the provision of additional disclosures and did not influence the net assets, financial position and results of the Group's operations in any way.

- IFRSs 2014–2016 Cycle "Annual Improvements to IFRSs 2014–2016": Amendments to IFRS 12 "Disclosure of Interests in Other Entities"
- Amendments to IAS 7 "Statement of Cash Flows"
- Amendments to IAS 12 "Income Taxes"

The following standards, amendments, clarifications and interpretations which have already been issued will be applied as soon as they become effective, provided they are adopted by the European Commission:

- IFRSs 2014–2016 Cycle "Annual Improvements to IFRSs 2014–2016" implements changes to following further standards:
  - IFRS 1 "First-time Adoption of International Financial Reporting Standards"
  - IAS 28 "Investments in Associates and Joint Ventures"

    The amendments are effective for annual periods beginning on or after 1 January 2018. Earlier adoption is allowed.
- IFRSs 2015–2017 Cycle "Annual Improvements to IFRSs 2015–2017" implements changes to following standards:
  - IFRS 3 "Business Combinations"
  - IFRS 11 "Joint Arrangements"
  - IAS 12 "Income Taxes"
  - IAS 23 "Borrowing Costs"

The amendments are effective for annual periods beginning on or after 1 January 2019. Earlier adoption is allowed. The adoption by the EU is still pending.

- IFRIC 22 "Foreign Currency Transactions and Advance Consideration": The interpretation is effective for annual periods beginning on or after 1 January 2018. Earlier adoption is allowed. The adoption by the EU is still pending.
- IFRIC 23 "Uncertainty over Income Tax Treatments": The interpretation is effective for annual periods beginning on or after 1 January 2019. Earlier adoption is allowed. The adoption by the EU is still pending.
- Amendments to IAS 40 "Investment Property": The amendments are effective for annual periods beginning on or after
   1 January 2018. Earlier adoption is allowed.
- IFRS 9 "Financial Instruments": The new guidelines are effective for fiscal years beginning on or after 1 January 2018.
   Earlier adoption is allowed.
- Amendments to IFRS 2 "Share-based payment": The amendments are effective for fiscal years beginning on or after
   1 January 2018. Earlier adoption is allowed.
- IFRS 15 "Revenue from contracts with customers": This standard is effective for fiscal years beginning on or after 1 January 2018. Earlier adoption is allowed.
- Clarifications to IFRS 15 "Revenues from contracts with customers": The clarifications are effective for fiscal years beginning on or after 1 January 2018. Earlier adoption is allowed.
- IFRS 16 "Leases": This standard is effective for fiscal years beginning on or after 1 January 2019. Earlier adoption is allowed.
- IFRS 17 "Insurance Contracts": This standard is effective for fiscal years beginning on or after 1 January 2021. Earlier adoption is allowed. The adoption by the EU is still pending.
- Amendments to IFRS 9 "Financial Instruments": The amendments are effective for annual periods beginning on or after
   1 January 2019. Earlier adoption is allowed. The adoption by the EU is still pending.
- Amendments to IAS 28 "Investments in Associates and Joint Ventures": The amendments are effective for annual periods beginning on or after 1 January 2019. Earlier adoption is allowed. The adoption by the EU is still pending.

Amendments to IAS 19 "Employee Benefits": The amendments are effective for annual periods beginning on or after
 1 January 2019. Earlier adoption is allowed. The adoption by the EU is still pending.

The application of these new and/or revised standards and interpretations may, in some cases, result in additional disclosure obligations in future consolidated financial statements. The amendments, except for IFRS 15 and IFRS 16, will presumably not have any effects on the Group's net assets, financial position and results of operations. Early adoption of IFRS 9 would not have led to the identification of default risks.

The application of IFRS 15 may have effects on the Group's net assets, financial position and results of operations in the future. PAION recognizes essential parts of its revenues from license agreements. According to IFRS 15, the analysis of revenue recognition is based on a process consisting of five steps. The application of IFRS 15 could particularly result in a different timing of the realization of revenues in regard to the achievement of contractually defined development milestones. The magnitude of these effects depends on the respective individual contractual agreement; particularly additional disclosure requirements might apply in the future. Existing contracts have been evaluated based on the five-step process with particular attention on differentiation between rights to access and rights to use as well as the distinction of sales-based royalties upon commercialization. In comparison to current accounting treatment, no effects of the application of the new standard have been identified. Therefore, application of IFRS 15 will neither have an effect on already recognized revenues nor on revenues to be recognized in the future from existing contracts. Future contracts will be subject to the same evaluation methodology. In terms of transition to IFRS 15, the cumulative effect method will be applied leading to no effects.

The application of IFRS 16 may have effects on the Group's net assets, financial position and results of operations in the future if leases existing at that time which are/would currently be treated off balance sheet would then need to be reflected in the balance sheet according to IFRS 16. The potential effects on existing leases are currently being analyzed; a final evaluation is outstanding.

The consolidated financial statements have been prepared in Euros. Amounts were stated in Euro or KEUR.

The income statement has been prepared using the cost of sales method. Research and development expenses are reported separately in the income statement in light of their material importance.

In accordance with IAS 1 "Presentation of Financial Statements", the balance sheet distinguishes between non-current and current assets and non-current and current liabilities. Assets, liabilities and provisions are deemed to be current if they mature within one year.

The consolidated financial statements do not contain any segment information as no reportable business or geographical segments could be identified.

The preparation of consolidated financial statements in accordance with IFRSs requires making estimates and assumptions which have an effect on the amount of recognized assets and liabilities, income and expenses and contingent liabilities. Actual amounts may differ from these estimates.

The estimations and discretionary valuations made in the course of preparing the consolidated financial statements apply primarily to the measurement of intangible assets, provisions and revenues. The development project remimazolam that was capitalized following the acquisition of the PAION UK group is amortized over the useful life based on forward-looking assumptions in respect of the time at which regulatory approval is obtained and of patent protection. PAION's revenues mainly result from license agreements which usually comprise the transfer of so far generated data, the achievement of development milestones as well as royalty payments depending on the commercial success. Revenues relating to technology access fees (e. g. in form of upfront payments), the achievement of milestones and services to be provided in that regard are recognized once the Management Board deems the underlying critera for revenue recognition according to IFRS as satisfied based on a scientific, technical and economic evaluation including the involvement of the relevant specialized departments.

The consolidation principles and accounting policies adopted in the previous year have been maintained and incorporate the new and/or revised standards and interpretations.

The application of the new and/or revised standards and interpretations did not result in additional disclosure obligations and did not have an influence on the net assets, financial position and results of the Group's operations.

### **Consolidation principles**

The consolidated financial statements include PAION AG, its subsidiaries PAION Deutschland GmbH, and PAION Holdings UK Ltd, and the latter's subsidiary companies as listed in A. "General disclosures". The financial statements of the companies included in the consolidated financial statements have been prepared in accordance with uniform accounting policies. Accounts receivable and payable, income and expenses and interim profits from intra-Group transactions have been eliminated.

# Foreign currency translation

The consolidated financial statements are shown in Euros, which is the functional currency of PAION AG and the reporting currency of the Group. Each company within the Group defines its own functional currency. This is the euro in the case of the German companies whereas the UK-based companies use the pound sterling as their functional currency. All items on the respective financial statements of each company are initially translated into the functional currency at the exchange rate applicable on the transaction date. Monetary assets and liabilities denominated in a foreign currency are translated to the functional currency on the reporting date at the exchange rate applicable on that date. All ensuing currency differences are recognized in profit or loss with the exception of exchange rate gains and losses from intra-group loans classified in accordance with IAS 21 as net investments in foreign business operations; these are recognized directly in equity.

The assets and liabilities of the foreign companies are translated into euro on the balance sheet date at the exchange rate applicable on that date (exchange rate as of 31 December 2017: 0.8887 GBP/EUR; exchange rate as of 31 December 2016: 0.8553 GBP/EUR). These include any goodwill in connection

with the acquisition of a foreign company and any fair value adjustments to the carrying amounts of the foreign company's assets and liabilities. Equity components are translated into euro at historical rates at the time of initial consolidation. Expenses and income are translated into euro at average monthly exchange rates (bandwith in 2017 from 0.8478 GBP/EUR to 0.9121 GBP/EUR; bandwith in 2016 from 0.7539 GBP/EUR to 0.8927 GBP/EUR). The resulting currency differences are accounted for separately within equity.

## **Accounting policies**

#### **Business combinations before 1 January 2010**

Business combinations are accounted for using the acquisition method. The cost of an acquisition is measured as the aggregate of the consideration transferred, measured at acquisition date fair value. Acquisition costs also include the costs directly attributable to the acquisition as well as liabilities arising from the acquisition. Assets, liabilities and contingent liabilities identifiable in the context of a business combination are measured at acquisition date fair value for first time consolidation.

 $\label{eq:there were no business combinations after 1 January 2010.$ 

## **Intangible assets**

Acquired intangible assets are measured at cost. They are subject to amortization over their respective useful life using the straight-line method and tested for possible impairment if there are any indications that the intangible asset may be impaired. A useful life of between three and five years is defined for software, while research and marketing rights for compounds are amortized over the term of the respective patent.

#### **Equipment**

Equipment is measured at cost less cumulative depreciation. These assets are subject to depreciation over their expected useful life using the straight-line method; their expected useful life is between three and twenty years. The recoverability of assets is always tested when events have occurred or circumstances have changed, which could have an effect on the recoverability

of the assets. The recoverability of the assets held and used by the company is measured on the basis of a comparison between the carrying amount and the higher of fair value less cost to sell and its value in use. If an asset is measured below its carrying amount, it is written down to the higher of fair value less cost to sell and its value in use. These impairment losses are reversed if the reasons for the prior impairments cease to exist.

Leased equipment that meets certain requirements defined in IAS 17 "Leases" is recognized as an asset and the present value of the leasing payment obligations is recognized as a liability. Leased assets that are recognized as assets are subject to depreciation over the term of the lease using the straight-line method.

#### **Financial assets**

Standard market purchases or sales of financial assets are recognized on the trading date, i.e. on the day on which the Group undertakes to purchase or sell the asset.

### **Financial Instruments**

The fair value of financial instruments is determined according to the three hierarchy levels defined in IFRS 13 based on the availability of respective input factors:

- Level 1: The fair value is determined based on quoted prices in active markets.
- Level 2: The fair value is determined based on valuation models depending on price-relevant information.
- Level 3: The fair value is determined based on valuation models that do not incorporate price-relevant information.

Changes in fair value are recognized through profit and loss.

## Receivables and other assets

Trade receivables and other assets are measured at amortized cost. Receivables denominated in a foreign currency are translated at the rate applicable on the balance sheet date. Exchange rate gains or losses are recognized in profit or loss.

#### Cash and cash equivalents

Cash and cash equivalents comprise cash balances, bank account balances and current deposits with an original residual term of less than three months. Cash and cash equivalents are measured at amortized cost.

#### **Equity**

The costs directly associated with the issuance of equity are not expensed in the income statement but deducted straight from the added equity after taking into account potential tax effects.

#### **Provisions**

Provisions for current obligations (legal or constructive), which originated in the past and whose maturity and amount are uncertain, are recognized to the extent to which these obligations will probably have to be satisfied by an outflow of resources that represent an economic benefit, and to which the amount of the obligations can be reliably estimated. Provisions with a term of more than one year are recognized at present value.

#### Financial liabilities

Financial liabilities are recognized at amortized cost using the effective interest method.

#### Trade payables/other liabilities

Trade payables and other liabilities are measured at repayment cost. Liabilities denominated in a foreign currency are measured at the exchange rate applicable on the reporting date. Exchange rate gains or losses are recognized in profit or loss.

## **Deferred income**

Non-refundable payments received in connection with outlicensing agreements are either directly recognized as income or reported as deferred income and recognized in profit over the period in which the corresponding underlying service is being rendered or over the probable development life of the respective product/indication, in each case depending on the individual contractual regulations.

#### **Revenues**

Revenues are recognized as realized during the fiscal year. Income is realized upon performance of the service owed and transfer of the risk, when the amount of anticipated consideration can be reliably estimated, when it is probable that the economic benefits will flow to the entity and when the cost incurred and to be potentially incurred in respect of the transaction can be measured reliably.

Since PAION is not selling products at the market yet, revenues are essentially realized by means of saling or outlicensing substances or drug candidates. Processually, the sale or outlicensing of substances or technological knowledge regularly starts with an extensive technology and know-how access by the buyer or licensee. Depending on the strategy of the licensee, subsequent services like the (support in regard to the) implementation of a production process, the conduct and completion of clinical trials in other regions or e.g. providing dossiers for market approvals from other regions are contractually agreed. Revenues in the context of services for which PAION owes a successful completion are only recognized once all services to be delivered based on the contractual agreements have been carried out completely in the respective period due to the high inherent risk in the development of medical and pharmaceutical products. Revenues in the context of quantifiable services for which PAION does not know a success, are recognized based on the stage of completion in the respective period.

For the assessment of the respective magnitude of revenues to be recognized, the contractual agreements, the complexity and specificity of the service, the potential costs for the licensee/buyer in case of an alternative purchase, the costs (incurred) as well as revenues from comparable transactions are being considered.

#### **Cost of revenues**

Development costs that are charged on to third parties are reported as costs of revenues.

#### Research and development expenses

Research costs are recognized as expenditure in the period in which they are incurred. Pursuant to IAS 38 "Intangible Assets",

development costs must be capitalized depending on the possible outcome of the development activities and when specific cumulative conditions are met. These conditions are not met at present, which is why all development costs are recognized as expenses in the period in which they occur.

#### Interest income/expense

Interest income/expense is recognized in the period in which it occurs. Any necessary deferrals are calculated using the effective interest method.

#### Income taxes/deferred taxes

Deferred taxes are recognized in accordance with IAS 12 "Income Taxes". They are recognized by applying enacted statutory tax rates applicable to future years to temporary differences between the IFRS carrying amounts and the tax bases of existing assets and liabilities. The effects of a change in the enacted tax rates on deferred taxes is recognized in the period in which the change is enacted. Deferred taxes are also recognized for losses carried forward. No deferred tax assets are recognized if it is probable that some portion or all of the deferred tax assets may not be recoverable. Tax reimbursements from the British tax authorities for subsidized research and development activities are disclosed under income taxes.

#### **Share-based payment transactions**

Stock options (equity-settled share-based payment instruments) are measured at fair value at the time they are granted. The fair value of the obligations is recognized both as a personnel expense and an increase in equity over the vesting period. The fair value is calculated using internationally accepted valuation methods (Black/Scholes).

### Consolidated balance sheet disclosures

# (I) Intangible assets

Intangible assets developed as follows:

		Industrial rights
		and similar rights
EUR	and assets	

Acquisition Cost	
1 Jan. 2016	15,208,246.58
Additions	57,073.05
Disposals	0.00
Reclassifications	0.00
Exchange rate differences	-2,111,121.09
31 Dec. 2016	13,154,198.54
Additions	22,318.63
Disposals	958.71
Reclassifications	0,00
Exchange rate differences	-484,835.31
31 Dec. 2017	12,690,723.15
Accumulated amortization, depreciation and	l impairment losses
1 Jan. 2016	11,846,744.65
Additions	271,078.37
Disposals	0.00
Exchange rate differences	-1,651,479.95
31 Dec. 2016	10,466,343.07
Additions	199,005.12
Disposals	958.71
Exchange rate differences	-388,536.88
31 Dec. 2017	10,275,852.60
Carrying amounts as of 31 Dec. 2016	2,687,855.47
Carrying amounts as of 31 Dec. 2017	2,414,870.55

The intangible assets mainly comprise the development project remimazolam (KEUR 2,353; 31 December 2016: KEUR 2,626). This development project is being written off over the expected useful

life until mid-2031 based on forward-looking assumptions in respect of the expected time at which regulatory approval is obtained, and of patent protection.

Amortization of intangible assets substantially relates to remimazolam and is recognized as research and development

expenses during the development period. A minor portion of the amortization of intangible assets relates to software and is recognized partly in the research and development expenses and partly in the general administrative and selling expenses.

# (2) Equipment

# Equipment developed as follows:

EUR	Plant and machinery	Other plant, factory and office equipment	Tota
A			
Acquisition Cost 1 Jan. 2016	171,785.20	694,347.12	866,132.32
Additions	3,132.14	169,177.74	172,309.88
Disposals	0.00	28,501.30	28,501.30
Reclassifications	0.00	0.00	0.00
Exchange rate differences	171.45	-21,813.17	-21,641.72
31 Dec. 2016	175,088.79	813,210.39	988,299.18
Additions	,	0.00	
	2,662.54		2,662.54
Disposals Reclassifications	4,820.42	12,672.78	17,493.20
	0.00	0.00	0.0
Exchange rate differences 31 Dec. 2017	-345.32 172,585.59	-9,453.71 791,083.90	-9,799.03 963,669.49
Accumulated amortization, depreciation and impairment losses			
1 Jan. 2016	137,956.13	672,585.42	810,541.5
Additions	13,147.48	39,772.73	52,920.2
Disposals	0.00	26,524.00	26,524.0
Exchange rate differences	55.34	-15,904.23	-15,848.8
31 Dec. 2016	151,158.95	669,929.92	821,088.8
Additions	9,537.02	37,535.34	47,072.3
Disposals	1,688.78	11,505.00	13,193.7
Disposais Exchange rate differences	-86.45	, i	,
		-4,893.52	-4,979.9
31 Dec. 2017	158,920.74	691,066.74	849,987.48
Carrying amounts as of 31 Dec. 2016	23,929.84	143,280.47	167,210.3
Carrying amounts as of 31 Dec. 2017	13,664.85	100,017.16	113,682.01

# (3) Trade receivables

Trade receivables entirely relate to the remimazolam license agreement for Japan entered into with Mundipharma in the reporting period.

# (4) Prepaid expenses and other assets

Prepaid expenses and other assets substantially comprise claims for reimbursement from the British tax authorities for subsidized research and development activities (KEUR 3,749; previous year: KEUR 4,737), prepaid expenses relating to research and development services for remimazolam (KEUR 409; previous year: KEUR 0), VAT refund claims (KEUR 129; previous year: KEUR 122) and prepaid expenses relating to insurance contributions, rents and other prepayments (KEUR 101; previous year: KEUR 113).

#### (5) Cash and cash equivalents

Cash and cash equivalents are comprised of the following:

	31 Dec. 2017 KEUR	31 Dec. 2016 KEUR
Current deposits  Bank balance and cash in	619	13,049
hand	24,220 <b>24,839</b>	17,062 <b>30,111</b>

Bank balances earn interest at the variable rates for call money. Current deposits are made for periods ranging from one to three months. These earn interest at the respective applicable interest rate for current deposits.

# (6) Equity

As of 31 December 2017, the share capital amounts to EUR 61,120,046.00 (previous year: EUR 55,757,094.00); it is divided into 61,120,046 no-par value shares (previous year: 55,757,094 shares). The increase of the share capital in the total amount of EUR 5,362,952.00 in the reporting period results from a capital increase with subscription rights conducted in February 2017 in the amount of EUR 2,439,023.00, from a capital increase without subscription rights conducted in July 2017 in the amount of EUR 2,824,515.00, and from the exercise of stock options in the amount of EUR 99,414.00. Details are described in the following.

The capital reserve amounts to EUR 135,854,744.31 as of 31 December 2017 (previous year: EUR 128,548,802.57) and contains the share premium from the issuance of shares and expenses in the amount of the fair value of granted stock options recognized over the vesting period.

On 7 February 2017, the Management Board decided with the approval of the Supervisory Board and based on the authorization by the General Meeting to issue 2,439,023 new, no-par value bearer shares at a subscription price of EUR 2.05, granting pre-emptive rights to existing shareholders. The existing shareholders were able to subscribe the new shares at a subscription ratio of 23:1 in the subscription period from 10 February 2017 to 27 February 2017. A U.S. institutional investor had committed to acquire any new shares not subscribed for by existing shareholders or other investors in connection with the rights offering at the subscription price. Upon completion of the capital increase, the company's share capital increased from EUR 55,757,094.00 by EUR 2,439,023.00 to EUR 58,196,117.00 through the issuing of 2,439,023 new shares. The capital increase with gross proceeds of EUR 5.0 million was recorded in the commercial register on 1 March 2017. Authorized Capital 2015 correspondingly decreased by EUR 2,439,023.00 to EUR 17,817,753.00.

By virtue of a resolution adopted by the Annual General Meeting on 17 May 2017, the Management Board was authorized to increase the share capital on or prior to 16 May 2022, with the consent of the Supervisory Board, on one or more occasions, by up to EUR 29,098,058.00 in total by issuing up

to 29,098,058 new no-par value bearer shares in return for cash contributions or contributions in kind (Authorized Capital 2017). Furthermore, the Management Board was authorized to use up to EUR 5,819,611.00 of the Authorized Capital 2017 to issue new shares for cash by excluding pre-emptive rights. The still available Authorized Capital 2015 in the amount of EUR 17,817,753.00 was revoked.

On 17 July 2017, the Management Board decided with the approval of the Supervisory Board and based on the authorization of the General Meeting to issue 2,824,515 no-par value bearer shares in return for cash contribution by excluding pre-emptive rights for the existing shareholders to two institutional U.S. investors. The new shares were issued at a price of EUR 2.8444. The capital increase led to gross proceeds of EUR 8.0 million. As a result, the share capital of the company was increased from EUR 58,256,591.00 by EUR 2,824,515.00 to EUR 61,081,106.00 through the issuing of 2,824,515 new shares. The capital increase was registered in the Commercial Register on 18 July 2017. The Authorized Capital 2017 was reduced by EUR 2,824,515.00 in the course of this capital measure and amounts to EUR 26,273,543.00 as of 31 December 2017.

Furthermore, by virtue of another resolution adopted by the Annual General Meeting on 17 May 2017, subject to the consent of the Supervisory Board, the Management Board was authorized to issue on or before 16 May 2022, on one or more occasions, bearer or registered convertible bonds, warrantlinked bonds, profit participation rights and/or participating bonds (or combinations thereof; hereinafter collectively "Bonds") of up to an aggregate of EUR 125,000,000.00 with or without a limited maturity period and to grant the holders or beneficiaries of the Bonds conversion rights or options to new shares in PAION AG with a proportionate amount of the share capital of up to EUR 26,200,000.00 in total (Conditional Capital 2017). Furthermore, the Management Board was authorized to use up to EUR 5,819,611.00 of the Conditional Capital 2017 for Bonds against cash by excluding pre-emptive rights. Conditional Capital 2015 in the amount of EUR 22,433,285.00 was revoked.

The Annual General Meeting of 17 May 2017 adopted a resolution to revoke the remaining Conditional Capital 2004 II

in the amount of EUR 34,847.00. The conditional capital increase could have been executed only to the extent that the holders of options granted by PAION AG in connection with the Stock Option Plan 2005 had exercised their options. All remaining stock options issued under the Stock Option Plan 2005 have lapsed in the reporting period.

A resolution was adopted by the Annual General Meeting on 5 May 2008 to conditionally increase the share capital of PAION AG by an aggregate of up to EUR 815,000.00 by issuing an aggregate of up to 815,000 new no-par value bearer shares (Conditional Capital 2008 I). A resolution was adopted by the Annual General Meeting on 19 May 2010 to adjust the Conditional Capital 2008 I to EUR 760,235.00. The conditional capital increase may be executed only to the extent that the holders of options granted by PAION AG in connection with the Stock Option Plan 2008 exercise their options. Under the Stock Option Plan 2008, 375,747 stock options were issued to current and former Management Board members and employees of the PAION Group as of 31 December 2017. To date, 341,045 stock options from the Stock Option Plan 2008 have been exercised, thereof 99,414 in fiscal year 2017. The exercises led to cash inflows of EUR 147,448.54 in the fiscal year. As of 31 December 2017, Conditional Capital 2008 I amounts to EUR 419,190.00.

A resolution was adopted by the Annual General Meeting on 19 May 2010 to conditionally increase the share capital of PAION AG by an aggregate of up to EUR 720,000.00 by issuing an aggregate of up to 720,000 new no-par value bearer shares (Conditional Capital 2010 I). The conditional capital increase may be executed only to the extent that the holders of options granted by PAION AG in connection with the Stock Option Plan 2010 exercise their options. Under the Stock Option Plan 2010, 696,626 stock options were issued to current and former Management Board members and employees of the PAION Group as of 31 December 2017. No stock options have been exercised yet.

A resolution was adopted by the Annual General Meeting on 21 May 2014 to conditionally increase the share capital of PAION AG by an aggregate of up to EUR 740,000.00 by issuing an aggregate of up to 740,000 new no-par value bearer shares (Conditional Capital 2014). The conditional capital increase may be executed only to the extent that the

holders of options granted by PAION AG in connection with the Stock Option Plan 2014 exercise their options. Under the Stock Option Plan 2014, 478,385 stock options were issued to current and former Management Board members and employees of the PAION Group as of 31 December 2017. No stock options have been exercised yet.

A resolution was adopted by the Annual General Meeting on 25 May 2016 to conditionally increase the share capital of PAION AG by an aggregate of up to EUR 840,000.00 by issuing an aggregate of up to 840,000 new no-par value bearer shares (Conditional Capital 2016). The conditional capital increase may be executed only to the extent that the holders of options granted by PAION AG in connection with the Stock Option Plan 2016 exercise their options. Under the Stock Option Plan 2016, 211,546 stock options were issued to employees of the PAION Group as of 31 December 2017. No stock options have been exercised yet.

The currency translation reserve amounted to EUR -630,192.60 as of 31 December 2017 (previous year: EUR -340,777.37). Of these, KEUR 8,017 concern cumulative exchange rate gains (as of 31 December 2016 cumulative exchange rate gains of KEUR 5,205) arising from the translation of the financial statements of the British subsidiaries from GBP into EUR (the prior year amount also included cumulative exchange rate losses from the translation of the financial statements of the former U.S. subsidiary from USD into EUR in the amount of KEUR -15) whereas KEUR -8,647 concern cumulative exchange rate losses (as of 31 December 2016 KEUR -5,546 cumulative exchange rate losses) incurred on loans from PAION AG to the British subsidiaries (the prior year amount also included cumulative exchange rate gains amounting to KEUR 48 from the loan from PAION AG to the former U.S. subsidiary). As of 31 December 2017, these loans amount to KEUR 89,461 (previous year: KEUR 72,435).

A U.S. investor has the right to subscribe for up to 2.8 million new shares until 30 April 2018 in a maximum of two tranches. In case the U.S. investor has not subscribed to a minimum of 0.9 million new shares until 30 April 2018, PAION can request that this minimum investment is to be made by the U.S. investor under certain conditions. The offer price will correspond to a volume-weighted average Xetra price at that time

minus a 5% discount. The U.S. investor has not made use of his right so far.

# (7) Provisions

### Provisions developed as follows:

	Premiums/ Management		ou.	m . 1
in KEUR	Bonuses	Taxes	Other	Total
31 Dec. 2015	162	0	62	224
Utilization	72	0	0	72
Addition	310	18	173	501
Release	88	0	0	88
Exchange rate differences	-3	0	-7	-10
31 Dec. 2016	309	18	228	555
Utilization	270	18	0	288
Addition	258	0	0	258
Release	1	0	127	128
Exchange rate differences	-1	0	-5	-6
31 Dec. 2017	295	0	96	391

# (8) Trade payables

Trade payables amounted to KEUR 5,921 as of 31 December 2017 (previous year: KEUR 6,353). These liabilities do not bear interest and are generally due for payment within 30 days after invoicing. In case of accrued liabilities as of the balance sheet date, the maturity may be later than 30 days after balance sheet date, depending on the respective invoice date.

# (9) Other current liabilities

Other current liabilities comprise the following:

	31 Dec. 2017 KEUR	31 Dec. 2016 KEUR
Wage taxes	172	194
Holiday allowances	100	82
Supervisory Board remuneration	34	27
Others	19	56
	325	359

# (10) Deferred income

Deferred income is current in the full amount as of 31 December 2017 and amounts to KEUR 19. The prior year amount contained the portion of the upfront payment of KEUR 10,000 received from Cosmo in the previous year amounting to KEUR 5,749 that was entirely recognized as revenue in the reporting period.

Consolidated statement of comprehensive income disclosures

# (II) Revenues

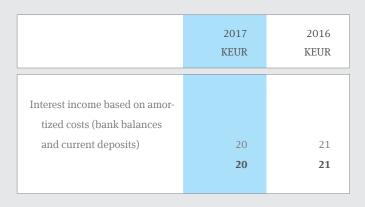
Revenues recognized in the reporting period amount to KEUR 5,811 and result from the upfront payment of KEUR 10,000 received from Cosmo in the course of the license agreement concluded in 2016 in the amount of KEUR 5,749. Revenue recognition of the received upfront payment was dependent on the progress of certain development components. Revenues from the remimazolam license agreement for Japan entered into with Mundipharma in the reporting period have been recognized in the amount of KEUR 37.

# (12) Other income (expenses), net

Other income (expenses) in the fiscal year comprise foreign exchange gains in the amount of KEUR 28 (previous year: foreign exchange losses of KEUR 1,064).

## (13) Financial income

Financial income consists of the following:



# (14) Income taxes / Deferred taxes

As of 31 December 2017, the tax losses carried forward by PAION Germany group (PAION AG and PAION Deutschland GmbH) amounted to about EUR 80 million (previous year: EUR 80 million). According to current German tax legislation, these losses can be carried forward indefinitely and offset against future earnings according to the relevant tax regulations (e. g. minimum taxation).

The tax losses carried forward by the British subsidiaries amount to GBP 108 million per 31 December 2017 (equivalent to EUR 121 million if translated at the exchange rate applicable on the reporting date). In the previous year, these amounted to GBP 100 million or EUR 117 million, respectively. According to British tax legislation, these can be carried forward indefinitely and a large portion of them can be offset against future earnings.

Overall, the losses carried forward within the Group amount to EUR 201 million (previous year: EUR 198 million). No deferred tax assets were recognized regarding a partial amount of EUR 198 million (previous year: EUR 195 million) of the total tax losses carried forward.

The composite German corporate income tax rate is 32.45% resulting from a corporate income tax rate of 15.0%, the solidarity surcharge of 5.5% that is levied on corporate income tax, and the trade earnings tax rate of 16.625%. The income tax rate in Great Britain is 19%. The expected tax rate for the Group overall is 30%.

Intangible assets were recognized in an amount of KEUR 13,844 as part of the purchase price allocation of PAION UK Group, which was acquired in 2008. The measurement of these development projects resulted in deferred tax liabilities in an amount of KEUR 3,876 based on the British income tax rate of 28% applicable at that time. These were offset by the same amount of deferred tax assets on losses carried forward. Deferred tax assets and liabilities are written down in line with the amortization of the development projects. Deferred taxes are reported as net balances in both the balance sheet and the statement of comprehensive income. As of the balance sheet date, deferred tax assets and liabilities each amounted to KEUR 447 (previous year: KEUR 525) after currency translation; these relate to the intangible asset remimazolam (deferred tax liabilities) as well as in the same amount to deferred taxes on losses carried forward (deferred tax assets).

If the combined income tax rate that is currently applicable in Germany was applied to the tax losses carried forward in Germany as of 31 December 2017, the resulting deferred tax assets would amount to EUR 26 million (previous year: EUR 26 million). Based on the income tax rate of 19% that is currently applicable in Great Britain, the losses carried forward in Great Britain as of 31 December 2017 would produce deferred tax assets in an amount of GBP 20 million (equivalent to EUR 23 million if translated at the rate applicable on the reporting date). In the previous year, these amounted to GBP 20 million or EUR 23 million, respectively. The temporary differences between the tax base and the IFRS carrying amount would produce a net balance as of 31 December 2017 of deferred tax assets in an amount of KEUR 28 (previous year: KEUR 26), of which Germany accounts for KEUR 0 (previous year: KEUR 2) and Great Britain for KEUR 28 (previous year: KEUR 24). The depicted differences in carrying amounts relate

mainly to fixed assets, provisions and deferred income. Total deferred tax assets would amount to EUR 49 million (previous year: EUR 49 million).

In the fiscal year, PAION Deutschland GmbH reported a low profit; all other companies of the PAION Group have reported losses. In coming years, further losses are expected to be generated. As a result, the realizability of the deferred tax assets mentioned above is not considered sufficiently likely before potential market approval and successful launch of remimazolam. In line with IAS 12.34 "Income Taxes", the excess assets of the deferred tax assets on losses carried forward and the excess

assets of deferred taxes on temporary differences are therefore not recognized.

In the reporting period, also the other comprehensive income (foreign currency translation of foreign subsidiaries) does not have any tax effects.

Based on an anticipated Group tax rate of 30%, the reconciliation of anticipated and actual income taxes is as follows:

in KEUR	2017	2016
Result for the period before taxes	-15,852	-25,061
Anticipated tax expense (+)/income (-)	-4,756	-7,518
Difference between anticipated Group tax rate and actual local tax rates	2,184	3,318
Non-recognition of deferred taxes on tax losses	1,613	4,074
Expenses in connection with stock options	54	69
Non-deductible expenses	34	29
Non-recognition of deferred taxes on temporary differences	18	-10
Correction of prior years' tax expenses	1	18
Deferred taxes on additional tax losses from previous years	0	-689
Non-recognition of deferred taxes on additional tax losses from previous years	0	689
Tax losses used	-70	-67
Cost in connection with capital increases	-223	-154
Effects from currency translation	-1,007	-2,724
Effects from tax credits	-1,608	-1,980
Other	1	1
Actual tax expense (+) / income (-)	-3,759	-4,944

The actual tax income results in an amount of KEUR 3,760 from the expected reimbursement of research and development costs through British tax authorities. The expected tax credits reduced the tax losses carried forward accordingly. The actual tax income also includes a tax expense of KEUR 1 relating to a tax payment for fiscal year 2012.

# (15) Earnings per Share

In accordance with IAS 33 "Earnings per Share", the earnings per share were calculated on the basis of the net result for the year and the weighted average number of shares outstanding. The underlying weighted average number of ordinary shares is derived as follows:

	2017	2016
Shares outstanding as of 1 January Weighted average number of shares issued	55,757,094 3,361,592	50,659,440 2,586,192
Weighted average number of ordinary shares	59,118,686	53,245,632

The calculation of basic and diluted earnings per share is based on the following figures:

	2017	2016
Net result for the year (in EUR) Weighted average number of ordinary shares for basic earnings per share Weighted average number of ordinary shares for diluted earnings per share	-12,093,427.29 59,118,686 59,558,627	-20,117,636.81 53,245,632 53,491,803
Earnings per share (in EUR): Basic Diluted	-0.20 -0.20	-0.38 -0.38

Potential ordinary shares from the exercise of stock options only have a dilutive effect if the new ordinary shares from the exercise of stock options led to a lower result per share. Under consideration of the current result of the PAION group, potential new ordinary shares do therefore not induce a dilutive effect.

#### Consolidated cash flow statement disclosures

The consolidated cash flow statement shows how additions and disposals have changed the cash and cash equivalents held by PAION over the course of the fiscal year. In accordance with IAS 7 "Statement of Cash Flows", a distinction is made between cash flows from operating activities, from investing activities and from financing activities. The cash and cash equivalents reported in the consolidated cash flow statement are comprised of cash and bank balances, together with current deposits that mature within three months from investment.

# Other disclosures

# **Stock Option Plans**

PAION has implemented a total of four stock option plans in the course of which stock options can be/have been granted to Management Board The stock options are accounted for in accordance with the provisions of IFRS 2. All stock option plans include vesting periods, waiting periods during a certain period of time before the grant. Details of the individual programs can be found in the following table (the presentation of the S period, is omitted):

	Stock Option Plan 2008	Stock Option Plan 2010
	Approved 5 May 2008	Approved 19 May 2010
Underlying Capital	Conditional Capital 2008 I	Conditional Capital 2010
Term of the options	10 years	10 year
Vesting period	2–4 years	2–4 year
Waiting period	2–4 years	4 year
Number of outstanding options for which the waiting		
period has expired as of 31 December 2017	375,747	
Exercise condition	Cumulative stock price increase of 5 % per year since grant in relation to exercise price	Cumulative stock price increase of 5 % per year since grant in relation to exercis price
Exercise price *	EUR 1.26 to EUR 2.69	EUR 2.0
Weighted average exercise price *	EUR 1.60	EUR 2.0
Exercise hurdle as of 31 Dec. 2017 *	EUR 1.84 to EUR 3.74	EUR 2.4
Weighted average remaining term as of 31 Dec. 2017	1.4 years	6.1 year
Further grants possible? (as of 31 Dec. 2017)	No	N
Number of totally granted options until 31 Dec. 2017	817,550	720,00
Number of outstanding options as of 31 Dec. 2017 **	375,747	696,62
granted to employees	181,720	392,87
granted to Management Board members	194,027	303,75
Number of totally lapsed options as of 31 Dec. 2017	100,758	23,37
thereof lapsed in the reporting period	0	
Number of totally exercised options until 31 Dec. 2017	341,045	
thereof exercised in the reporting period	99,414	
Personnel expenses in the reporting period	EUR O	EUR
Fair value per option at the time of the grant ***	EUR 0.57 to EUR 2.48	EUR 1.6
Elements of calculation		
Valuation model	Black/Scholes	Black/Schole
Risk-free rate	2.5-4.47%	0.79
Volatility	83.31-88.44%	73.75%
Staff turnover	0–5% per year	10% per yea
) in relation to outstanding options as of 31 Dec. 2017 *) in relation to employee/Management Board member sta **) in relation to totally granted options	tus at the time of the grant	

members and employees of PAION AG and its subsidiaries at the time of the grant. and exercise hurdles. The respective exercise price is based on the average stock price tock Option Plan 2005, from which the last stock options lapsed in the reporting

Stock Option Plan 2014	Stock Option Plan 2016
Approved 21 May 2014	Approved 25 May 2016
Conditional Capital 2014	Conditional Capital 2016
10 years	10 years
2-4 years	2–4 years
4 years	4 years
0	0
Cumulative stock price increase of 5 % per year since grant in relation to exercise price	Cumulative stock price increase of 5 % per year since grant in relation to exercise price
EUR 1.99 to EUR 2.40	EUR 2.48
EUR 2.16	EUR 2.48
EUR 2.14 to EUR 2.73	EUR 2.53
7.7 years	9.6 years
Yes	Yes
684,500	212,500
478,385	211,546
235,572	211,546
242,813	0
206,115	954
58,840	954
0	0
0	0
KEUR 111	KEUR 63
EUR 1.02 to EUR 1.39	EUR 1.70
Black/Scholes	Black/Scholes
-0.26-0.08%	-0.25%
82.64-83.76%	81.61%
8–14.5% per year	8% per year

#### Other financial obligations/Contingent liabilities

PAION has rented office space and leased parts of its factory and office equipment. The rental contracts for the office spaces in some cases include an automatic extension of the respective contract unless it is terminated by one of the two contract parties at a certain point in time prior to its expiry. The minimum future rental and lease obligations arising from these contracts are as follows:

	31 Dec. 2017 KEUR	31 Dec. 2016 KEUR
Due within one year Due after more than	318 13	327 82
one year <b>Total</b>	331	409

Rental and lease expenses amounted to KEUR 290 in fiscal year 2017 (previous year: KEUR 322). The long-term rental and lease obligations in the amount of KEUR 13 exist for the year 2019.

Based on assigning the conduct of (non-)clinical studies to Clinical Research Organizations (CROs) and having contractual manufacturers perform the production development and manufacture the study medication, PAION has contractually committed financial obligations in the amount of approx. EUR 8.6 million. The underlying contracts have variable notice periods of several months at the maximum. If contracts were terminated, the depicted financial obligations would decrease.

PAION has an obligation to pay Mr. Greg Papaz, former CEO of the former subsidiary PAION, Inc., 0.5% of income from milestone payments from Cosmo.

In the context of an amendment to the remimazolam license agreement with the Chinese partner Yichang Humanwell in light of the distinct features of the Chinese market, PAION is obliged to pay the partner EUR 1.5 million in case of certain market conditions. Also, future license payments could be reduced. PAION and Yichang Humanwell cooperatively work together on preventing this scenario.

#### **Headcount and personnel expenses**

In fiscal year 2017, PAION employed an average of 33 persons (previous year: 36 employees). Of these 33 employees, 23 worked in development and ten in administration and sales. PAION UK Group had an average headcount of five employees. As of 31 December 2017, the headcount was 34 (31 December 2016: 34).

The following personnel expenses were incurred in fiscal years 2017 and 2016:

	2017 KEUR	2016 KEUR
Wages and salaries	3,786	4,905
Social security contributions	380	470
Total	4,166	5,375

The personnel expenses stated above include (net) expenses from the granting of stock options in connection with the Stock Option Plan 2014 and the Stock Option Plan 2016 in an amount of KEUR 174 (previous year: KEUR 198). The figures also include contributions to the German and British social insurance schemes in an amount of KEUR 370 (previous year: KEUR 414).

#### **Related parties**

In accordance with IAS 24 "Related Party Disclosures", information must be provided on related parties. Members of both the Management Board and the Supervisory Board, and shareholders, are classified as related parties in the context of IAS 24.9. As far as the remuneration paid to and equity interests owned by the members of the Management and Supervisory Board are concerned, please refer to the explanations in the subsections "Members of the Management Board" and "Members of the Supervisory Board" in this section.

No relationships with related parties existed otherwise.

#### Objectives and methods of financial risk management

PAION's business activities currently focus on clinical development, the production development and to a minor extent preclinical development of remimazolam. Since these development activities are not yet generating any revenues from the sale of launched products, the scheduled expenses are correspondingly high. PAION aims at bringing remimazolam through the clinical development and regulatory approval phases either itself or through partners as well as to ensure the availability of the requisite short-term and mid-term funding. This funding is primarily secured by means of equity and through cooperation agreements, pursuant to which the cooperation partners effect milestone payments and assume direct and indirect responsibility for the development and/or commercialization. Future possibilities to attract additional equity or receive technology access and further milestone payments from cooperation partners will depend to a large extent on the positive clinical development progress and the regulatory process, especially in the U.S., as well as the success of the license partner Cosmo in regard to a potential market approval and subsequent commercialization of remimazolam. PAION's management therefore concentrates on managing and monitoring the individual development projects, its liquidity and its future liquidity requirements.

The financial liabilities are comprised of provisions, trade payables and part of the other liabilities. PAION owns various financial assets, such as trade receivables, part of the other assets as well as bank balances and current deposits. These financial assets and liabilities are direct products of PAION's business operations and/or are used to finance ongoing business activities.

PAION AG uses derivative financial instruments in the context of foreign exchange risk management. In doing so, only financial instruments with an explicit hedging relationship are used.

The financial instruments expose PAION to the following risks:

PAION is exposed to **currency risks** arising from its trade payables, in particular in connection with the clinical development of remimazolam in the U.S. and from the loans granted to its British subsidiaries. Liquid assets are mainly

invested in euros, but also funds in U.S. dollar and Pound Sterling are held.

The expected U.S. dollar share of remaining cash outflows for the completion of the development of remimazolam in the U.S. in 2018 amounts to approximately USD 1.5 million. As of 31 December 2017, PAION held an amount of USD 0.9 million. This way, per year-end, about 60% of the current U.S. dollar risk in connection with the completion of the development of remimazolam in the U.S. were hedged. Taking into account further U.S. dollar purchases after the balance sheet date, the U.S. dollar risk in connection with the development of remimazolam in the U.S. is hedged nearly entirely.

The loans granted by PAION AG to its foreign subsidiaries produced exchange rate losses of KEUR 3,102 in 2017, which were recognized in equity. These nearly entirely relate to the British subsidiaries. If the EUR/GBP exchange rate had been 5% higher on the balance sheet date, the currency component recognized in equity in the reporting period would have decreased by KEUR 4,536 compared to the change in the currency component actually recognized in equity in 2017. If the EUR/GBP exchange rate had been 5% lower on the balance sheet date, the currency component recognized in equity in the reporting period would have decreased by KEUR 4,536 less compared to the change in the currency component actually recognized in equity in 2017.

PAION's bank balances and current deposits are mainly held with two major German banks, a savings bank and a major British bank. The choice of short-term capital investments is based on various security criteria (e.g. rating, capital guarantee, safeguarded by the deposit protection fund (Einlagensicherungsfonds)). In light of these selection criteria and the ongoing monitoring of its capital investments, PAION deems the occurrence of a **counterparty credit risk** in this area unprobable. The amounts stated in the balance sheet always represent the maximum possible default risk.

PAION uses a customized business planning tool to monitor and manage its cash flows; this tool comprises both short- and medium-term, and long-term business planning. **Liquidity risks** are identified at an early stage by simulating different scenarios and conducting sensitivity analyses. Current liquidity is recorded and monitored on a daily basis.

The interest earned on bank balances and current deposits is dependent on the development of market interest rates. As such, these assets held by PAION are exposed to the risk of changing interest rates. A reduction of 10 basis points in the interest rates would have reduced consolidated result by KEUR 27 in fiscal year 2017 (previous year: KEUR 31).

The other assets mainly comprise claims for tax refunds from the tax authorities in Great Britain in connection with the partial reimbursement of research and development costs. The calculation of the refund claims is based on the calculation method agreed in previous years between the PAION UK companies and the British tax authorities. A final review of the tax credit recognized for 2017 by the British tax authorities has however not taken place as of the balance sheet date.

### **Financial instruments**

The following table shows the carrying amounts and fair values of the financial instruments included in the consolidated financial statements:

		Carrying amount		Fair value	
in KEUR		31 Dec. 2017	31 Dec. 2016	31 Dec. 2017	31 Dec. 2016
Financial assets:					
Cash and cash equivalents	(1)	24,839	30,111	24,839	30,111
Trade receivables	(1)	37	0	37	0
Other assets	(1)	7	3	7	3
Financial liabilities:					
Provisions	(2)(3)	391	537	391	537
Trade payables	(2)(3)	5,921	6,353	5,921	6,353
Other liabilities	(2)(3)	154	165	154	165

Measurement category according to IAS 39:

- (I) Loans and receivables
- (2) Liabilities recognized at amortized cost
- (3) lead to cash outflows

In light of the short residual terms of the cash and cash equivalents, other assets, provisions, trade payables and other liabilities, their carrying amounts are equivalent to the fair values as of the balance sheet date. Thus, the determination of the fair values of these financial instruments was based on unobservable input factors (input factors of level 3 according to IFRS 13). In fiscal year 2017, there were no movements between the hierarchy levels.

#### **Members of the Management Board**

The members of the company's Management Board are:

- Dr. Wolfgang Söhngen, CEO, Chairman
- Abdelghani Omari, CFO
- Dr. Jürgen Beck, CDO (since 1 January 2018)

Dr. Jürgen Raths left the Management Board as of 14 March 2017.

Management Board remuneration totalled KEUR 928 in fiscal year 2017. As of 31 December 2017, a total of 562,067 stock options (fair value at time of granting: EUR 806,699) had been issued to active Management Board members as of 31 December 2017. For more information on Management Board remuneration, please see the disclosures in the remuneration report, which is part of the group management report.

Dr. Wolfgang Söhngen and Mr. Abdelghani Omari are also Managing Directors of PAION Deutschland GmbH.
Mr. Abdelghani Omari is also Managing Director of PAION Holdings UK Ltd and its subsidiaries. Dr. Jürgen Beck is Managing Director of PAION Deutschland GmbH since 11 December 2017 and Managing Director of PAION Holdings UK Ltd and its subsidiaries since 25 January 2018. All Management Board members work full-time for the company and its subsidiaries.

As of 31 December 2017, Dr. Wolfgang Söhngen owned 1.06% (648,546 voting rights) of the shares in PAION AG. This equity interest includes 0.01% (6,425 voting rights) of the shares in PAION AG that are held by Dres. Söhngen Beteiligungs GmbH, in which Dr. Wolfgang Söhngen holds 50%.

## Members of the Supervisory Board

The members of the Supervisory Board are:

- Dr. Jörg Spiekerkötter, Kleinmachnow/Germany, Chairman;
   Managing Partner of JSP-Invest GmbH, Potsdam/Germany
   Other supervisory board memberships or similar positions:
  - Dr. Loges + Co. GmbH, Winsen (Luhe)/Germany, Chairman of the Board
- Dr. Karin Louise Dorrepaal, Amsterdam/The Netherlands, Vice Chairman; Chairman of the HR and Nomination Committee, former Member of the Management Board of Schering AG

Other supervisory board memberships or similar positions:

- Gerresheimer AG, Dusseldorf/Germany, Member of the Supervisory Board
- Almirall S.A., Barcelona/Spain, Member of the Board of Directors
- Triton Beteiligungsberatung GmbH, Frankfurt/Germany, Member of the Triton Industry Board
- Kerry Group plc, Tralee/Ireland, Non-executive director
- Humedics GmbH, Berlin/Germany, Chairman of the Board
- Julius Clinical Research BV, Bunnik/The Netherlands, Member of the Supervisory Board
- John Dawson, Fetcham/England, Chairman of the Audit Committee; CEO of Oxford BioMedica plc, Oxford/England
- Dr. Dr. Irina Antonijevic (since 12 June 2017), Boston,
   MA/U.S., Chairman of the Research and Development Committee; Vice President Translational Medicine at Wave Life Sciences Ltd., Cambridge, MA/U.S.

Other supervisory board memberships or similar positions:

- 4SC AG, Planegg (Munich)/Germany, Member of the Supervisory Board
- Dr. Hans Christoph Tanner (since 12 June 2017), Zurich/
   Switzerland, Member of the Supervisory Board, Head of
   Transactions of Cosmo Pharmaceuticals N.V., Amsterdam/The
   Netherlands, Head of Finance of Cassiopea SpA, Milan/Italy
   Other supervisory board memberships or similar positions:
  - Cosmo Pharmaceuticals N.V., Amsterdam/The Netherlands, Member of the Board of Directors
  - Private Equity Holding AG, Zug/Switzerland, Member of the Board of Directors and Chairman of the Compensation Committee
  - DKSH Holding AG, Zurich/Switzerland, Member of the Board of Directors and Chairman of the Audit Committee
  - CureVac AG, Tübingen/Germany, Member of the Supervisory Board and Chairman of the Audit Committee
  - Joimax GmbH, Karlsruhe/Germany, Member of the Advisory Board

- Qvanteq AG, Zurich/Switzerland, Member of the Board of Directors
- Wyss Zurich (ETH Zürich), Zurich/Switzerland, Member of the Evaluation Board

Remuneration to the members of the Supervisory Board totalled KEUR 141 in fiscal year 2017. For more information on Supervisory Board remuneration, please see the disclosures in the remuneration report of the group management report.

As of 31 December 2017, none of the members of the Supervisory Board owned shares in PAION AG.

#### Financial statements auditor

The Annual General Meeting on 17 May 2017 appointed Ernst & Young GmbH Wirtschaftsprüfungsgesellschaft, Cologne office, Germany, as auditor of the annual and consolidated financial statements for fiscal year 2017. The auditor has received or will invoice the following fees for services rendered to PAION AG and its subsidiaries in fiscal year 2017:

	2017 KEUR	2016 KEUR
Audits of financial statements Other services	97 0 <b>97</b>	128 203 <b>331</b>

The fees for audits of financial statements include remuneration for reviewing the interim financial statements in the amount of KEUR 11 (previous year: KEUR 23). The other services in the previous year comprised the preparation of a comfort letter in the context of the preparation of a potential capital increase, which was ultimately not conducted.

#### **Corporate Governance**

The Supervisory Board and Management Board of PAION AG declare that they are committed to responsible and transparent

management and control of the company focused on adding value in the long term.

The company complied with the recommendations set forth in the most recent version of the German Corporate Governance Code dated 7 February 2017 until 18 June 2017 with one exception. Since 19 June 2017, the company complies with all recommendations without exception. In December 2017, the Supervisory Board and the Management Board issued the declaration of compliance with the Corporate Governance Code pursuant to Section 161 AktG. This declaration of compliance is published on PAION AG's website (http://www.paion.com/media-and-investors/corporate-governance/declaration-of-conformity/).

#### Report on post-balance sheet date events

Dr. Jürgen Beck has been appointed member of the Management Board of PAION AG effective 1 January 2018.

There were no further significant events in the period between the reporting date, 31 December 2017, and the preparation of this report.

Aachen, Germany, 21 March 2018

PAION AG

Dr. Wolfgang Söhngen

Abdelghani Omani

Responsibility Statement (Bilanzeid) in accordance with section 117 no.1 of the Wertpapierhandelsgesetz (WpHG – German Securities Trading Act) in conjunction with sections 297(2) sentence 4 and 315(1) sentence 5 of the Handelsgesetzbuch (HGB – German Commercial Code)

"To the best of our knowledge, and in accordance with the applicable reporting principles, the consolidated financial statements give a true and fair view of the assets, liabilities, financial position and profit or loss of the group, and the group management report includes a fair review of the development and performance of the business and the position of the group, together with a description of the principal opportunities and risks associated with the expected development of the group."

Aachen, Germany, 21 March 2018

PAION AG

Dr. Wolfgang Söhngen

Dr. Jürgen Beck

# Reproduction of the auditor's report

We issued the following auditor's report on the consolidated financial statements and the group management report:

#### "Independent auditor's report

To PAION AG, Aachen

# Report on the audit of the consolidated financial statements and of the group management report

#### **Opinions**

We have audited the consolidated financial statements of PAION AG, Aachen, and its subsidiaries (the Group), which comprise the consolidated balance sheet as at 31 December 2017, and the consolidated statement of comprehensive income, consolidated statement of changes in equity and consolidated cash flow statement for the fiscal year from 1 January 2017 to 31 December 2017, and notes to the consolidated financial statements, including a summary of significant accounting policies. In addition, we have audited the group management report of PAION AG for the fiscal year from 1 January 2017 to 31 December 2017. In accordance with the German legal requirements, we have not audited the content of the reference to the group statement on corporate governance contained in the group management report.

In our opinion, on the basis of the knowledge obtained in the audit,

- the accompanying consolidated financial statements comply, in all material respects, with the IFRSs as adopted by the EU, and the additional requirements of German commercial law pursuant to Sec. 315e (1) HGB ["Handelsgesetzbuch": German Commercial Code] and, in compliance with these requirements, give a true and fair view of the assets, liabilities, and financial position of the Group as at 31 December 2017, and of its financial performance for the fiscal year from 1 January 2017 to 31 December 2017, and
- the accompanying group management report as a whole
  provides an appropriate view of the Group's position. In all
  material respects, this group management report is consistent with the consolidated financial statements, complies
  with German legal requirements and appropriately presents

the opportunities and risks of future development. Our opinion on the group management report does not cover the content of the group statement on corporate governance contained in the group management report in the form of a reference

Pursuant to Sec. 322 (3) Sentence 1 HGB, we declare that our audit has not led to any reservations relating to the legal compliance of the consolidated financial statements and of the group management report.

#### **Basis for the opinions**

We conducted our audit of the consolidated financial statements and of the group management report in accordance with Sec. 317 HGB and the EU Audit Regulation (No 537/2014, referred to subsequently as "EU Audit Regulation") and in compliance with German Generally Accepted Standards for Financial Statement Audits promulgated by the Institut der Wirtschaftsprüfer [Institute of Public Auditors in Germany] (IDW). We performed our audit of the consolidated financial statements in supplementary compliance with the International Standards on Auditing (ISAs). Our responsibilities under those requirements, principles and standards are further described in the "Auditor's responsibilities for the audit of the consolidated financial statements and of the group management report" section of our auditor's report. We are independent of the group entities in accordance with the requirements of European law and German commercial and professional law, and we have fulfilled our other German professional responsibilities in accordance with these requirements. In addition, in accordance with Art. 10 (2) f) of the EU Audit Regulation, we declare that we have not provided non-audit services prohibited under Art. 5 (1) of the EU Audit Regulation. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinions on the consolidated financial statements and on the group management report.

# Key audit matters in the audit of the consolidated financial statements

Key audit matters are those matters that, in our professional judgment, were of most significance in our audit of the consolidated financial statements for the fiscal year from

1 January 2017 to 31 December 2017. These matters were addressed in the context of our audit of the consolidated financial statements as a whole, and in forming our opinion thereon; we do not provide a separate opinion on these matters.

Below, we describe what we consider to be the key audit matters:

- 1. Tax credit for certain research and development expenses in the UK
- 1.1 Reasons why the matter was determined to be a key audit matter

Due to the ongoing development activities pertaining to remimazolam, there is a risk that the research and development expenses incurred during the fiscal year will be only partially or not at all recognized by the British tax authorities as taxprivileged research and development expenses. Tax recognition depends on the categorization of the individual cost components as well as the other requirements of British tax law. There is therefore a risk that, in the event of an incorrect categorization of the cost components, research and development expenses will be partially or in total not recognised, which would mean that the receivable from the British tax authorities reported as of 31 December 2017 would be only partially or not at all recoverable. The potential non-recognition of the research and development expenses and the corresponding resulting lack of cash inflow would give rise to higher financing requirements on the part of PAION AG. In light of this and the related use of judgment, the recoverability of the tax credit for certain research and development expenses was a key audit matter.

#### 1.2 Auditor's response

With regard to the calculation of refundable research and development expenses, we analysed the process implemented within the Group and the related controls in connection with the full and correct categorization of the cost components. We obtained an understanding of the composition, completeness

and origination of the research and development expenses by comparing the individual cost components with accounting evidence on a sample basis, examining whether the type and amount of the costs agree with the evidence. Additionally, we analysed the tax return of PAION UK Limited for 2017 prepared by an external tax advisor by checking the tax return for arithmetical accuracy and also assessed whether the return was prepared in accordance with the requirements of the British tax authorities. We also involved our tax specialists in the UK for this purpose. Additionally, we checked that the data basis was correct by comparing the figures in the tax return with the figures from the internal accounts.

Our audit procedures did not lead to any reservations regarding the recognition and measurement of the tax credit for certain research and development expenses in the UK.

#### 1.3 Reference to related disclosures

With regard to the accounting bases applied to the tax credits as well as other disclosures, refer to section Accounting policies, paragraph: Income taxes/deferred taxes and section Consolidated balance sheet disclosures (4) Prepaid expenses and other assets in the notes to the Company's consolidated financial statements.

#### Other information

The executive directors are responsible for the other information. The other information comprises the reference to the group statement on corporate governance.

Our opinions on the consolidated financial statements and on the group management report do not cover the other information, and consequently we do not express an opinion or any other form of assurance conclusion thereon.

In connection with our audit, our responsibility is to read the other information and, in so doing, to consider whether the other information

- is materially inconsistent with the consolidated financial statements, with the group management report or our knowledge obtained in the audit, or
- otherwise appears to be materially misstated.

# Responsibilities of the executive directors and the Supervisory Board for the consolidated financial statements and the group management report

The executive directors are responsible for the preparation of the consolidated financial statements that comply, in all material respects, with IFRSs as adopted by the EU and the additional requirements of German commercial law pursuant to Sec. 315e (1) HGB, and that the consolidated financial statements, in compliance with these requirements, give a true and fair view of the assets, liabilities, financial position, and financial performance of the Group. In addition, the executive directors are responsible for such internal control as they have determined necessary to enable the preparation of consolidated financial statements that are free from material misstatement, whether due to fraud or error.

In preparing the consolidated financial statements, the executive directors are responsible for assessing the Group's ability to continue as a going concern. They also have the responsibility for disclosing, as applicable, matters related to going concern. In addition, they are responsible for financial reporting based on the going concern basis of accounting unless there is an intention to liquidate the Group or to cease operations, or there is no realistic alternative but to do so.

Furthermore, the executive directors are responsible for the preparation of the group management report that, as a whole, provides an appropriate view of the Group's position and is, in all material respects, consistent with the consolidated financial statements, complies with German legal requirements, and appropriately presents the opportunities and risks of future development. In addition, the executive directors are responsible for such arrangements and measures (systems) as they have considered necessary to enable the preparation of a group management report that is in accordance with the applicable German legal requirements, and to be able to provide sufficient appropriate evidence for the assertions in the group management report.

The Supervisory Board is responsible for overseeing the Group's financial reporting process for the preparation of the consolidated financial statements and of the group management report.

# Auditor's responsibilities for the consolidated of the annual financial statements and of the group management report

Our objectives are to obtain reasonable assurance about whether the consolidated financial statements as a whole are free from material misstatement, whether due to fraud or error, and whether the group management report as a whole provides an appropriate view of the Group's position and, in all material respects, is consistent with the consolidated financial statements and the knowledge obtained in the audit, complies with the German legal requirements and appropriately presents the opportunities and risks of future development, as well as to issue an auditor's report that includes our opinions on the consolidated financial statements and on the group management report.

Reasonable assurance is a high level of assurance, but is not a guarantee that an audit conducted in accordance with Sec. 317 HGB and the EU Audit Regulation and in compliance with German Generally Accepted Standards for Financial Statement Audits promulgated by the Institut der Wirtschaftsprüfer (IDW) and in supplementary compliance with ISAs will always detect a material misstatement. Misstatements can arise from fraud or error and are considered material if, individually or in the aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of these consolidated financial statements and this group management report.

We exercise professional judgment and maintain professional skepticism throughout the audit.

#### We also:

• Identify and assess the risks of material misstatement of the consolidated financial statements and of the group management report, whether due to fraud or error, design and perform audit procedures responsive to those risks, and obtain audit evidence that is sufficient and appropriate to provide a basis for our opinions. The risk of not detecting a material misstatement resulting from fraud is higher than for one resulting from error, as fraud may involve collusion, forgery, intentional omissions, misrepresentations, or the override of internal control.

- Obtain an understanding of internal control relevant to the audit of the consolidated financial statements and of arrangements and measures (systems) relevant to the audit of the group management report in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of these systems.
- Evaluate the appropriateness of accounting policies used by the executive directors and the reasonableness of estimates made by the executive directors and related disclosures.
- Conclude on the appropriateness of the executive directors' use of the going concern basis of accounting and, based on the audit evidence obtained, whether a material uncertainty exists related to events or conditions that may cast significant doubt on the Group's ability to continue as a going concern. If we conclude that a material uncertainty exists, we are required to draw attention in the auditor's report to the related disclosures in the consolidated financial statements and in the group management report or, if such disclosures are inadequate, to modify our respective opinions. Our conclusions are based on the audit evidence obtained up to the date of our auditor's report. However, future events or conditions may cause the Group to cease to be able to continue as a going concern.
- Evaluate the overall presentation, structure and content of the consolidated financial statements, including the disclosures, and whether the consolidated financial statements present the underlying transactions and events in a manner that the consolidated financial statements give a true and fair view of the assets, liabilities, financial position and financial performance of the Group in compliance with IFRSs as adopted by the EU and the additional requirements of German commercial law pursuant to Sec. 315e (1) HGB.
- Obtain sufficient appropriate audit evidence regarding the financial information of the entities or business activities within the Group to express opinions on the consolidated financial statements and on the group management report.
   We are responsible for the direction, supervision and performance of the group audit. We remain solely responsible for our audit opinions.

- Evaluate the consistency of the group management report with the consolidated financial statements, its conformity with [German] law, and the view of the Group's position it provides.
- Perform audit procedures on the prospective information presented by the executive directors in the group management report. On the basis of sufficient appropriate audit evidence we evaluate, in particular, the significant assumptions used by the executive directors as a basis for the prospective information, and evaluate the proper derivation of the prospective information from these assumptions. We do not express a separate opinion on the prospective information and on the assumptions used as a basis. There is a substantial unavoidable risk that future events will differ materially from the prospective information.

We communicate with those charged with governance regarding, among other matters, the planned scope and timing of the audit and significant audit findings, including any significant deficiencies in internal control that we identify during our audit.

We also provide those charged with governance with a statement that we have complied with the relevant independence requirements, and communicate with them all relationships and other matters that may reasonably be thought to bear on our independence and where applicable, the related safeguards.

From the matters communicated with those charged with governance, we determine those matters that were of most significance in the audit of the consolidated financial statements of the current period and are therefore the key audit matters. We describe these matters in our auditor's report unless law or regulation precludes public disclosure about the matter.

#### Other legal and regulatory requirements

# Further information pursuant to Art. 10 of the EU Audit Regulation

We were elected as group auditor by the Annual General Meeting on 17 May 2017. We were engaged by the Supervisory Board on 12 July 2017. We have been the group auditor of PAION AG without interruption since fiscal year 2004.

We declare that the opinions expressed in this auditor's report are consistent with the additional report to the Audit Committee pursuant to Art. 11 of the EU Audit Regulation (long-form audit report).

# German Public Auditor responsible for the engagement

The German Public Auditor responsible for the engagement is Peter Gockel."

Cologne, 21 March 2018

Ernst & Young GmbH Wirtschaftsprüfungsgesellschaft

(s) Gockel (s) Conrad

Wirtschaftsprüfer Wirtschaftsprüfer

[German Public Auditor] [German Public Auditor]

# Management Board and Supervisory Board

## Management Board

### Dr. Wolfgang Söhngen

Founder, Chief Executive Officer of PAION AG, Managing Director of PAION Deutschland GmbH Dr. Wolfgang Söhngen is founder and CEO of PAION AG and Managing Director of PAION Deutschland GmbH. He has raised more than EUR 180 million through fund raising and about EUR 90 million through partnering.

Wolfgang has many years of experience in the pharmaceutical industry. He worked in clinical development, project management, corporate development, and strategic planning at Grünenthal GmbH for ten years. Before founding PAION in 2000 with his wife Mariola, he was head of his own consulting firm, Virtueality, which specialized in healthcare and clinical development.

In 1985, Wolfgang received his doctoral degree in medicine from RWTH Aachen (Technical University of Aachen). He spent two years as a resident in internal medicine and then held a post-doc position in cardiovascular pharmacology at the University of Michigan, Ann Arbor (USA). He also holds a Master of Business Communication and a Diploma in Pharmaceutical Medicine (DGPharMed).

## Abdelghani Omari

UK subsidiaries

Chief Financial Officer of PAION AG, Managing Director of PAION Deutschland GmbH and the Abdelghani Omari joined PAION in 2008 as Vice President Finance. Between 2012 and 2014 Abdel was responsible for the entire finance department. In 2014 he was appointed Chief Financial Officer of PAION AG.

Abdel has more than 17 years of experience in Finance. At KPMG, he advised international clients on accounting, post-merger integration and financial reporting. Previously, he worked several years in the audit department of KPMG with a focus on the chemical industry.

 $\label{eq:continuous} \mbox{He holds a degree in Business Administration from the University of Aachen.}$ 

Abdel has been instrumental in financings and partnering deals, particularly for remimazolam. He has raised more than EUR 80 million through raising capital and concluded a total of nine license agreements with more than EUR 110 million in upfront and milestone payments.

# Dr. Jürgen Beck

Chief Development Officer of PAION AG, Managing Director of PAION Deutschland GmbH and the UK subsidiaries Dr. Jürgen Beck was appointed Chief Development Officer of PAION AG with effect from 01 January 2018.

Within the Management Board, he is responsible for product development, in particular for the remimazolam development program in procedural sedation in the U.S. and for the EU Phase III program in general anesthesia.

Jürgen has over 25 years of experience in the European pharma business, with positions held in various drug development projects. As a graduated physician and having a diploma in business administration, he held inter alia various senior management positions at Synthélabo for many years, was longtime Managing Director of the contract research organization Monitoring Force GmbH, Senior Vice President of Medical Affairs at Epigenomics and Vice President of Clinical Operations Europe at InterMune International AG

## Supervisory Board

# Dr. Jörg Spiekerkötter

Chairman of the Supervisory Board Dr. Jörg Spiekerkötter is a member of PAION's Supervisory Board since June 2007 and the Supervisory Board appointed Dr. Spiekerkötter as Chairman in May 2010.

Dr. Jörg Spiekerkötter has many years of experience in the pharmaceutical industry where he has held executive positions in the areas of finance, law and human resources. Until May 2007, he was the Chief Financial Officer of Organon BioSciences N.V., Oss (Netherlands). He left after the acquisition of the company by the U.S. pharmaceutical company Schering-Plough. Until September 2006, he was the Chief Financial Officer at Schering AG in Berlin (Germany), and before that he was Head of the Legal Department at Hoechst Schering AgrEvo GmbH in Berlin (Germany). Dr. Spiekerkötter is Managing Partner of JSP-Invest GmbH and Chairman of Dr. Loges + Co. GmbH since August 2016. Dr. Spiekerkötter studied in Bielefeld (Germany), Lausanne (Switzerland) and Freiburg (Germany) and has a PhD in law. Until December 2010, he was the Chief Financial Officer of Conergy AG, Hamburg (Germany).

### Dr. Karin Dorrepaal

Vice-Chairman of the Supervisory Board, Chairman of the HR & Nomination Committee

Dr. Karin Dorrepaal is a member of PAION's Supervisory Board since October 2012.

She has broad experience in the Life Science Industry. After four years as a research fellow at the Netherlands Cancer Institute, Dr. Dorrepaal received her PhD from the Free University of Amsterdam, Netherlands. She went on to study at the Rotterdam School of Management where she obtained an MBA. In 1990, Dr. Dorrepaal joined Booz Allen Hamilton, Management Consultants. She specialized in the pharmaceutical industry and advised major companies on issues regarding strategy, sales, marketing and supply chain. In 2000, Dr. Dorrepaal was appointed Vice President of Booz Allen.

In 2004, the Supervisory Board of Schering AG appointed Dr. Dorrepaal to the Board of Executive Directors of Schering AG.

After Bayer AG acquired Schering AG, Dr. Dorrepaal left the company in 2006 and since that time she holds several non-executive roles in Germany, Ireland, Spain and the Netherlands.

#### **John Dawson**

Chairman of the Audit Committee  ${\it John Dawson is a member of PAION's Supervisory Board since May 2014.}$ 

From 1996 to 2007, he held senior management positions in the European operations of Cephalon Inc., including from 2005, a management board position as Chief Financial Officer and Head of Business Development Europe. In his time at Cephalon he led many of the deals that built the European business to over 1,000 employees, taking the business from having no sales in 1998 to a turnover of several hundred million U.S. dollars. In 2005, he led the USD 360 million acquisition of Zeneus by Cephalon.

Between 1991 and 1996 he was Director of Finance and Administration of Serono Laboratories (UK) Limited.

John Dawson joined Oxford BioMedica as Non-executive Director in August 2008. He was then appointed Chief Executive Officer in October 2008.

**Dr. Dr. Irina Antonijevic**Chairman of the R&D
Committee

Dr. Dr. Irina Antonijevic is a member of PAION's Supervisory Board since June 2017

Dr. Dr. Irina Antonijevic has more than 17 years of drug development experience in different pharmaceutical organizations, with a focus on neuropsychiatric and rare diseases. She completed her medical studies at the Technical University of Munich (1991), received her MD from the Max Planck Institute in Munich (1992) and her PhD from the University of Edinburgh, UK (1995). She completed her residency at the Max Planck Institute of Psychiatry in Munich and received her Venia Legendi from the Charité, Berlin, in 2004. Dr. Dr. Antonijevic has been a regular reviewer for the German Ministry of Research (BMBF) since 2006 and joined Wave Life Sciences, Cambridge (MA, U.S.) in 2018 as Vice President Translational Medicine.

**Dr. Chris Tanner** 

Dr. Chris Tanner is a member of PAION's Supervisory Board since June 2017.

Dr. Chris Tanner was a member of the Executive Board since 2005 and has been a member of the Supervisory Board of Cosmo Pharmaceuticals N.V. since 2006 for which he conducted the IPO as Chief Financial Officer and Head of Investor Relations. In 2015, Cosmo span off the daughter Cassiopea SpA where he also acts as Chief Financial Officer and Head of Investor Relations. Moreover, he is a member of the board of directors or advisory board (Beirat) of listed DKSH AG, Private Equity Holding AG and the private medtec companies Qvanteq AG, CureVac AG and Joimax GmbH. From 1998 to 2001, he was a partner of Dr. Ernst Mueller-Moehl and co-founder of the 20 Minutes group of newspapers and founded A&A Active Investor, a SIX-listed investment company. From 1992 to 1998, he was the Head of Corporate Finance & Capital Markets at UBS in Zurich, and from 1976 to 1991 he had various functions in the Corporate Banking Department at UBS in Zurich, Madrid and Los Angeles. Dr. Tanner has a PhD in economics and a diploma as economist from the University of St. Gallen.

# Glossary

Anesthesia

Anesthesia is characterized by unconsciousness resulting from the administration of a general anesthetic, to facilitate very painful procedures. Apart from the loss of consciousness, also pain perception, defensive reflexes as well as muscle tension are thereby inactivated throughout the body.

Anesthetic

A drug which induces anesthesia/narcosis.

Clinical Phase I

In clinical Phase I studies, drug candidates are explored in healthy volunteers (so-called probands). The main focus of these studies is usually safety and tolerability. Moreover, the concentration of the substance in the blood is typically being determined, among other parameters. Interaction with other drugs is also frequently studied. Potential participants freely decide about inclusion in Phase I studies after being informed about scope, risks and the study protocol.

Clinical Phase II

In clinical Phase II studies, drug candidates are for the first time therapeutically evaluated in patients. A successful Phase II thus is considered a major step forward regarding the commercial valuation of the drug and the company developing it. Phase II studies mainly focus on finding the right dose for effective therapy. While statistical significance usually is achieved through larger scale Phase III studies, Phase II studies often give important indications whether the drug candidate can meet expectations. In most cases, if major side effects exist, they will be discovered in Phase II. Potential participants or their relatives, respectively, freely decide about inclusion in Phase II studies after being informed about scope, risks and the study protocol.

Clinical Phase III

Clinical Phase III studies concentrate on showing efficacy in a statistically significant manner with an acceptable safety profile. In Phase III and sometimes already in Phase II, studies are normally carried out as double-blind, placebo-controlled trials. "Placebo control" refers to the fact that one sub-group of patients receives only an inactive substance (placebo). As neither the patient nor the physician knows who received drug candidate or placebo, these studies are dubbed "double-blind". Through this study design, one can rule out that measured effects are due to other factors than the drug candidate. Potential participants or their relatives, respectively, freely decide about inclusion in Phase III studies after being informed about scope, risks and the study protocol. After successful completion of Phase III, the next step is usually filing for regulatory approval.

Clinical studies

Well-controlled assessment of the effects of drug candidates or new medical devices.

INN (international non-proprietary name)

The non-proprietary or generic name given to a pharmaceutical substance by the World Health Organisation (WHO). Whereas many substances are distributed under different trade names, INNs are internationally uniform and thereby facilitate a clear distinction. In contrast to internal substance names used by companies (e.g. CNS 7056), it is custom to use the INN in scientific publications (i.e. remimazolam).

Narcotic

A drug which induces anesthesia/narcosis.

Opiate

Any of various sedative narcotics containing opium or one or more of its natural or synthetic derivatives.

Peri-operative pain

Pain experienced during and/or after an operation, originating from the

surgery.

Placebo

Inactive substance. In clinical studies, one patient group receives an inactive substance (placebo) instead of the drug candidate in order to rule out that effects are caused by other factors than the drug.

Pre-clinical research

Laboratory tests of a new drug candidate or a new medical device on animals or cell cultures. These tests are conducted to explore the mode of action as well as to detect potential risks prior to testing in humans.

**Proband** 

Volunteer (Phase I studies)

Remimazolam

Remimazolam is an ultra-short-acting intravenous sedative and anesthetic in Phase III clinical development. It is a member of the class of substances known as benzodiazepines. In the human body, remimazolam is rapidly metabolized to an inactive metabolite by tissue esterases, and not metabolized by hepatic or renal pathways. Like other benzodiazepines, remimazolam can be reversed with flumerapil

lam can be reversed with flumazenil.

Sedation

Reduction of anxiety, stress, irritability, or excitement by administration of

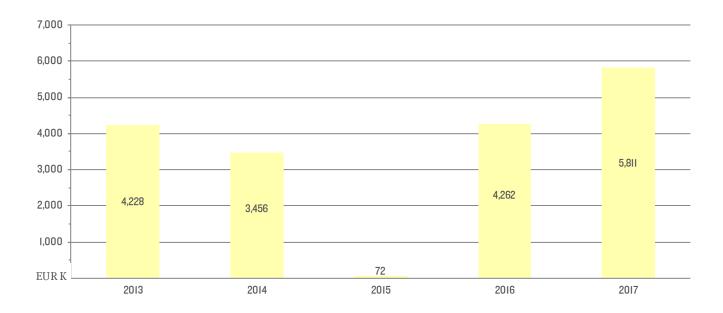
a sedative to facilitate a medical procedure.

Sedative

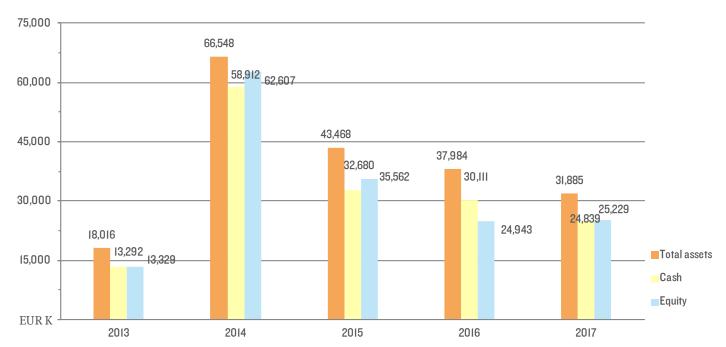
A drug which generally promotes sedation.

# Development of Selected Consolidated Financial Key Figures (IFRS)

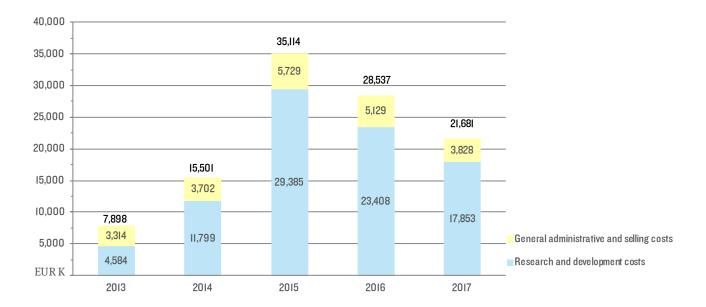
# Revenues



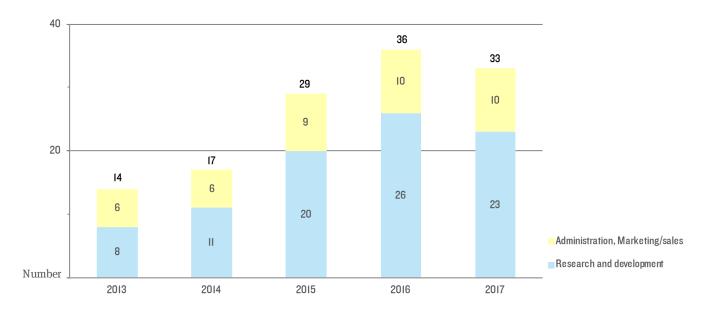
Total Assets / Cash and Cash Equivalents / Equity



# **Cost Segments**



# **Employee Structure**



# Five-Year Comparison of Key Consolidated Financial Figures (IFRS)

(all figures in EUR K unless otherwise noted)	2017	2016	2015	2014	2013
Profit and loss statement					
Revenues	5,811	4,262	72	3,456	4,22
Research and development expenses	-17,853	-23,408	-29,385	-11,799	-4,58
General administrative and selling expenses	-3,828	-5,129	-5,729	-3,702	-3,31
Net result	-12,093	-20,118	-28,212	-9,105	-2,21
Personnel expenses included therein	-4,166	-5,375	-4,996	-3,233	-2,293
Number of shares outstanding (weighted ave-					
rage, basic)	59,118,686	53,245,632	50,652,563	39,881,039	25,379,90
Number of shares outstanding (weighted ave-					
rage, diluted)	59,558,627	53,491,803	50,895,530	40,346,159	25,379,90
Earnings per share in EUR (basic)	-0.20	-0.38	-0.56	-0.23	-0.0
Earnings per share in EUR (diluted)	-0.20	-0.38	-0.56	-0.23	-0.0
Balance sheet					
Intangible assets	2,415	2,688	3,362	3,440	3,49
Cash and cash equivalents	24,839	30,111	32,680	58,912	13,29
Equity	25,229	24,943	35,562	62,607	13,32
Current liabilities	6,656	13,040	7,900	3,924	4,65
Balance sheet total	31,885	37,983	43,468	66,548	18,01
Cash flow					
Cash flow from operating activities	-17,720	-11,586	-26,287	-12,044	-1,74
Cash flow from investing activities	-25	-192	-33	-26	-
Cash flow from financing activities	12,494	9,212	22	57,618	-7,16
Employees					
Group employees (average)	33	36	29	17	1

# Information on PAION Shares

Market segment Regulated Market/Prime Standard Frankfurt Stock Exchange

Ticker symbol PA8

Reuters symbol PASG.DE (Xetra)
Bloomberg PAS GY (Xetra)
ISIN DE000A0B65S3
First day of trading 11 February 2005
Designated Sponsor Oddo Seydler

Key figures	2017	2016
Numbers of shares at year-end	61,120,046	55,757,094
Average daily trading volume (Xetra, FSE)	193,073	194,107
Year high (Xetra closing price)	EUR 3.30 (26 Jun 2017)	EUR 2.95 (17 Oct 2016)
Year low (Xetra closing price)	EUR 2.15 (22 Mar 2017)	EUR 1.08 (11 Feb 2016)
Share price at year-end	EUR 2.71	EUR 2.45
Market capitalization at the end of the financial year (Xetra)	EUR 166 million	EUR 137 million

# Imprint

**Editor, Conception, Design & Text** 

PAION AG, Martinstrasse 10–12, 52062 Aachen

# Corporate Calendar 2018

22 March 2018 Publication of financial results 2017

09 May 2018 Publication of the financial results for the first quarter 2018

23 May 2018 Annual general meeting, Aachen

08 August 2018 Publication of the financial results for the second quarter and the first half-year 2018

07 November 2018 Publication of the financial results for the third quarter and first nine months 2018

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