PAION AG, Aachen

Annual Financial Report

for the Fiscal Year 2018

PAION

PAION AG, Aachen

Consolidated Financial Statements

as of 31 December 2018 and

Group Management Report

for the Fiscal Year 2018

PAION

Group management report for fiscal year 2018

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, PAION has licensees in the U.S., China, South Korea, Canada, Russia/CIS, Turkey, the MENA region and Japan. For the use of remimazolam for procedural sedation, clinical development has already been completed; a market approval dossier has been filed in China. For the indication general anesthesia, remimazolam is in the final stage of clinical development and has already been completed for Japan where a market approval dossier has been filed in the reporting period. The different indications for application of remimazolam will be described in detail in the following chapters.

Fiscal year 2018 was marked by the concentration of PAION on the continuation of the development of remimazolam and regulatory activities, in particular the preparation and start of a Phase III study in general anesthesia in the EU and preparations for the market approval dossiers in the U.S. and 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 licensees. The progress of these activities is being documented and discussed continuously. PAION has already signed several regional license agreements. The licensees operate independently in their respective license territory. However, the cooperation agreements require the licensees to exchange relevant information. Development in the U.S. has been completed by PAION. The U.S. licensee Cosmo Pharmaceuticals (Cosmo) plans to file for market approval in procedural sedation shortly and will be responsible for all further development activities in the U.S.

The central coordination of the information flow worldwide between the licensees 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

I. Macroeconomic and sector-specific environment

a. Macroeconomic development

German economy has continued its growth also in 2018. Drivers in particular were investments with an increase of 4.8% and consumption with an increase of 1.0% as compared to the prior year.

With an increase of the gross domestic product (GDP) of 1.5% (2017: 2.2%), growth has lost momentum as compared to 2017 however.[1]

A decrease in economic growth has also manifested in the Euro area: The GDP in the Euro zone only increased by 1.8% in 2018 after 2.4% growth in 2017, and a further decrease to 1.6% is expected for 2019. Growth of the world GDP however only decreased slightly from 3.8% in the prior year to 3.7% in 2018 to which an increase of growth of the U.S. GDP from 2.2% in the previous year to 2.9% in 2018 has contributed significantly, contrary to the development in the Euro area.[2] While the decrease in growth in the Euro area significantly resulted from declining global demand, in particular from China, U.S. economy has benefited from the impact of the U.S. tax reform.[3]

For 2019, a further slowdown of worldwide growth from 3.7% in the prior year to now 3.5% is expected. A decrease in growth of developed economies contributes to this trend in particular. There is major uncertainty in regard to consequences and potential expansions of international trade restrictions and tariffs most notably. Moreover, the short- and mid-term outlook is tarnished by a potential exit of the United Kingdom from the EU without a follow-up agreement (so-called "No-deal Brexit"), geopolitical tensions and an increasingly reserved financial market sentiment.[4]

This is also reflected on the stock markets: The DAX registered a decrease by 18.3% in 2018 in comparison to the prior year's end closing value; the EUROSTOXX 50 also closed 2018 with a minus of 14.3% as compared to the previous year. The Dow Jones decreased less significantly in 2018 and closed 2018 with a minus of 5.6% in comparison to the prior year's end closing value.

b. Development of the pharmaceutical and biotechnology industry

The pharmaceutical and biotechnology industry continues to be marked by steadily increasing costs for pharmaceutical development due to advancing portfolio complexity, the trend to personalized therapies and increasingly extensive and challenging regulatory requirements which in turn are faced by increasingly lower income particularly due to higher competition, patent expiry of formerly high-selling products and price pressure from governmental regulation.[5] Average development costs of a new drug increased by approx. 82% from 2010 to 2018 on average for big pharma companies while peak sales potential approximately halved.[6]

Although the worldwide transaction volume in the pharmaceutical industry increased again with USD 198 billion in 2018, it was about USD 90 billion lower than the average of the years 2014 to 2016 in spite of the availability of respective funds. In addition to high valuations which increased by 78% from 2014 to 2018 on average for biotechnology companies, the transaction

[1] Federal Statistical Office: Deutsche Wirtschaft ist im Jahr 2018 um 1,5 % gewachsen, press release dated 15 January 2019.
[2] International Monetary Fund: World Economic Outlook Update, January 2019.
[3] Commerzbank Research: Economic and Market Monitor – Chart Book February 2019.
[4] International Monetary Fund: World Economic Outlook Update, January 2019.
[5] Deloitte Centre for Health Solutions: Unlocking R&D productivity: Measuring the return from pharmaceutical innovation 2018, 2018; Ernst & Young: 2019 EY M&A Firepower report: When data and technology expedite growth, how can dealmaking power the value equation?, 2018.
[6] Deloitte Centre for Health Solutions: Unlocking R&D productivity: Measuring the return from pharmaceutical innovation 2018, 2018.

volume was particularly curbed by uncertainty in regard to (potential) internal trade restrictions and geopolitical tensions.[7]

The financing environment for the pharmaceutical and biotechnology industry was very good in 2018. With a volume of USD 8.3 billion, more funds were raised through IPOs in 2018 than ever before; the previous high from 2014 was exceeded by nearly 32%.[8] Also in Germany, with funds raised in the amount of EUR 1.3 billion, a new all-time high of financing volume was reached in the industry.[9] In terms of valuation, this is at least also reflected in the DAXsubsector Biotechnology Index which increased by 14.3% in 2018 in comparison to the prior year's end closing value, while the NASDAQ Biotechnology Index closed the year 2018 with a minus of 9.3%.

The significant competitive drivers in the pharmaceutical and biotechnology industry are likely to also persist in 2019 and to maintain consolidation pressure. In addition to intensifying competition and continuously increasing challenges for the industry, for instance in regard to digitalization, individualization of therapies and regulatory requirements, companies with a clear therapeutic focus are more successful than their less focused competitors. Under consideration of the strong fragmentation in the industry, the availability of significant amounts of funds due to the tax reform that came into force in the U.S. and the central banks' continuing loose monetary policy, a high acquisition and transaction volume worldwide can be expected in the pharmaceutical industry in 2019.[10] However, it remains to be seen to what extent the design and potential expansion of international trade restrictions and protective tendencies have a damping effect on acquisition and transaction volumes.

2. Presentation of the course of business and development activities

The development portfolio of PAION Group essentially comprises 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 is 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,

[7] Ernst & Young: 2019 EY M&A Firepower report: When data and technology expedite growth, how can deal-making power the value equation?, 2018.
[8] Morrison, C. (2019): Boom: 2018's biotech IPOs, in: Nature Reviews Drug Discovery, Vol. 18, January 2019.
[9] transkript: Finanzierungen auf 1,3 Mrd. Euro verdoppelt, announcement from 11 January 2019.
[10] Ernst & Young: 2019 EY M&A Firepower report: When data and technology expedite growth, how can deal-making power the value equation?, 2018; Deloitte Centre for Health Solutions: Unlocking R&D productivity: Measuring the return from pharmaceutical innovation 2018, 2018; PwC Health Research Institute: Top health industry issues of 2019: The New Health Economy comes of age, 2018; Commerzbank Research: Economic and Market Monitor – Chart Book February 2019.

remimazolam demonstrated efficacy and safety with around 2,400 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.

PAION has completed clinical development of remimazolam for procedural sedation in the U.S. The U.S. licensee Cosmo plans to file for market approval in procedural sedation shortly and is responsible for any further development activities in the U.S. In Japan, remimazolam licensee Mundipharma filed for market approval in general anesthesia in December 2018 and in China, licensee Yichang Humanwell filed for market approval in procedural sedation in November 2018. In Europe, PAION initiated a Phase III study in general anesthesia in July 2018, for which patient recruitment is expected to be completed by the end of 2019.

In addition to procedural sedation and general anesthesia, based on positive Phase II study results, ICU sedation (beyond 24 hours) is another possible attractive indication for further development in the EU by PAION as well as by its licensees.

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

Procedural Sedation Market

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 colonoscopy 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 costs and higher risks, since there is no reversal agent available for propofol in order to be able to quickly stop sedation if required. 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 prices will be paid for 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.[11] 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 expects that remimazolam, subject to FDA approval (FDA = Food and Drug Administration) 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.

PAION is currently evaluating the possibility of submitting a Marketing Authorization Application (MAA) for remimazolam in procedural sedation in **Europe** with the European Medicines Agency (EMA) based on the completed U.S. development program.

In the EU, based on its own projections for procedural sedation, PAION currently estimates an annual peak sales potential of approx. EUR 75 million. In contrast to the U.S. market which has a large freestanding ambulatory surgery healthcare infrastructure, procedural sedation in Europe

[11] Liu, H. et al. (2012): Utilization of Anesthesia Services During Outpatient Endoscopies and Colonoscopies and Associated Spending in 2003-2009, The Journal of the American Medical Association, 2012 307(11):1178-1184; Al-Awabdy, B. and Wilcox, C.M. (2013): Use of anesthesia on the rise in gastrointestinal endoscopy, World Journal of Gastrointestinal Endoscopy, January 2013 5(1): 1-5.

is mainly a hospital-based activity where anesthesiologists have the overall responsibility for the sedation of patients. This entails a high potential for synergies with the planned commercialization of remimazolam for use in general anesthesia.

General Anesthesia Market

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 aging 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. In the EU, based on its own projections for general anesthesia, PAION currently estimates an annual peak sales potential of approx. EUR 150 million to EUR 200 million.

In adults, myocardial injury during noncardiac surgery (MINS) is the most common cardiovascular complication associated with such surgery. Investigations conclude that MINS occurs in about 8% of the approximately 200 million patients yearly worldwide and leads to an increased morbidity. Approximately 10% of patients suffering such injury die within 30 days after surgery. The suspected cause of this is, inter alia, a (too) low blood pressure and a concomitant temporary undersupply of the heart muscle with oxygen during the procedure.[12] Based on the safety data available to date, remimazolam could contribute significantly to reducing this mortality rate by reducing intraoperative blood pressure drops.

[12] Khan, J. et al. (2014), Myocardial injury after noncardiac surgery, Current Opinion in Cardiology, 2014 Jul, 29(4):307-11; Abbott, T. E. F. et al. (2019): Depth of Anesthesia and Postoperative Delirium in JAMA, 2019, 321(5):459-460.

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 bears an attractive market potential. 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.

Clinical Development

Clinical Development	
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 combined 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 Anesthesia (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. 500)**	
ICU Sedation (Japan)	
Phase II in ICU patients (49)*	
Studies in other territories	
Phase III in general anesthesia - Russia (150)	Phase I single ascending dose in China (62)
Phase III in general anesthesia - South Korea (198)	Phase I continuous infusion in China (12)
Phase II in procedural sedation - China (150)	
Phase III in procedural sedation - China (480)	
Phase IIa dose finding study - China (24)	

Patient/volunteer numbers in brackets
*) Discontinued studies, no safety concerns
**) Ongoing study

Procedural sedation (U.S. + China)

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. In China, one Phase II and one Phase III trial have also been successfully 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.

The first U.S. Phase III study was successfully completed in 2016, and the primary efficacy endpoint was achieved. 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.

The study was successfully completed in 2017, and the primary efficacy endpoint was achieved. 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 (American Society of Anesthesiologists classification) patients undergoing colonoscopy (American Society of Anesthesiologists classification) was performed which was successfully completed in 2017. 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 to start of procedure	4.0–5.0 min	17–19.5 min	16.0–19.0 min
Time from end of procedure to fully alert	3.0–7.2 min	5.0–21.3 min	7.0–15.7 min
Time to back to normal	331–404 min	572–935 min	478.5–553 min

*) 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.

In July 2018, PAION's licensee Cosmo attended a pre-NDA meeting (NDA = New Drug Application) with the FDA for remimazolam for the indication procedural sedation together with PAION delegates.

Pre-NDA meetings with the FDA represent the final step during drug development before submission of an NDA. These meetings allow companies to discuss with the FDA the appropriateness of the content of their submission package as well as the approval pathway and the preferred label.

During the pre-NDA meeting with the FDA, there was no indication that would prevent the submission of the market approval dossier as planned.

General anesthesia (Japan, EU, Russia, China + South Korea)

A total of six Phase I, three Phase II and four Phase III 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.

In order to allow using the Japanese data for filing in the EU, the same induction and maintenance doses were used in the Phase II trial performed in Germany in 2014 as part of the European development program, 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.

Subsequently, 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 has started an EU Phase III clinical trial with remimazolam for the induction and maintenance of general anesthesia in July 2018.

The randomized, single-blind, propofol-controlled, confirmatory Phase III trial is expected to enroll approx. 500 ASA III/IV patients (American Society of Anesthesiologists classification III to IV) undergoing non-emergency surgery at more than 20 European trial centers. Patient recruitment is expected to be completed by the end of 2019.

The primary objective of the trial is to demonstrate the non-inferiority of remimazolam compared to propofol for the induction and maintenance of general anesthesia during elective surgery. The key secondary objective is to show improved hemodynamic stability (avoidance of intraoperative drop of blood pressure and vasopressor usage) compared to propofol.

The trial was designed in consultation with EU key opinion leaders in general anesthesia. Based on Scientific Advice obtained from the EMA in January 2018, PAION expects that a positive Phase III trial in combination with previously completed clinical studies in Europe and Japan should be sufficient for filing for market approval for the indication of general anesthesia in the EU.

In November 2018, PAION's licensee R-Pharm announced the successful completion of a Phase III trial in general anesthesia and PAION's licensee Hana Pharm has successfully completed patient recruitment of a Phase III trial in general anesthesia in October 2018.

ICU sedation

PAION's former licensee 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.

Pediatric development

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.

The aims of sedation and general anesthesia are the same in both adults and children: to enable diagnostic, surgical or dental procedures to be carried out safely and successfully while minimizing distress and discomfort to the patient. Advances in the diagnostics and treatment of pediatric diseases has led to an increase in the number of painful or distressing procedures for which many children need effective sedation or general anesthesia. While in adults many procedures can be undertaken with local anesthesia and verbal reassurance, this is often not possible with children and teenagers. Particularly for children, procedures are often too frightening, too painful, or need to be performed in children who are uncooperative, ill or in pain. In 2018, PAION submitted a pediatric investigation plan to the EMA. Subject to the EMA's approval for this development plan, the various trials are planned to be carried out sequentially over several years, starting with procedural sedation, followed by general anesthesia and finally ICU sedation. The clinical trials will initially be conducted with teenagers and further studies will be performed with increasingly younger children. At the same time, while at the beginning less serious diseases are included in the trials, increasingly severe diseases will be included in the trials in the later course of the development program.

Partnerships, regulatory and commercial activities

Development and commercialization collaborations with partners with local expertise or with a specific therapeutic focus with respect to remimazolam are an effective way of funding and

advancing remimazolam's 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 licensees 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. In order to exploit remimazolam's full potential, it is PAION's defined target to commercialize remimazolam on its own in selected European markets immediately after a potential market approval. PAION is well positioned to find further licensees. 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. (Cosmo Pharmaceuticals), Japan (Mundipharma), China (Yichang Humanwell), Canada (Pharmascience), Russia/CIS (R-Pharm), Turkey and the MENA region (TR-Pharm) and South Korea (Hana Pharm). For all other markets outside the EU, remimazolam is available for licensing.

PAION's **Chinese** remimazolam licensee Yichang Humanwell submitted a market approval dossier to the Chinese National Medical Products Administration (NMPA) for remimazolam in the indication procedural sedation in November 2018.

PAION's **Japanese** remimazolam licensee Mundipharma submitted a market approval dossier to the Japanese Pharmaceuticals and Medical Devices Agency PMDA for remimazolam in the indication general anesthesia in December 2018.

Together with Cosmo, PAION has prepared the market approval dossier in procedural sedation in the **U.S.** to a degree that allows for filing for market approval shortly as planned.

In November 2018, PAION's **Russian** remimazolam licensee R-Pharm announced the successful completion of a Phase III trial in general anesthesia. R-Pharm currently plans to file for market approval in Russia by the end of 2019.

For **Canada**, PAION currently expects its remimazolam licensee Pharmascience to use the U.S. market approval dossier as the basis for their own filing for market approval.

PAION's remimazolam licensee TR-Pharm (**Turkey, the Middle East** and **North Africa**) plans to file for market approval in Turkey based on the U.S. or Japanese dossier.

PAION's remimazolam licensee Hana Pharm has successfully completed patient recruitment of a Phase III trial in general anesthesia in October 2018. Before filing for market approval, the production process for remimazolam needs to be established in **South Korea**. Accordingly, Hana Pharm plans to file for market approval in 2020.

For **Europe** PAION is currently evaluating the possibility of submitting a Marketing Authorization Application for remimazolam in procedural sedation with the EMA based on the completed U.S. development program. In the course of a so-called pre-submission meeting with the EMA held in February 2019, the U.S. Phase III clinical development program including key safety data and efficacy results was discussed with the EMA in regard to a potential regulatory filing in the EU. Based on this pre-submission meeting, PAION assumes that the existing data package is sufficient to be able to submit the MAA for procedural sedation in the EU.

Pre-submission meetings with the EMA are intended to give companies the opportunity to ask the EMA process questions about a planned MAA submission for a drug, not to discuss the probability of approval. Therefore, the EMA has not provided PAION with any feedback on whether the results of the trials and the contents of the planned MAA will be sufficient to obtain regulatory approval of remimazolam.

Upfront and milestone payments			
	Total received	Maximum outstanding amount	Royalty rate
Ono, Japan (2007) (terminated in 2015)	USD 8 m	None	None
Yichang Humanwell, China (2012)	EUR 3.5 m[6]	EUR 0.5 m	10%[6]
Hana Pharm, S. Korea (2013)	EUR 1.5 m[4]	EUR 1.5 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
Pharmascience, Canada (2014)	EUR 0.4 m[1]	~ EUR 3.6 m	Tiered (starting at 15%)
Cosmo, U.S. (2016)	EUR 20 m[2]	EUR 42.5 m	20–25%[3]
Mundipharma, Japan (2017)	EUR 2 m[4]	EUR 24 m	Up to over 20%[5]
Total	EUR 36.8 m	~ EUR 83.6 m	

[1]) 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.
[2]) 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.
[3]) Subject to adjustments under specific circumstances, but not below 15% of net sales.
[4]) Partially received after the balance sheet date
[5]) Tiered royalties starting in the low double-digits to over 20%
[6]) In case of occurrence of certain market conditions in China, PAION is obliged to pay back 50% of the milestone payments already received (partially to bet set off against royalties). In this case, royalties would drop to 5%.

Vision: Specialty Pharma Company with own sales in the EU

In order to become a leader in the anesthesia field, forward integration, particularly in the EU, is essential for PAION in the near future. For PAION, forward integration does not only imply the buildup of an own distribution for the future commercialization of remimazolam in the EU, but also the use of these structures as a platform for future products in order to develop the greatest possible synergy potential. Forward integration provides an opportunity to find partners as there are only relatively few players in this area. At the same time, this reduces the potential dependence on any chosen partner. The goal is to grow significantly in the medium to long term. Until then, the product portfolio in the field of anesthesia is planned to be enriched with innovative medicines.

3. Net assets, financial position and results of operations

a. Results of operations

	2018 KEUR	2017 KEUR	Change in result KEUR
Revenues	2,766	5,811	-3,045
Gross profit	2,766	5,811	-3,045
Research and development	-12,167	-17,853	5,686
General administrative and selling	-3,408	-3,828	420
Other income (expenses)	354	-2	356
Operating expenses	-15,221	-21,683	6,462
Operating result	**-12,455**	**-15,872**	**3,417**
Financial result	6	20	-14
Income taxes	2,510	3,759	-1,249
Net result	**-9,939**	**-12,093**	**2,154**

Revenues recognized in the reporting period amounted to KEUR 2,766 and result from the remimazolam license agreement with Mundipharma in the amount of KEUR 1,963, thereof KEUR 1,000 from the filing of the market approval dossier in Japan and KEUR 963 from the recognition of the remaining part of the upfront payment of KEUR 1,000 received in January 2018. Moreover, KEUR 500 relate to the remimazolam license agreement with Hana Pharm resulting from the filing for market approval in Japan, and KEUR 250 relate to the remimazolam license agreement with Yichang Humanwell resulting from the filing for market approval in China. Revenues in the previous year mainly resulted from the remimazolam license agreement with Cosmo.

Research and development expenses amounted to KEUR 12,167 and mainly related to expenses in connection with the EU Phase III trial in general anesthesia started in July 2018, the validation of commercial scale production as well as activities for filings for market approval for remimazolam. The decrease of KEUR 5,686 compared to the prior year is mainly due to lower costs for Phase III and particularly Phase I studies which had been incurred to a significant extent in the prior year, especially in connection with the U.S. development program.

General administrative and selling expenses amounted to KEUR 3,408 and decreased by KEUR 420 compared to the previous year. Administrative expenses decreased by KEUR 39 to KEUR 3,040 and selling expenses decreased by KEUR 381 to KEUR 368. The decrease of selling expenses mainly results from lower expenses for market research activities in the reporting period.

Other income (expenses) mainly results from recharges to licensees.

Income taxes of the fiscal year 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 research and development expenses for remimazolam in the reporting period.

PAION closes fiscal year 2018 with a **net loss** of KEUR 9,939 after a net loss of KEUR 12,093 in the previous year.

b. Net assets

	31 Dec. 2018 KEUR	31 Dec. 2017 KEUR	Change KEUR
Non-current assets	2,286	2,528	-242
Current assets	22,037	29,357	-7,320
Assets	**24,323**	**31,885**	**-7,562**
Equity	20,822	25,229	-4,407
Current liabilities	3,501	6,656	-3,155
Equity and liabilities	**24,323**	**31,885**	**-7,562**

Non-current assets mainly comprise the book value of the development project remimazolam (KEUR 2,159; 31 December 2017: KEUR 2,353) resulting from the purchase price allocation in the course of the CeNeS acquisition in 2008 reduced by scheduled amortization.

Compared to 31 December 2017, **current assets** decreased by KEUR 7,320 to KEUR 22,037 and comprised cash and cash equivalents, prepaid expenses and other assets as well as trade receivables as of 31 December 2018. Cash and cash equivalents decreased by KEUR 7,612 in the reporting period from KEUR 24,839 as of 31 December 2017 to KEUR 17,227 as of 31 December 2018. Prepaid expenses and other assets decreased from KEUR 4,481 as of 31 December 2017 by KEUR 1,170 to KEUR 3,311 as of 31 December 2018. The decrease is substantially due to a KEUR 1,268 lower tax claim for reimbursement of parts of the research and development expenses from the British tax authorities as compared to 31 December 2017 amounting to KEUR 2,481 as of 31 December 2018. Trade receivables amounted to KEUR 1,500 as of

31 December 2018, increased by KEUR 1,463 as compared to 31 December 2017, and result from milestone payments from licensees Mundipharma and Hana Pharm for filing of the market approval dossier in Japan received after the balance sheet date.

The decrease in **equity** by KEUR 4,407 compared to 31 December 2017 mainly results from the net loss of the year and the capital increase conducted in June 2018. The equity ratio amounts to 85.6% as of 31 December 2018 (31 December 2017: 79.1%).

The decrease of **current liabilities** by KEUR 3,155 to KEUR 3,501 is primarily due to KEUR 3,703 lower trade payables compared to 31 December 2017 which amount to KEUR 2,218 as of 31 December 2018 and have decreased as planned due to the completion of certain development activities.

c. Financial position

Compared to 31 December 2017, **cash and cash equivalents** decreased by KEUR 7,612 to KEUR 17,227. The change in cash and cash equivalents stems from the following areas:

	2018 KEUR	2017 KEUR	Change KEUR
Cash flow from operating activities	-12,813	-17,720	4,907
Cash flow from investing activities	-13	-25	12
Cash flow from financing activities	5,214	12,494	-7,280
Effect of exchange rate changes	0	-21	21
Change in cash and cash equivalents	**-7,612**	**-5,272**	**-2,340**

The **cash flow from operating activities** primarily results from the net loss of the year in the amount of KEUR 9,939, changes in the working capital, particularly the decrease of trade payables of KEUR 3,703, as well as the tax credit payment from the British tax authorities in the amount of KEUR 3,729 received in September 2018, adjusted for the current tax credit claim towards the British tax authorities (KEUR 2,481) which has not had a cash effect yet.

The **cash flow from financing activities** results from the gross proceeds from the capital increase under exclusion of subscription rights conducted in June 2018 (KEUR 5,200), the cost of funds in this context (KEUR 160) and the exercise of stock options (KEUR 174). In the prior year, the cash flow from financing activities mainly resulted from the net proceeds from the capital increase with subscription rights conducted in February 2017 and from the capital increase under exclusion of subscription rights conducted in July 2017.

d. Overall appraisal

The net loss of EUR 9.9 million is below the forecast range of approx. EUR 12.5 million to approx. EUR 15 million projected for fiscal year 2018 in the previous year. This is particularly due to lower research and development expenses than expected for 2018 in the prior year.

Recognized revenues of EUR 2.8 million are slightly below the amount of approx. EUR 3 million forecasted per prior year for 2018 since milestones were partly achieved earlier and partly achieved later than planned.

General administrative and selling expenses of EUR 3.4 million are slightly below the range of approx. EUR 3.5 million to approx. EUR 4 million forecasted per prior year for 2018.

With EUR 12.2 million, research and development expenses are below the forecast range of approx. EUR 15 million to approx. EUR 17 million projected for fiscal year 2018 in the previous year since parts of the costs will only be incurred in 2019.

Tax income of EUR 2.5 million is also below the prior-year forecast for 2018 of approx. EUR 3 million due to the lower research and development expenses.

In total, results of operations, net assets and financial position have evolved better than expected in the reporting period due to the lower net loss.

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

Headcount

In fiscal year 2018, PAION had an average of 39 employees (previous year: 33 employees). Of these 39 employees, 30 worked in development and nine in administration and sales. PAION UK Group had an average headcount of seven employees. As of 31 December 2018, the headcount was 40 (31 December 2017: 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 1.84 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 2018, the exercise hurdle was EUR 2.66.

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 2018, the exercise hurdle was EUR 2.50.

From the Stock Option Plan 2014 approved by the Annual General Meeting on 21 May 2014, a total of 333,000 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 1.99, EUR 2.30 or EUR 2.60 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 2018, the exercise hurdle was EUR 2.24, EUR 2.75 or EUR 2.72, depending on the grant date.

From the Stock Option Plan 2016 approved by the Annual General Meeting on 25 May 2016, a total of 244,500 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 2.25 or EUR 2.60 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 2018, the exercise hurdle was EUR 2.31 or EUR 2.72, 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 2018 can be gathered from the following tables (according to German Corporate Governance Code):

Benefits granted in EUR	Dr. Wolfgang Söhngen CEO				
	2017	**2018**	**2018 (Min)**	**2018 (Max)**	
Fixed compensation	275,000	275,000	275,000	275,000	
Other remuneration	45,592	45,301	45,301	45,301	
Total	**320,592**	**320,301**	**320,301**	**320,301**	
One-year variable compensation	175,000	175,000	0	175,000	
Multi-year variable compensation					
Stock Option Plan 2014 - Grant 2018 (Waiting period 2018 to 2022) *	0	0	-	-	
Stock Option Plan 2016 - Grant 2018 (Waiting period 2018 to 2022) *	0	102,000	-	-	
Total	**495,592**	**597,301**	**320,301**	**495,301**	
Service cost	0	0	0	0	
Total remuneration	**495,592**	**597,301**	**320,301**	**495,301**	

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

Allocation in EUR	Dr. Wolfgang Söhngen CEO		
	2017	**2018**	
Fixed compensation	275,000	275,000	
Other remuneration	45,592	45,301	
Total	**320,592**	**320,301**	
One-year variable compensation	132,405	114,100	
Multi-year variable compensation			
Stock Option Plan 2008 - Grant 2008 (Waiting period 2008 to 2010)	0	50,028 *	
Total	**452,997**	**484,429**	
Service cost	0	0	
Total remuneration	**452,997**	**484,429**	

*) Dr. Söhngen exercised 41,517 stock options in the reporting period

	Abdelghani Omari CFO				Dr. Jürgen Beck CDO since 1 January 2018			
	2017	**2018**	**2018 (Min)**	**2018 (Max)**	**2017**	**2018**	**2018 (Min)**	**2018 (Max)**
	175,833	180,000	180,000	180,000	0	200,000	200,000	200,000
	15,127	15,127	15,127	15,127	0	15,127	15,127	15,127
	190,961	**195,127**	**195,127**	**195,127**	**0**	**215,127**	**215,127**	**215,127**
	90,000	90,000	0	90,000	0	70,000	0	70,000
	0	0	-	-	0	76,035	-	-
	0	102,000	-	-	0	60,965	-	-
	280,961	**387,127**	**195,127**	**285,127**	**0**	**422,127**	**215,127**	**285,127**
	0	0	0	0	0	0	0	0
	280,961	**387,127**	**195,127**	**285,127**	**0**	**422,127**	**215,127**	**285,127**

	Abdelghani Omari CFO		Dr. Jürgen Beck CDO since 1 January 2018	
	2017	**2018**	**2017**	**2018**
	175,833	180,000	0	200,000
	15,127	15,127	0	15,127
	190,961	**195,127**	**0**	**215,127**
	68,094	58,680	0	45,640
	0	0	0	0
	259,055	**253,807**	**0**	**260,767**
	0	0	0	0
	259,055	**253,807**	**0**	**260,767**

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

Management Board remuneration in fiscal year 2018 amounted to KEUR 1,290 in total (previous year: KEUR 928) and is composed as follows:

in EUR	2018	2017
Fixed remuneration	655,000	666,483
Other remuneration	75,556	60,741
Total non-performance based remuneration	**730,555**	**727,224**
Short-term variable remuneration	218,420	200,499
Total short-term remuneration	**948,975**	**927,723**
Long-term variable remuneration	341,000	0
Total long-term remuneration	**341,000**	**0**
Total remuneration	**1,289,975**	**927,723**

The increase of total remuneration compared to the previous year mainly results from the grant of stock options in the reporting period while no stock options were granted in the previous year.

The Management Board members held the following stock options as of 31 December 2018:

Status of non-exercised stock options as of 31 December 2018:		Dr. Wolfgang Söhngen	Abdelghani Omari	Dr. Jürgen Beck
Stock options 2008	No.	56,550	0	0
Stock options 2008 - fair value *	EUR	140,244	-	-
Stock options 2010	No.	162,000	80,000	0
Stock options 2010 - fair value *	EUR	270,540	133,600	-
Stock options 2014	No.	111,000	111,000	55,500
Stock options 2014 - fair value *	EUR	119,325	119,325	76,035
Stock options 2016	No.	100,000	100,000	44,500
Stock options 2016 – fair value *	EUR	102,000	102,000	60,965

*) 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, Mr. Omari and Dr. Beck are each entitled to contractual termination benefits, which correspond to an amount of two annual fixed basic remunerations. For Dr. Beck, a claim to

termination benefits in connection with a change of control can only be exerted if the change of control also entails a significant change in business strategy, in responsibilities or in regard to the company domicile.

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, 2014 and 2016, 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 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. Supervisory Board remuneration for fiscal year 2018 can be gathered from the following table:

	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	4,000	24,000
Dr. Dr. Irina Antonijevic	20,000	5,000	25,000
Dr. Hans Christoph Tanner	20,000	5,000	25,000

Supervisory Board remuneration in fiscal year 2018 amounted to KEUR 162. In the previous year the remuneration amounted to KEUR 141. The increase stems from the extension of the Supervisory Board by two members during the prior-year period.

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

Composition of subscribed capital
As of 31 December 2018, PAION AG had a subscribed capital of EUR 63,858,143.00, divided into 63,858,143 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 shareholder 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 2018 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 22 May 2023, with the consent of the Supervisory Board, on one or more occasions, by up to EUR 30,560,023.00 in total by issuing up to 30,560,023 new no-par value bearer shares in return for cash contributions or contributions in kind (Authorized Capital 2018). 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 23 May 2018 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 21 June 2018, the Authorized Capital 2018 was used in the amount of EUR 2,600,000.00 and amounts to EUR 27,960,023.00 as of 31 December 2018.

Furthermore, subject to the consent of the Supervisory Board, the Management Board is authorized to issue on or before 22 May 2023, 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 2018 I). Conditional Capital 2018 I has not yet been used. Furthermore, the company is authorized to issue 281,093 shares (Conditional Capital 2008 I), 720,000 shares (Conditional Capital 2010 I), 740,000 shares (Conditional Capital 2014), 840,000 shares (Conditional Capital 2016) and 900,000 shares (Conditional Capital 2018 II) in connection with the Stock Option Plans 2008, 2010, 2014, 2016 and 2018.

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, 2016 and 2018 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 the reporting period, no audit was carried out by the internal auditors. 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 quarterly statements and half-year 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 quarterly statements as well as half-year and annual financial statements are published and are discussed with the Audit Committee of the Supervisory Board or 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 high risk	Very high risk
Very probable 60%-90%	Very low risk	Low risk	Increased risk	High risk	Very 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.[13]

In order to ensure timely filings for market approval of remimazolam, 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.

PAION is currently conducting an EU Phase III study in general anesthesia. 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 have been 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 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

[13] Tufts Center for the Study of Drug Development (2014): Briefing – Cost of Developing a New Drug.

may not be confirmed to the same degree in subsequent studies and primary and secondary study endpoints defined in advance cannot be achieved. 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 and the achievement of primary and secondary endpoints, a throroughly chosen study design defined in advance under consultation with external experts and/or in the course of the study potential dosage modifications and amendments to clinical trial protocols if there are indications for their necessity 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 high risk. In case of occurrence, the potential damage level could pose a threat to the continued existence of the group. The risk classification increased by two categories compared to the previous year in light of (the relevance of) the EU Phase III study in general anesthesia which is currently being conducted.

In the course of the development of remimazolam for adults, in the U.S. as well as in the EU the subsequent development for pediatric use is a requirement. Should the start or conduct of this development not be possible within the timetable proposed to EMA due to delays, there is a risk that acceptance of filing of a market approval dossier in the EU is denied by EMA at first. PAION actively works on the completion and implementation of the pediatric development plan in the EU and is in regular contact with EMA in this regard in order to minimize this risk. This is an increased 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 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. Also after filing of a market approval dossier, there is a risk that the competent authority rejects a dossier e.g. due to formal reasons and demands rework, appoints external expert committees for the evaluation of single issues and/or initially rejects dossiers demanding the conduct of further studies. This may lead to significant delays in the approval process, higher than initially planned costs (e.g. in case of the necessity to conduct additional studies) and discontinuation of further development of the product candidate (in the respective market) in the worst case. 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 and its licensees in all important markets consult the regulatory authorities informally as well as within the frame of official consultations, as e.g. in pre-NDA meetings. Moreover, PAION consults

regulatory experts. This is a high risk. In case of occurrence, the potential damage level could pose a threat to the continued existence of the group.

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 and first filings of market approval dossiers 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 can only be influenced to a minor degree. It is planned to conduct additional smaller studies which clearly emphasize the value added by remimazolam in the respective indication in the affected market in order to allow for commercialization in the respective target groups as planned. 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 licensees will not be able to sufficiently prepare the market for launch by means of pre-marketing and market access activities as for example communication and/or exchange 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 and establishing a network of key opinion leaders. Moreover, there is regular information exchange with the U.S. licensee Cosmo and the licensees in the other regions. 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 an own commercialization in the EU) and licensees' distribution set-ups, if not existent yet, 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 is preparing implementation under consultation of external experts. Moreover, there is a regular information exchange with the U.S. licensee Cosmo and the licensees in the other regions. This is an increased risk. In case of occurrence, the potential damage level could pose a threat to the continued existence of the group.

For commercial supply of remimazolam, certain regulatory permissions and licenses need to be acquired. There is a risk that potentially required changes of processes or in the documentation at PAION cannot be implemented fast enough or that extensive inspections are undertaken by the authorities prior to the grant of such permissions leading to a delay in the supply of the commercially usable medicine for the licensees as well as for PAION itself. In order to avoid this risk, requirements and potentially necessary changes at PAION are being analyzed and implemented well in advance. This is an increased risk.

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, low to medium quantities of remimazolam have been produced in course of the clinical trials and the preparation of commercialization. Up until the start of commercialization, the so-called scale-up process still needs to be entirely completed. 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. Moreover, PAION has considered feedback from the respective regulatory authorities from formal and informal consultations in the product development program for remimazolam accordingly. 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 entirely completed until then. This could lead to a delay of studies and incur additional costs. PAION is therefore working on the timely completion of 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, not all 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.

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 licensees cannot be fulfilled if production development has not been completed yet, commercial supply agreements and purchasing infrastructures are not in place yet or if production orders cannot be submitted to the contractual manufacturers early enough. Also, PAION's own commercialization in the EU could be delayed by occurrence of these risks. In cooperation with its contractual manufacturers, PAION is working on the completion of relevant work for the production development and, under involvement of the licensees, on the finalization of commercial supply agreements and planning of production orders. Moreover, PAION has analyzed purchasing

infrastructures and is preparing implementation. This is a high risk. In case of occurrence, the potential damage level could pose a threat to the continued existence of the group.

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 licensees 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 a moderate risk. The risk classification decreased by one category compared to the previous year.

For the Chinese market, a competing remimazolam product is being developed by a competitor of PAION's Chinese licensee Yichang Humanwell. Should this product be granted market approval within a certain timeframe and should commercialization be possible without infringement of Yichang Humanwell's and PAION's existing patents, Yichang Humanwell's revenues from sales could be reduced significantly. Moreover, PAION would be obliged to pay an amount of EUR 1.75 million (partially to bet set off against royalties) to Yichang Humanwell, and the royalty rate would be halved from 10% to 5%. PAION expects the existing patent protection to avoid a successful commercialization of such competing product and would assess legal measures in cooperation with Yichang Humanwell in case of a potential market approval of this product should existing patents be infringed. This is a high risk.

ee) Risks in relation to licensees

In light of the progress of the development activities for remimazolam, increasingly bigger clinical studies are being conducted by licensees and important regulatory coordinations, meetings with the respective regulatory authorities and filings of market approval dossiers are increasingly in the focus for PAION's licensees. There is a risk that results from clinical studies, discussions with the authorities or evaluations of market approval dossiers by the authorities render the further development of remimazolam unattractive for existing licensees 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 licensees and engages in the evaluation of development plans and market approval dossiers 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 in regard to

studies as well as market approval dossiers. 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 licensees 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 further 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 Phase III study in general anesthesia which is currently being conducted 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 licensees are not met.

PAION's future ability to secure additional funding will depend on the success of its development, licensee 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 as well as (potential) pharma partners and licensees. 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. A strong rise of these currencies 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 and pound sterling. Currency risks also arise from potential future royalties which will be payable in different currencies by licensees depending on the respective licensed market, particularly in U.S. dollars from the potential commercialization in the U.S., as well

as 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, the consequences of a potential Brexit could also lead to tax payments on potential earnings expected in the future, e.g. due to controlled foreign corporation rules. 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 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. Due to a legislation change already enacted, tax credits will be significantly lower for PAION in future periods.

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 based on the current state of negotiations between the United Kingdom and the EU as well as the ongoing controversial discussion of potential (exit) scenarios within the UK. At the time of creation of this report, it is neither certain if the notified exit date end of 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 since the negotiations as well as possibilities and scenarios controversially discussed particularly within the UK have gained significant momentum since the fourth quarter of 2018. 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, trade restrictions of any kind as well as 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. Among others, free movement of employees of the PAION Group could be restrained.

Moreover, also apart from intragroup services, tax risks in particular could result from a potential Brexit, e.g. due to controlled foreign corporation rules.

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.

Clinical development of remimazolam in procedural sedation for minor medical interventions in the U.S. has already been completed and PAION's U.S. licensee Cosmo, who will be responsible for all further activities in the U.S., expects filing for market approval shortly. The start of commercialization of remimazolam in the U.S. is expected in 2020. PAION's Chinese licensee Yichang Humanwell filed for market approval in procedural sedation in China in November 2018. For Europe, PAION is currently evaluating the possibility of submitting a market approval dossier for remimazolam in procedural sedation with the EMA based on the completed U.S. development program. Based on a pre-submission meeting with the EMA, PAION assumes that the existing data package is sufficient to be able to submit the MAA for procedural sedation in the EU. Development in general anesthesia in Japan is completed and the Japanese licensee Mundipharma filed for market approval of remimazolam in general anesthesia in Japan in December 2018. PAION's Russian licensee R-Pharm currently plans to file for market approval in Russia by the end of 2019 based on the Phase III trial in general anesthesia successfully completed in November 2018. After successfully completed patient recruitment of a Phase III study in general anesthesia in October 2018, the South Korean licensee Hana Pharm plans to initially establish the production process for an own manufacture of remimazolam in South Korea and to file for market approval in general anesthesia in 2020. PAION expects that no further study in addition to the Phase III trial currently being conducted in the EU will be required for filing for market approval in general anesthesia in the EU. 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 licensees in Japan, China, Canada, Russia/CIS, Turkey, the MENA region, and South Korea financially in the form of milestone payments and royalties from launch onwards as well as in the form of additional development data. For selected European markets, an own commercialization is targeted. For all other regions, it is targeted to find licensees or distribution partners. In 2019, PAION will primarily focus on the completion of the ongoing Phase III study in general anesthesia in Europe, the support of its licensees for filings for market approvals and subsequent interactions with regulatory authorities as well as the establishment of the supply chain in order to be able to provide remimazolam for PAION's own commercial use in the EU as well as for licensees in their respective territories in time.

Overall, PAION has the chance of generating 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 filings for market approval in China and Japan in the reporting period were important milestones on the way to first market approvals for remimazolam in even more than one region and indication. Also, filing for market approval in the U.S. is expected shortly and the licensees in the other regions have made good development progress in 2018 on the way to potential filings for market approval in their licensed territories. Thus, the risk of failure of the development of remimazolam has further decreased.

The capital increase conducted in the reporting period has further reduced the required funds until filing for market approval in general anesthesia in the EU. Thus, the risk situation has improved compared to the previous year.

It is expected that the market approval dossier for procedural sedation in the U.S. will be filed shortly and that commercialization in the market could start in 2020. In Japan and China, a potential market approval could each be granted towards end of 2019 or in 2020. Moreover, further filings for market approval by licensees in their respective territories could take place in 2019. 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

There were no significant events in the period between the reporting date, 31 December 2018, and the preparation of this report.

Report on expected developments

Outlook on development and commercialization

PAION's focus for 2019 is on the development program in Europe, approval processes in the U.S. and other regions, manufacture of and supply chain for remimazolam. Moreover, PAION expects the development and approval activities in all territories to also further promote the other indications.

Europe

For the EU, PAION is working on the advancement of the clinical development program of remimazolam. Focus for 2019 are the conduct and completion of the ongoing Phase III study in general anesthesia as well as first development work to address the pediatric development plan stretching over several years. As a result of the consultation with EMA, PAION is currently evaluating the possibility of filing for market approval in procedural sedation in the EU based on the data from the U.S. development program.

U.S.

For the U.S., filing for market approval in procedural sedation by licensee Cosmo, which is expected shortly, has priority. With a regular course of the approval process, start of commercialization of remimazolam in the U.S. can be expected in 2020.

Rest of the World

PAION supports its licensees in the preparation and filing of approval dossiers. In China, licensee Yichang Humanwell filed for market approval in November 2018 leading to a potential market approval end of 2019 the earliest in case of a positive approval process. In Japan, licensee Mundipharma filed for market approval in December 2018; market approval could be granted end of 2019 the earliest.

PAION expects its other regional remimazolam licensees to continue their development activities and/or the preparation of market approval dossiers for remimazolam. Licensee R-Pharm plans to file for market approval in Russia by the end of 2019. Licensee TR-Pharm plans to file for market approval in Turkey based on the U.S. or Japanese dossier in the course of 2019, and in South Korea, Hana Pharm plans to file for market approval in 2020 after establishment of the production process for remimazolam.

Further activities

PAION is working on setting up the supply chain in order to be able to provide remimazolam product to the licensees timely for commercial use as well as having it available early enough for PAION's own commercialization.

Also, PAION plans small-scale pre-marketing activities for the preparation of an own commercialization subject to possible dates of filing its own market approval dossiers for remimazolam in Europe.

Financial outlook 2019

PAION expects revenues of about EUR 8 million in 2019, thereof EUR 7.5 million in connection with the planned regulatory filing for remimazolam in the U.S. by Cosmo. Moreover, EUR 0.5 million are related to revenues from TR-Pharm in connection with the transfer of the Japanese filing dossier translated into English or transfer of the U.S. filing dossier.

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 between approx. EUR 13 million and approx. EUR 15 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 2 million. General administrative and selling expenses are expected to amount to between approx. EUR 4 million and approx. EUR 5 million depending on the volume of precommercial activities. Net loss is expected to amount to between approx. EUR 7 million and approx. EUR 10 million in 2019.

This outlook assumes that PAION and licensee activities progress as expected. In case of delays, essential cost blocks and/or revenues would shift into 2020 or subsequent periods. Plans are also based on the current status of discussions with regulatory authorities. Additional unexpected requirements by regulatory authorities could lead to higher costs than planned and to delays in approvals and revenues based thereon.

Based on current planning, cash and cash equivalents at hand, including expected tax credits from the British tax authorities on parts of research and development expenses and the expected milestone payment in connection with filing for market approval in the U.S., secure a liquidity runway until approx. mid-2020. PAION expects to require further funds of approx. EUR 10 million until filing for market approval in general anesthesia in the EU based on current planning.

Moreover, additional funds will be required in the next years for the planned own commercialization in selected European markets. The magnitude of the required funds will be dependent on the actual setup of commercialization and which European countries PAION will initially focus on. Also, there is an additional requirement for funds for the intended development of the indication ICU sedation as well as for the multi-year pediatric development plan. PAION expects that the total requirement for funds can be partially covered by potential future milestone payments and royalties.

Aachen, Germany, 19 March 2019
PAION AG

Dr. Wolfgang Söhngen Dr. Jürgen Beck Abdelghani Omari

Consolidated Financial Statements

PAION AG

Consolidated Balance Sheet as of 31 December 2018

ASSETS	Note	31 Dec. 2018 EUR	31 Dec. 2017 EUR
Non-current assets			
Intangible assets	1.	2,212,476.80	2,414,870.55
Equipment	2.	73,569.84	113,682.01
Other assets		13.93	13.95
		2,286,060.57	2,528,566.51
Current assets			
Trade receivables	3.	1,500,000.00	37,433.15
Prepaid expenses and other assets	4.	3,310,694.39	4,480,716.05
Cash and cash equivalents	5.	17,226,658.20	24,838,652.24
		22,037,352.59	29,356,801.44
Total assets		**24,323,413.16**	**31,885,367.95**

EQUITY AND LIABILITIES	Note	31 Dec. 2018 EUR	31 Dec. 2017 EUR
Equity	6.		
Share capital		63,858,143.00	61,120,046.00
Capital reserve		138,730,764.25	135,854,744.31
Translation reserve		-712,030.72	-630,192.60
Loss carryforward		-171,115,423.14	-159,021,995.85
Result for the period		-9,939,410.76	-12,093,427.29
		20,822,042.63	25,229,174.57
Current liabilities			
Trade payables	8.	2,217,979.06	5,920,968.99
Provisions	7.	629,506.26	390,855.94
Other current liabilities	9.	653,885.21	325,453.79
Current portion of deferred income		0.00	18,914.66
		3,501,370.53	6,656,193.38
Total equity and liabilities		**24,323,413.16**	**31,885,367.95**

Consolidated Statement of Comprehensive Income for Fiscal Year 2018

	Note	2018 EUR	2017 EUR
Revenues	10.	2,765,900.33	5,811,199.73
Gross profit		2,765,900.33	5,811,199.73
Research and development expenses		-12,167,169.44	-17,853,505.83
General administrative and selling expenses		-3,407,785.10	-3,827,551.76
Other income (expenses), net	11.	353,802.76	-2,355.95
Operating expenses		-15,221,151.78	-21,683,413.54
Operating result		-12,455,251.45	-15,872,213.81
Financial income	12.	6,183.15	19,811.94
Financial result		6,183.15	19,811.94
Result for the period before taxes		-12,449,068.30	-15,852,401.87
Income taxes	13.	2,509,657.54	3,758,974.58
Result for the period		**-9,939,410.76**	**-12,093,427.29**
of which attributable to other shareholders		0.00	0.00
of which attributable to shareholders of PAION AG		-9,939,410.76	-12,093,427.29
Foreign currency translation of subsidiaries		-81,838.12	-279,641.89
Total income and expense recognized directly in equity that will be reclassified to profit or loss when specific conditions are met		-81,838.12	-279,641.89
Cumulative foreign currency translation reclassified to profit or loss due to changes in the scope of consolidation		0.00	-9,773.34
Other comprehensive income		-81,838.12	-289,415.23
Total comprehensive income		**-10,021,248.88**	**-12,382,842.52**
of which attributable to other shareholders		0.00	0.00
of which attributable to shareholders of PAION AG		-10,021,248.88	-12,382,842.52
Earnings per share (basic)	14.	-0.16	-0.20
Earnings per share (diluted)	14.	-0.16	-0.20

Consolidated Cash Flow Statement for Fiscal Year 2018

	2018 EUR	2017 EUR
Cash flows from operating activities:		
Net result for the period	-9,939,410.76	-12,093,427.29
Reconciliation of net profit (loss) for the period to cash flows from operating activities:		
Income taxes	-2,509,657.54	-3,758,974.58
Amortization/depreciation and non-cash changes of fixed assets	255,574.27	347,254.29
Loss/Profits from the disposal of non-current assets	0.00	4,240.19
Interest expenses and interest income	-6,183.15	-19,811.94
Release of deferred income	-982,405.73	-5,478,666.89
Expenses from stock option plans	399,691.16	174,474.72
Changes in assets and liabilities which are not attributable to investing or financing activities:		
Trade receivables	-1,462,566.85	-37,433.15
Prepaid expenses and other assets	-48,372.59	-300,545.32
Trade payables	-3,702,989.93	-431,647.13
Provisions	238,650.32	-145,609.20
Other current liabilities	328,431.42	-33,360.32
Deferred income	963,491.07	-276,453.88
Non-cash exchange losses/gains	-81,364.70	-267,717.27
	-16,547,113.01	-22,317,677.77
Tax payments	0.00	-19,696.15
Tax payments received	3,729,251.01	4,596,583.91
Interest received	4,983.92	20,346.50
Net cash used in operating activities	-12,812,878.08	-17,720,443.51
Cash flows from investing activities:		
Cash paid for investments in intangible assets and equipment	-13,068.33	-24,981.17
Net cash used in investing activities	-13,068.33	-24,981.17
Cash flows from financing activities:		
Capital increase	2,738,097.00	5,362,952.00
Contributions to the capital reserve	2,635,905.22	7,818,544.16
Payments in connection with raising capital	-159,576.44	-687,077.14
Net cash provided from financing activities	5,214,425.78	12,494,419.02
Change in cash and cash equivalents	-7,611,520.63	-5,251,005.66
Effect of exchange rate changes on cash	-473.41	-21,697.97
Cash and cash equivalents at beginning of the period	24,838,652.24	30,111,355.87
Cash and cash equivalents at end of the period	**17,226,658.20**	**24,838,652.24**
Composition of cash and cash equivalents at the end of the period:		
Cash and cash equivalents	**17,226,658.20**	**24,838,652.24**

Consolidated Statement of Changes in Equity for Fiscal Year 2018

EUR	Share capital	Capital reserve	Translation reserve	Loss carryforward	Equity
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**
Total comprehensive income	0.00	0.00	-81,838.12	-9,939,410.76	-10,021,248.88
Issue of shares	2,738,097.00	0.00	0.00	0.00	2,738,097.00
Contribution to the capital reserve	0.00	2,635,905.22	0.00	0.00	2,635,905.22
Cost of raising capital	0.00	-159,576.44	0.00	0.00	-159,576.44
Additional contribution to the capital reserve due to the issue of options	0.00	399,691.16	0.00	0.00	399,691.16
31 December 2018	**63,858,143.00**	**138,730,764.25**	**-712,030.72**	**-181,054,833.90**	**20,822,042.63**

Consolidated Notes

PAION AG

Notes to the consolidated financial statements for fiscal year 2018

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 consolidated financial statements as of 31 December 2018 are scheduled for authorization and approval for publication by the Supervisory Board in its meeting on 19 March 2019.

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 2018, 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 2018 according to IAS 1.

The following new and/or revised standards, amendments and interpretations were applied for the first time in the fiscal year.

- IFRS 15 “Revenue from contracts with customers“ and clarifications to IFRS 15 “Revenue from contracts with customers“
- IFRS 9 “Financial Instruments”
- IFRSs 2014–2016 Cycle “Annual Improvements to IFRSs 2014–2016”. The following further standards were changed:
  - IFRS 1 “First-time Adoption of International Financial Reporting Standards”
  - IAS 28 “Investments in Associates and Joint Ventures”
- Amendments to IAS 40 “Investment Property”
- Amendments to IFRS 2 “Share-based payment”
- IFRIC 22 “Foreign Currency Transactions and Advance Consideration”

The application of IFRS 15 had no effects on the Group’s net assets, financial position or results of operations. In comparison to the accounting treatment until fiscal year 2017, no effects of the application of the new standard have been identified. Therefore, application of IFRS 15 neither has an effect on already recognized revenues nor on revenues to be recognized in the future from contracts entered into until and including 2017. In the course of first-time adoption of IFRS 15, the cumulative effect method was applied leading to no effects. The application of IFRS 15 has led to additional notes disclosures.

The application of IFRS 9 had no effects on the Group’s net assets, financial position or results of operations but has led to additional notes disclosures.

The application of the other standards and interpretations applicable for the first time did not necessitate the provision of additional disclosures and did not influence the Group’s net assets, financial position or results of operations.

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 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.

– 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.
– 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.
– 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.
– Amendments to IAS 19 “Employee Benefits”: The amendments are effective for annual periods beginning on or after 1 January 2019. Earlier adoption is allowed.
– Amendments to References to the Conceptual Framework in IFRS Standards: The amendments are effective for annual periods beginning on or after 1 January 2020. Earlier adoption is allowed. The adoption by the EU is still pending.
– Amendments to IFRS 3 “Business Combinations”: The amendments are effective for annual periods beginning on or after 1 January 2020. Earlier adoption is allowed. The adoption by the EU is still pending.
– Amendments to IAS 1 and IAS 8 (Definition of Material): The amendments are effective for annual periods beginning on or after 1 January 2020. 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 16, will presumably not have any effects on the Group’s net assets, financial position and results of operations.

The application of IFRS 16 will have effects on the Group’s net assets, financial position and results of operations in the future which are however immaterial at the time of first-time adoption and which will lead to an increase of the balance sheet total of less than EUR 0.5 million due to first-time capitalization of leases previously not recognized on the balance sheet and corresponding recognition of lease liabilities. For contracts subject to a different accounting treatment due to first-time adoption of the new standard, rent and lease expenses previously entirely recognized in the operating expenses will be recognized mostly as depreciation of tangibles and as financial expenses to a small degree. Financial expenses will initially be higher and decrease over the respective lease term due to application of the effective interest method. Overall, this will lead to an earlier recognition of expenses by tendency and to a shift of a small part of expenses previously recognized as general administrative and selling as well as research and development costs to the financial expenses.

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 neither reportable business nor geographical segments according to IFRS 8 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 criteria for revenue recognition according to IFRS as satisfied based on a scientific, technical and economic evaluation including the involvement of the relevant specialized departments. Provisions are recognized for current obligations if they originated in the past and are uncertain in regard to maturity and amount, and if it is probable after consideration and evaluation of all relevant information that these obligations will have to be satisfied by an outflow of resources that represent an economic benefit and if the amount of the obligations can be reliably estimated.

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 or results of the Group's operations except for IFRS 9 and IFRS 15 for which the application did not have an effect on the Group's net assets, financial position or results of operations but led to additional notes disclosures.

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 "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 2018: 0.8969 GBP/EUR; exchange rate as of 31 December 2017: 0.8887 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 2018 from 0.8720 GBP/EUR to 0.8978 GBP/EUR; bandwith in 2017 from 0.8478 GBP/EUR to 0.9121 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.

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.

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 out-licensing 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 according to IFRS 15. Income is realized once PAION's performance obligation has been satisfied by transfer of the promised good or service. Such an asset is deemed transferred when the customer obtains control of it and is therefore able to direct the use of and substantially obtain the remaining benefits from it. Some performance obligations are satisfied over time while others are satisfied at a point in time.

Since PAION is not selling products at the market yet, revenues are essentially realized by means of selling 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 from performance obligations satisfied at a point in time are realized at the time of satisfaction. Revenues from performance obligations satisfied over time, comprising research and development activities and/or milestones and 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 connection with performance obligations which are satisfied over time, quantifiable and for which PAION does not owe a success, are recognized based on the stage of completion in the respective reporting 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.

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:

EUR	Industrial rights and similar rights and assets
Acquisition Cost	
1 Jan. 2017	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
Additions	12,164.83
Disposals	0.00
Reclassifications	0.00
Exchange rate differences	-113,494.43
31 Dec. 2018	12,589,393.55
Accumulated amortization, depreciation and impairment losses	
1 Jan. 2017	10,466,343.07
Additions	199,005.12
Disposals	958.71
Exchange rate differences	-388,536.88
31 Dec. 2017	10,275,852.60
Additions	195,428.46
Disposals	0.00
Exchange rate differences	-94,364.31
31 Dec. 2018	10,376,916.75
Carrying amounts as of 31 Dec. 2017	**2,414,870.55**
Carrying amounts as of 31 Dec. 2018	**2,212,476.80**

The intangible assets mainly comprise the development project remimazolam (KEUR 2,159; 31 December 2017: KEUR 2,353). 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	Total
Acquisition Cost			
1 Jan. 2017	175,088.79	813,210.39	988,299.18
Additions	2,662.54	0.00	2,662.54
Disposals	4,820.42	12,672.78	17,493.20
Reclassifications	0.00	0.00	0.00
Exchange rate differences	-345.32	-9,453.71	-9,799.03
31 Dec. 2017	172,585.59	791,083.90	963,669.49
Additions	0.00	903.50	903.50
Disposals	0.00	0.00	0.00
Reclassifications	0.00	0.00	0.00
Exchange rate differences	0.00	-2,213.32	-2,213.32
31 Dec. 2018	172,585.59	789,774.08	962,359.67
Accumulated amortization, depreciation and impairment losses			
1 Jan. 2017	151,158.95	669,929.92	821,088.87
Additions	9,537.02	37,535.34	47,072.36
Disposals	1,688.78	11,505.00	13,193.78
Exchange rate differences	-86.45	-4,893.52	-4,979.97
31 Dec. 2017	158,920.74	691,066.74	849,987.48
Additions	5,090.06	35,504.37	40,594.43
Disposals	0.00	0.00	0.00
Exchange rate differences	0.00	-1,792.08	-1,792.08
31 Dec. 2018	164,010.80	724,779.03	888,789.83
Carrying amounts as of 31 Dec. 2017	**13,664.85**	**100,017.16**	**113,682.01**
Carrying amounts as of 31 Dec. 2018	**8,574.79**	**64,995.05**	**73,569.84**

(3) Trade receivables

Trade receivables relate in the amount of KEUR 1,000 to the remimazolam license agreement for Japan with Mundipharma and in the amount of KEUR 500 to the license agreement for South Korea with Hana Pharm.

(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 2,481; previous year: KEUR 3,749), claims for reimbursement from recharges to licensees (KEUR 304; previous year: KEUR 53), prepaid expenses relating to research and development services for remimazolam (KEUR 221; previous year: KEUR 409), prepaid expenses relating to insurance contributions, rents and other prepayments (KEUR 155; previous year: KEUR 101) and VAT refund claims (KEUR 81; previous year: KEUR 129).

(5) Cash and cash equivalents

Cash and cash equivalents are comprised of the following:

	31 Dec. 2018 KEUR	31 Dec. 2017 KEUR
Current deposits	0	619
Bank balance and cash in hand	17,227	24,220
	17,227	**24,839**

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 2018, the share capital amounts to EUR 63,858,143.00 (previous year: EUR 61,120,046.00); it is divided into 63,858,143 no-par value shares (previous year: 61,120,046 shares). The increase of the share capital in the total amount of EUR 2,738,097.00 in the reporting period results from a capital increase without subscription rights conducted in June 2018 in the amount of EUR 2,600,000.00 and from the exercise of stock options in the amount of EUR 138,097.00. Details are described in the following.

The capital reserve amounts to EUR 138,730,764.25 as of 31 December 2018 (previous year: EUR 135,854,744.31) 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.

By virtue of a resolution adopted by the Annual General Meeting on 23 May 2018, the Management Board was authorized to increase the share capital on or prior to 22 May 2023, with the consent of the Supervisory Board, on one or more occasions, by up to EUR 30,560,023.00 in total by issuing up to 30,560,023 new no-par value bearer shares in return for cash contributions or contributions in kind (Authorized Capital 2018). Furthermore, the Management Board was authorized to use up to EUR 6,112,004.00 of the Authorized Capital 2018 to issue new shares for cash by excluding pre-emptive rights. The still available Authorized Capital 2017 in the amount of EUR 26,273,543.00 was revoked.

On 21 June 2018, the Management Board decided with the approval of the Supervisory Board and based on the authorization of the General Meeting to issue 2,600,000 no-par value bearer shares in return for cash contribution by excluding pre-emptive rights for the existing shareholders to a French institutional investor. The new shares were issued at a price of EUR 2.00 per share. The capital increase led to gross proceeds of EUR 5.2 million. As a result, the share capital of the company was increased from EUR 61,127,526.00 by EUR 2,600,000.00 to EUR 63,727,526.00 through the issuing of 2,600,000 new shares. The capital increase was registered in the Commercial Register on 25 June 2018. The Authorized Capital 2018 was reduced by EUR 2,600,000.00 in the course of

this capital measure and amounts to EUR 27,960,023.00 as of 31 December 2018.

Furthermore, by virtue of another resolution adopted by the Annual General Meeting on 23 May 2018, subject to the consent of the Supervisory Board, the Management Board was authorized to issue on or before 22 May 2023, 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 2018 I). Furthermore, the Management Board was authorized to use up to EUR 6,112,004.00 of the Conditional Capital 2018 I for Bonds against cash by excluding pre-emptive rights. Conditional Capital 2017 in the amount of EUR 26,200,000.00 was revoked.

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, 205,250 stock options were issued to current and former Management Board members and employees of the PAION Group as of 31 December 2018. To date, 479,142 stock options from the Stock Option Plan 2008 have been exercised, thereof 138,097 in fiscal year 2018. The exercises led to cash inflows of EUR 174,002.22 in the fiscal year. As of 31 December 2018, Conditional Capital 2008 I amounts to EUR 281,093.00.

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 2018. 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, 533,885 stock options were issued to current and former Management Board members and employees of the PAION Group as of 31 December 2018. 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, 701,185 stock options were issued to Management Board members and employees of the PAION Group as of 31 December 2018. No stock options have been exercised yet.

A resolution was adopted by the Annual General Meeting on 23 May 2018 to conditionally increase the share capital of PAION AG by an aggregate of up to EUR 900,000.00 by issuing an aggregate of up to 900,000 new no-par value bearer shares (Conditional Capital 2018 II). 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 2018 exercise their options. Under the Stock Option Plan 2018, no stock options were granted yet as of 31 December 2018.

The currency translation reserve amounted to EUR -712,030.72 as of 31 December 2018 (previous year: EUR -630,192.60). Of these, KEUR 7,523 concern cumulative exchange rate gains (as of 31 December 2017 cumulative exchange rate gains of KEUR 8,017) arising from the translation of the financial statements of the British subsidiaries from GBP into EUR, KEUR -6,319 concern cumulative exchange rate losses (as of 31 December 2017 cumulative exchange rate losses of KEUR 0) from (parts of) the loans granted to the British subsidiaries by PAION AG which were swapped into shares in the respective entities in the reporting period, and KEUR -1,916 concern cumulative exchange rate losses (as of 31 December 2017 cumulative exchange rate losses of KEUR -8,647) incurred on the loan from PAION AG to the British subsidiary PAION UK Ltd (the prior-year amount also included cumulative exchange rate losses amounting to KEUR -285 from the loan from PAION AG to the British subsidiary PAION Holdings UK Ltd). As of 31 December 2018, the loan granted to PAION UK Ltd amounts to KEUR 22,434 (in the previous year, the loans granted to the British subsidiaries amounted to KEUR 89,461).

(7) Provisions

Provisions developed as follows:

in KEUR	Premiums/ Management Bonuses	Taxes	Other	Total
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**
Utilization	252	0	0	252
Addition	497	0	0	497
Release	6	0	0	6
Exchange rate differences	0	0	0	0
31 Dec. 2018	**534**	**0**	**96**	**630**

(8) Trade payables

Trade payables amount to KEUR 2,218 as of 31 December 2018 (previous year: KEUR 5,921). 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 the balance sheet date, depending on the respective invoice date.

(9) Other current liabilities

Other current liabilities comprise the following:

	31 Dec. 2018 KEUR	31 Dec. 2017 KEUR
Refund liability	250	0
Wage taxes	220	172
Holiday allowances	93	100
Supervisory Board remuneration	55	34
Others	36	19
	654	**325**

Consolidated statement of comprehensive income disclosures

(10) Revenues

Revenues recognized in the reporting period amount to KEUR 2,766 and result from the remimazolam license agreement with Mundipharma in the amount of KEUR 1,963, thereof KEUR 1,000 from the filing of the market approval dossier in Japan and KEUR 963 from the recognition of the remaining part of the upfront payment of KEUR 1,000 received in January 2018. Moreover, KEUR 500 relate to the remimazolam license agreement with Hana Pharm resulting from the filing for market approval in Japan, and KEUR 250 relate to the remimazolam license agreement with Yichang Humanwell resulting from the filing for market approval in China. Revenues in the previous year mainly resulted from the remimazolam license agreement with Cosmo Pharmaceuticals (Cosmo).

Disaggregation of revenue

Revenues in the reporting period nearly entirely result from consideration from (remimazolam) licensees for data, technology and know-how transfers as well as the achievement of (development) milestones whose licenses each grant rights (e.g. for development and commercialization) in certain geographical regions. Revenues of the reporting period are therefore disaggregated based on geographical regions in the following overview. Revenues are allocated to a certain region if they result from contracts with licensees for the respective region.

Revenues per region:

Japan: KEUR 1,963
China: KEUR 269
South Korea: KEUR 500
Others/worldwide: KEUR 34

Contract balances and performance obligations

Contract balances at the beginning and end of the reporting period were as follows:

	01 Jan. 2018 KEUR	31 Dec. 2018 KEUR
Trade receivables	37	1,500
Refund liabilities	0	250
Deferred Income	19	0

In the reporting period, revenues amounting to KEUR 19 were realized from (parts of) consideration recognized as deferred income as of 31 December 2017. Revenues amounting to KEUR 982 were recognized in the reporting period from performance obligations partially satisfied in prior years; the amount recognized in the reporting period only relates to performances carried out in the reporting period.

As a specialty pharma group, PAION develops new product candidates in anesthesia aiming at outlicensing these and commercializing these itself in certain regions. In addition to the grant of the license for development and commercialization, typical performances in the course of outlicensing product candidates and entering into license agreements regularly comprise extensive data, technology, process and/or know-how transfers, development services, the achievement of (regulatory) milestones and the provision of market approval dossiers from other regions.

Based on the development stage of PAION's currently only product candidate remimazolam which has not been granted market approval yet, PAION does not generate sustainable revenues in the form of royalties yet. Before the potential (future) recognition of royalties upon commercialization of remimazolam, there are mostly upfront payments at the beginning of the contract regularly compensating an extensive data, technology, process and/or know-how transfer as the typically first performance obligation in the course of entering into license agreements. Based on the respective contract, this performance can either be carried out at a point in time or over time. In case of satisfaction of the performance obligation at a point in time, payment regularly occurs shortly before the services are

rendered or closely around the time the performance is carried out. In case of satisfaction of the performance obligation over time, payment regularly occurs before completion of the performance, and deferred income is being recognized for the part of the consideration that is not to be recognized as revenue yet which is then being realized as revenue over the time of the satisfaction of the performance obligation. Revenue is regularly either being recognized over a contractually defined period or over a period resulting from (planned) development steps in this case.

Chronologically following upfront payments, the license contracts regularly include consideration linked to the achievement of certain (development) milestones (see above). These can either compensate development services to be carried out or development results to be achieved by PAION or the license itself. Due to the high risk of failure in drug development, underlying revenues are only being recognized upon complete and successful achievement of the defined milestones. Therefore, no contract assets or liabilities are being recognized during the time of satisfaction of the performance obligation. Upon achievement of the milestone, revenue and corresponding trade receivables are being recognized. Achievement of a milestone is in close timely relation to the corresponding consideration to be paid by the licensee.

Payments are usually due within 30 days either after satisfaction of the performance obligation or after contract signature in case of upfront payments. There is a potential repayment obligation in the amount of KEUR 1,500 from the license contract with Yichang Humanwell (also see the notes to contingent liabilities). In this context, there is also a potential refund liability in the amount of KEUR 250 which can be (potentially partially) set off against future royalties. The license agreements regularly do not comprise guarantees and do not include further material obligations in addition to a regular data exchange with the licensees, potential support of the licensees in their regulatory and development activities and the contractually defined performance obligations, in the course of which however not only the sole rendering of services but also the successful result of the underlying performance may be owed, as e.g. the successful conduct of studies under achievement of primary and secondary endpoints as defined in advance.

The transaction price allocated to (partially) unsatisfied performance obligations is KEUR 0 for all existing license contracts as of 31 December 2018. Performance obligations existing as of 31 December 2018 entirely relate to variable consideration which is constrained according to IFRS 15.56 and therefore not included in the transaction price due to the high risk of pharmaceutical development.

Material changes of contract balances in the reporting period relate to the increase of trade receivables. As of 31 December 2018, these result from the filing of the market approval dossier in Japan. Moreover, a refund liability amounting to KEUR 250 as of 31 December 2018 has been recognized resulting from the milestone payment received from licensee Yichang Humanwell in the context of the filing of the market approval dossier in China which is repayable (and (potentially partially) to be set off against future royalties) if a competing remimazolam product is being sold in China within a certain timeframe.

Significant judgements

Each performance obligation is individually being analyzed in regard to the point in time or the timeframe of satisfaction. In case of satisfaction of a performance obligation over time, output methods are regularly being used for recognition of revenue. For data, technology, process and/or know-how transfers, a finalization date is typically defined until which revenues are being realized on a straight-line basis, or revenue is recognized over the timeframe resulting from the (planned) development steps otherwise. Due to the objective verifiability for the licensor as well as for the licensee, these methods depict an appropriate state of the transfer of the services. For performance obligations for which successful satisfaction contractually requires the achievement of defined milestones, revenues are only being recognized at the point in time of complete achievement of the respective defined milestone in spite of the service being rendered over time since variable consideration for these services is constrained according to IFRS 15.56. As it is not certain if milestones can be achieved or not before actual achievement of these milestones due to the high risk of pharmaceutical development, actual achievement of the milestones depicts the best measurement for revenue recognition.

Performance obligations satisfied at a point in time regularly exist for data, technology, process and/or know-how transfers on the one hand, and for the grant of licenses with a right to use on the other hand. In the case of satisfaction of performance obligations from data, technology, process and/or know-how transfers at a point in time, this point in time is regularly contractually defined and both parties confirm the successful transfer in writing allowing for a clear determination of when the control has been transferred. For the grant of licenses with a right to use according to IFRS 15.B56b), the license is regularly deemed granted at the time of conclusion of the contract and thus control of it is deemed transferred.

For determination of the transaction price of a contract, all potential payments from a contract are initially being analyzed and included in the calculation of a potential transaction price. Variable consideration is then being analyzed in regard to a potential constraint according to IFRS 15.56 et seqq. This regularly leads to variable consideration from the achievement of (development) milestones and royalties not being included in the transaction price. Each variable consideration is individually analysed and evaluated in this context under consideration of the specific contractual background and the conditions for which fulfillment is required for receipt of the respective variable consideration. The high risk environment of the pharmaceutical industry in particular is taken into account for this evaluation. Within the contracts which are negotiated highly individually for the respective regions, variable consideration for the individual performance obligations is already depicted in the contractually defined payments linked to those performances. The transaction price at the time of conclusion of a contract regularly only includes the first payment mostly linked to a data, technology, process and/or know-how transfer which then consequentially the transaction price is allocated to. As soon as performance obligations have been satisfied by achievement of certain development steps or milestones and variable consideration is not constrained anymore, the total transaction price increases in the amount of the variable consideration which is not constrained anymore. This increase of the transaction price is allocated to the (development) performance (usually the achievement of a milestone) the variable consideration is linked to.

Returns, refunds and other similar obligations are evaluated individually based on the specific contracts and do not require estimations or measurements based on the contracts in place.

Assets recognized from costs to obtain or fulfill a contract and practical expedients

Since there are regularly no costs to obtain a contract that are only incurred in case of conclusion of a contract, no additional costs in connection with obtaining contracts have been capitalized.

In the course of first-time adoption of IFRS 15, the cumulative effect method according to IFRS 15.C3b) in connection with IFRS 15.C7 and IFRS 15.C8 has been applied retrospectively. Since there are no effects of first-time adoption there are no additional disclosures according to IFRS 15.C8.

(11) Other income (expenses), net

Other income (expenses) in the fiscal year includes income from recharges to licensees in the amount of KEUR 417 (previous year: KEUR 56).

(12) Financial income

Financial income consists of the following:

	2018 KEUR	2017 KEUR
Interest income based on amortized costs (bank balances and current deposits)	6	20
	6	**20**

(13) Income taxes / Deferred taxes

As of 31 December 2018, the tax losses carried forward by PAION Germany group (PAION AG and PAION Deutschland GmbH) amounted to about EUR 79 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 111 million per 31 December 2018 (equivalent to EUR 124 million if translated at the exchange rate applicable on the reporting date). In the previous year, these amounted to GBP 108 million or EUR 121 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 according to the relevant tax regulations (e.g. minimum taxation).

Overall, the losses carried forward within the Group amount to EUR 202 million (previous year: EUR 201 million). No deferred tax assets were recognized regarding a partial amount of EUR 200 million (previous year: EUR 198 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% and will be reduced to 17% starting 1 April 2020. 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 367 (previous year: KEUR 447) 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 2018, the resulting deferred tax assets would amount to EUR 26 million (previous year: EUR 26 million). Based on the income tax rate of 17% that will be applicable in Great Britain in the future, the losses carried forward in Great Britain as of 31 December 2018 would produce deferred tax assets in an amount of GBP 19 million (equivalent to EUR 21 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, based on the currently still applicable income tax rate of 19% in Great Britain. The temporary differences between the tax base and the IFRS carrying amount would produce a net balance as of 31 December 2018 of deferred tax assets in an amount of KEUR 240 (previous year: KEUR 28), of which Germany accounts for KEUR 0 (previous year: KEUR 0) and Great Britain for KEUR 240 (previous year: KEUR 28). The depicted differences in carrying amounts relate mainly to fixed assets and provisions. Total deferred tax assets would amount to EUR 47 million (previous year: EUR 49 million).

In the fiscal year, PAION AG and PAION Deutschland GmbH reported a (low) profit; the 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	2018	2017
Result for the period before taxes	-12,449	-15,852
Anticipated tax expense (+)/income (-)	-3,735	-4,756
Revaluation of tax losses due to tax rate changes	2,473	0
Difference between anticipated Group tax rate and actual local tax rates	1,413	2,184
Non-recognition of deferred taxes on tax losses	826	1,613
Non-recognition of deferred taxes on temporary differences	139	18
Effects from currency translation	136	-1,007
Expenses in connection with stock options	119	54
Correction of non-recognition of deferred taxes on temporary differences in prior years	112	0
Non-deductible expenses	40	34
Correction of prior years' tax expenses	0	1
Cost in connection with capital increases	-52	-223
Correction of non-recognition of deferred taxes on tax losses in prior years	-112	0
Tax losses used	-315	-70
Effects from tax credits	-1,082	-1,608
Adjustment non-recognition of deferred taxes on tax losses due to tax rate changes	-2,473	0
Other	1	1
Actual tax expense (+) / income (-)	**-2,510**	**-3,759**

The actual tax income results from the expected reimbursement of research and development costs through British tax authorities. The expected tax credits reduced the tax losses carried forward accordingly.

(14) 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:

	2018	2017
Shares outstanding as of 1 January	61,120,046	55,757,094
Weighted average number of shares issued	1,392,329	3,361,592
Weighted average number of ordinary shares	**62,512,375**	**59,118,686**

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

	2018	2017
Net result for the year (in EUR)	-9,939,410.76	-12,093,427.29
Weighted average number of ordinary shares for basic earnings per share	62,512,375	59,118,686
Weighted average number of ordinary shares for diluted earnings per share	62,754,424	59,558,627
Earnings per share (in EUR):		
Basic	**-0.16**	**-0.20**
Diluted	**-0.16**	**-0.20**

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 five active stock option plans in the course of which stock options can be/have been granted to Management Board members and employees of PAION AG and its subsidiaries at the time of the grant. The stock options are accounted for in accordance with the provisions of IFRS 2. All stock option plans include vesting periods, waiting periods and exercise hurdles. The respective exercise price is based on the average stock price during a certain period of time before the grant. Details of the individual plans can be found in the following table (the presentation of Stock Option Plan 2018, from which no stock options have been granted yet, is omitted):

	Stock Option Plan 2008 Approved 5 May 2008
Underlying Capital	Conditional Capital 2008 I
Term of the options	10 years
Vesting period	2–4 years
Waiting period	2–4 years
Number of outstanding options for which the waiting period has expired as of 31 December 2018	205,250
Exercise condition	Cumulative stock price increase of 5% per year since grant in relation to exercise price
Exercise price *	EUR 1.84 to EUR 2.69
Weighted average exercise price *	EUR 1.89
Exercise hurdle as of 31 Dec. 2018 *	EUR 2.66 to EUR 3.88
Weighted average remaining term as of 31 Dec. 2018	1.0 years
Further grants possible? (as of 31 Dec. 2018)	No
Number of totally granted options until 31 Dec. 2018	817,550
Number of outstanding options as of 31 Dec. 2018 **	205,250
granted to employees	91,000
granted to Management Board members	114,250
Number of totally lapsed options as of 31 Dec. 2018	133,158
thereof lapsed in the reporting period	32,400
Number of totally exercised options until 31 Dec. 2018	479,142
thereof exercised in the reporting period	138,097
Personnel expenses in the reporting period	EUR 0
Fair value per option at the time of the grant ***	EUR 0.57 to EUR 2.48
Elements of calculation	
Valuation model	Black/Scholes
Risk-free rate	2.5% to 4.47%
Volatility	83.31% to 88.44%
Staff turnover****	0% to 5% per year

*) in relation to outstanding options as of 31 Dec. 2018

**) in relation to employee/Management Board member status at the time of the grant

***) in relation to totally granted options

****) turnover last used for update of the quantity structure conducted until the end of the respective vesting period

Stock Option Plan 2010 Approved 19 May 2010	Stock Option Plan 2014 Approved 21 May 2014	Stock Option Plan 2016 Approved 25 May 2016
Conditional Capital 2010 I	Conditional Capital 2014	Conditional Capital 2016
10 years	10 years	10 years
2 years	2–4 years	2–4 years
4 years	4 years	4 years
696,626	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	Cumulative stock price increase of 5% per year since grant in relation to exercise price
EUR 2.01	EUR 1.99 to EUR 2.60	EUR 2.25 to EUR 2.60
EUR 2.01	EUR 2.21	EUR 2.34
EUR 2.50	EUR 2.24 to EUR 2.84	EUR 2.31 to EUR 2.72
5.1 years	7.0 years	9.2 years
No	No	Yes
720,000	740,000	706,500
696,626	533,885	701,185
392,876	235,572	456,685
303,750	298,313	244,500
23,374	206,115	5,315
0	0	4,361
0	0	0
0	0	0
EUR 0	KEUR 100	KEUR 300
EUR 1.67	EUR 1.02 to EUR 1.39	EUR 1.02 to EUR 1.70
Black/Scholes	Black/Scholes	Black/Scholes
0.7%	-0.26% to 0.08%	-0.25% to -0.14%
73.75%	72.34% to 83.76%	67.62% to 81.61%
10% per year	7% per year	7% 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 payments arising from these contracts are as follows:

	31 Dec. 2018 KEUR	31 Dec. 2017 KEUR
Due within one year	283	318
Due after more than one year	64	13
Total	**347**	**331**

Rental and lease expenses amounted to KEUR 295 in fiscal year 2018 (previous year: KEUR 290). The long-term rental and lease payments in the amount of KEUR 64 will be due in the years 2020 to 2023.

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 commited financial obligations in the amount of approx. EUR 6.8 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.

PAION is obliged to pay the Chinese licensee Yichang Humanwell an amount of EUR 1.5 million if a competing remimazolam product is commercialized by a competitor within a certain timeframe. Moreover, KEUR 250 from the milestone payment received in 2018 in connection with the filing of the market approval dossier in China have been recognized as a refund liability and would become repayable in the above-mentioned case but would bet set off against future royalties. Also, future royalties would be reduced in the above-mentioned case. PAION and Yichang Humanwell cooperatively work together on preventing this scenario. In case of a potential market approval of this product, PAION would assess legal measures in cooperation with Yichang Humanwell should existing patents be infringed.

Headcount and personnel expenses

In fiscal year 2018, PAION had an average of 39 employees (previous year: 33 employees). Of these 39 employees, 30 worked in development and nine in administration and sales. PAION UK Group had an average headcount of seven employees. As of 31 December 2018, the headcount was 40 (31 December 2017: 34).

The following personnel expenses were incurred in fiscal years 2018 and 2017:

	2018 KEUR	2017 KEUR
Wages and salaries	4,598	3,786
Social security contributions	482	380
Total	**5,080**	**4,166**

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 400 (previous year: KEUR 174). The figures also include contributions to the German and British social insurance schemes in an amount of KEUR 448 (previous year: KEUR 370) and expenses for defined contribution plans in the amount of KEUR 33.

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.

Dr. Mariola Söhngen, wife of the Chairman of PAION AG's Management Board, Dr. Wolfgang Söhngen, exercised 38,260 stock options with an exercise price of EUR 1.26 per stock option in the reporting period. These stock options had been granted during her term as Management Board member of PAION AG.

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 potentially debt as well as 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 and debt 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 licensee 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. For all financial assets it is intended to collect the original cash flows. These only include the original claim and potential interest.

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 the loan granted to the British subsidiary PAION UK Ltd. as well as from its trade payables to a currently only minor degree anymore. Liquid assets are mainly invested in euros, but also funds in Pound Sterling and to a low extent in U.S. dollar are held.

The loans granted by PAION AG to its British subsidiaries produced exchange rate gains of KEUR 412 in fiscal year 2018 which were recognized in equity, including cumulated exchange rate losses of KEUR -6,319 from (parts of) the loans swapped into shares in affiliated companies in the reporting period remaining in the currency component. 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 1,132 compared to the change in the currency component actually recognized in equity in 2018. 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 increased by KEUR 1,132 compared to the change in the currency component actually recognized in equity in 2018.

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 21 in fiscal year 2018.

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 2018 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. 2018	31 Dec. 2017	31 Dec. 2018	31 Dec. 2017
Financial assets:					
Cash and cash equivalents	(1)	17,227	24,839	17,227	24,839
Trade receivables	(1)	1,500	37	1,500	37
Other assets	(1)	369	7	369	7
Financial liabilities:					
Provisions	(2) (3)	630	391	630	391
Trade payables	(2) (3)	2,218	5,921	2,218	5,921
Other liabilities	(2) (3)	434	154	434	154

Measurement category according to IFRS 9:
(1) 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, trade receivables, 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 2018, there were no movements between the hierarchy levels.

Recoverability of financial assets was assessed based on historical and expected payment defaults. No default risks were identified and no impairment was recognized.

Members of the Management Board

The members of the company's Management Board are:

- Dr. Wolfgang Söhngen, CEO, Chairman (appointed until 22 November 2019)
- Abdelghani Omari, CFO (appointed until 31 August 2020)
- Dr. Jürgen Beck, CDO (since 1 January 2018) (appointed until 31 December 2019)

Management Board remuneration totalled KEUR 1,290 in fiscal year 2018. As of 31 December 2018, a total of 820,550 stock options (fair value at time of granting: EUR 1,124,034) had been issued to active Management Board members as of 31 December 2018. For more information on Management Board remuneration, please see the disclosures in the remuneration report, which is part of the group management report.

All Management Board members are also Managing Directors of PAION Deutschland GmbH. Mr. Abdelghani Omari and Dr. Jürgen Beck are also Managing Directors of PAION Holdings UK Ltd and its subsidiaries. All Management Board members work full-time for the company and its subsidiaries.

As of 31 December 2018, Dr. Wolfgang Söhngen owned 1.08% (690,063 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%.

As of 31 December 2018, Dr. Jürgen Beck owned 0.02% (10,000 voting rights) of the shares in PAION AG.

Members of the Supervisory Board

The members of the Supervisory Board are:

- Dr. Jörg Spiekerkötter, Berlin/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, Boston, MA/U.S., Chairman of the Research and Development Committee; Vice President Translational Medicine and Development at Wave Life Sciences Ltd., Cambridge, MA/U.S.
  Other supervisory board memberships or similar positions:
  - 4SC AG, Planegg-Martinsried (Munich)/Germany, Member of the Supervisory Board

- Dr. Hans Christoph Tanner, Zurich/Switzerland, Member of the Supervisory Board, Head of Transactions of Cosmo Pharmaceuticals N.V., Amsterdam/The Netherlands, Head of Finance & Investor Relations 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

- 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 of the Supervisory Board totalled KEUR 162 in fiscal year 2018. For more information on Supervisory Board remuneration, please see the disclosures in the remuneration report of the group management report.

As of 31 December 2018, none of the members of the Supervisory Board owned shares in PAION AG.

Financial statements auditor

The Annual General Meeting on 23 May 2018 appointed Ernst & Young GmbH Wirtschaftsprüfungsgesellschaft, Cologne office, Germany, as auditor of the annual and consolidated financial statements for fiscal year 2018. The auditor has received or will invoice the following fees for services rendered to PAION AG and its subsidiaries in fiscal year 2018:

	2018 KEUR	2017 KEUR
Audits of financial statements	96	97
	96	**97**

The fees for audits of financial statements include remuneration for reviewing the interim financial statements in the amount of KEUR 11 (previous year: KEUR 11).

Corporate governance

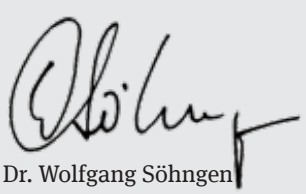
The Supervisory Board and Management Board of PAION AG declare that they are committed to responsible and transparent management and control of the company focused on adding value in the long term.

The company complies with all recommendations set forth in the most recent version of the German Corporate Governance Code dated 7 February 2017. In December 2018, 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

There were no significant events in the period between the reporting date, 31 December 2018, and the preparation of this report.

Aachen, Germany, 19 March 2019
PAION AG



Dr. Wolfgang Söhngen

Abdelghani Omari

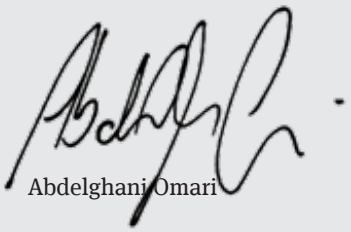
Dr. Jürgen Beck

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, 19 March 2019
PAION AG

Dr. Wolfgang Söhngen



Abdelghani Omari

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 2018, 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 2018 to 31 December 2018, 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 2018 to 31 December 2018. 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 2018, and of its financial performance for the fiscal year from 1 January 2018 to 31 December 2018, 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 the 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 2018 to 31 December 2018. 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. Recognition and measurement of the 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 performed by PAION UK Ltd. 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 tax-privileged 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 only partially or not at all recognised, which would mean that the receivable from the British tax authorities reported as of 31 December 2018 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. 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 for 2018 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 law. We also involved our tax specialists in the UK for this purpose. Additionally, we compared the figures in the tax return with the figures from the financial 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 pursuant to Sec. 315d HGB, of which we received a version intended for publication before issuing our auditor's report.

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 audit of the consolidated 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 scepticism 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 23 May 2018. We were engaged by the Supervisory Board on 23 May 2018. We have been the group auditor of PAION 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 Titus Zwirner."

Cologne, 19 March 2019

Ernst & Young GmbH
Wirtschaftsprüfungsgesellschaft

Zwirner	Conrad
Wirtschaftsprüfer	Wirtschaftsprüfer
[German Public Auditor]	[German Public Auditor]

PAION AG
Martinstrasse 10–12
52062 Aachen Germany
Phone +49 241 4453-0
Fax +49 241 4453-100
info@paion.com www.paion.com

PAION AG, Aachen

Financial Statements

as of 31 December 2018

Management Report

for Fiscal Year 2018

PAION

Management report for fiscal year 2018

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, PAION has licensees in the U.S., China, South Korea, Canada, Russia/CIS, Turkey, the MENA region and Japan. For the use of remimazolam for procedural sedation, clinical development has already been completed; a market approval dossier has been filed in China. For the indication general anesthesia, remimazolam is in the final stage of clinical development and has already been completed for Japan where a market approval dossier has been filed in the reporting period. The different indications for application of remimazolam will be described in detail in the following chapters.

Fiscal year 2018 was marked by the concentration of PAION on the continuation of the development of remimazolam and regulatory activities, in particular the preparation and start of a Phase III study in general anesthesia in the EU and preparations for the market approval dossiers in the U.S. and 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 licensees. The progress of these activities is being documented and discussed continuously. PAION has already signed several regional license agreements. The licensees operate independently in their respective license territory. However, the cooperation agreements require the licensees to exchange relevant information. Development in the U.S. has been completed by PAION. The U.S. licensee Cosmo Pharmaceuticals (Cosmo) plans to file for market approval in procedural sedation shortly and will be responsible for all further development activities in the U.S.

The central coordination of the information flow worldwide between the licensees 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

I. Macroeconomic and sector-specific environment

a. Macroeconomic development

German economy has continued its growth also in 2018. Drivers in particular were investments with an increase of 4.8% and consumption with an increase of 1.0% as compared to the prior year.

With an increase of the gross domestic product (GDP) of 1.5% (2017: 2.2%), growth has lost momentum as compared to 2017 however.[1]

A decrease in economic growth has also manifested in the Euro area: The GDP in the Euro zone only increased by 1.8% in 2018 after 2.4% growth in 2017, and a further decrease to 1.6% is expected for 2019. Growth of the world GDP however only decreased slightly from 3.8% in the prior year to 3.7% in 2018 to which an increase of growth of the U.S. GDP from 2.2% in the previous year to 2.9% in 2018 has contributed significantly, contrary to the development in the Euro area.[2] While the decrease in growth in the Euro area significantly resulted from declining global demand, in particular from China, U.S. economy has benefited from the impact of the U.S. tax reform.[3]

For 2019, a further slowdown of worldwide growth from 3.7% in the prior year to now 3.5% is expected. A decrease in growth of developed economies contributes to this trend in particular. There is major uncertainty in regard to consequences and potential expansions of international trade restrictions and tariffs most notably. Moreover, the short- and mid-term outlook is tarnished by a potential exit of the United Kingdom from the EU without a follow-up agreement (so-called "No-deal Brexit"), geopolitical tensions and an increasingly reserved financial market sentiment.[4]

This is also reflected on the stock markets: The DAX registered a decrease by 18.3% in 2018 in comparison to the prior year's end closing value; the EUROSTOXX 50 also closed 2018 with a minus of 14.3% as compared to the previous year. The Dow Jones decreased less significantly in 2018 and closed 2018 with a minus of 5.6% in comparison to the prior year's end closing value.

b. Development of the pharmaceutical and biotechnology industry

The pharmaceutical and biotechnology industry continues to be marked by steadily increasing costs for pharmaceutical development due to advancing portfolio complexity, the trend to personalized therapies and increasingly extensive and challenging regulatory requirements which in turn are faced by increasingly lower income particularly due to higher competition, patent expiry of formerly high-selling products and price pressure from governmental regulation.[5] Average development costs of a new drug increased by approx. 82% from 2010 to 2018 on average for big pharma companies while peak sales potential approximately halved.[6]

Although the worldwide transaction volume in the pharmaceutical industry increased again with USD 198 billion in 2018, it was about USD 90 billion lower than the average of the years 2014 to 2016 in spite of the availability of respective funds. In addition to high valuations which increased by 78% from 2014 to 2018 on average for biotechnology companies, the transaction

[1] Federal Statistical Office: Deutsche Wirtschaft ist im Jahr 2018 um 1,5 % gewachsen, press release dated 15 January 2019.
[2] International Monetary Fund: World Economic Outlook Update, January 2019.
[3] Commerzbank Research: Economic and Market Monitor – Chart Book February 2019.
[4] International Monetary Fund: World Economic Outlook Update, January 2019.
[5] Deloitte Centre for Health Solutions: Unlocking R&D productivity: Measuring the return from pharmaceutical innovation 2018, 2018; Ernst & Young: 2019 EY M&A Firepower report: When data and technology expedite growth, how can dealmaking power the value equation?, 2018.
[6] Deloitte Centre for Health Solutions: Unlocking R&D productivity: Measuring the return from pharmaceutical innovation 2018, 2018.

volume was particularly curbed by uncertainty in regard to (potential) internal trade restrictions and geopolitical tensions.[7]

The financing environment for the pharmaceutical and biotechnology industry was very good in 2018. With a volume of USD 8.3 billion, more funds were raised through IPOs in 2018 than ever before; the previous high from 2014 was exceeded by nearly 32%.[8] Also in Germany, with funds raised in the amount of EUR 1.3 billion, a new all-time high of financing volume was reached in the industry.[9] In terms of valuation, this is at least also reflected in the DAXsubsector Biotechnology Index which increased by 14.3% in 2018 in comparison to the prior year's end closing value, while the NASDAQ Biotechnology Index closed the year 2018 with a minus of 9.3%.

The significant competitive drivers in the pharmaceutical and biotechnology industry are likely to also persist in 2019 and to maintain consolidation pressure. In addition to intensifying competition and continuously increasing challenges for the industry, for instance in regard to digitalization, individualization of therapies and regulatory requirements, companies with a clear therapeutic focus are more successful than their less focused competitors. Under consideration of the strong fragmentation in the industry, the availability of significant amounts of funds due to the tax reform that came into force in the U.S. and the central banks' continuing loose monetary policy, a high acquisition and transaction volume worldwide can be expected in the pharmaceutical industry in 2019.[10] However, it remains to be seen to what extent the design and potential expansion of international trade restrictions and protective tendencies have a damping effect on acquisition and transaction volumes.

2. Presentation of the course of business and development activities

The development portfolio of PAION Group essentially comprises 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 is 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,

[7] Ernst & Young: 2019 EY M&A Firepower report: When data and technology expedite growth, how can deal-making power the value equation?, 2018.
[8] Morrison, C. (2019): Boom: 2018's biotech IPOs, in: Nature Reviews Drug Discovery, Vol. 18, January 2019.
[9] transkript: Finanzierungen auf 1,3 Mrd. Euro verdoppelt, announcement from 11 January 2019.
[10] Ernst & Young: 2019 EY M&A Firepower report: When data and technology expedite growth, how can deal-making power the value equation?, 2018; Deloitte Centre for Health Solutions: Unlocking R&D productivity: Measuring the return from pharmaceutical innovation 2018, 2018; PwC Health Research Institute: Top health industry issues of 2019: The New Health Economy comes of age, 2018; Commerzbank Research: Economic and Market Monitor – Chart Book February 2019.

remimazolam demonstrated efficacy and safety with around 2,400 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.

PAION has completed clinical development of remimazolam for procedural sedation in the U.S. The U.S. licensee Cosmo plans to file for market approval in procedural sedation shortly and is responsible for any further development activities in the U.S. In Japan, remimazolam licensee Mundipharma filed for market approval in general anesthesia in December 2018 and in China, licensee Yichang Humanwell filed for market approval in procedural sedation in November 2018. In Europe, PAION initiated a Phase III study in general anesthesia in July 2018, for which patient recruitment is expected to be completed by the end of 2019.

In addition to procedural sedation and general anesthesia, based on positive Phase II study results, ICU sedation (beyond 24 hours) is another possible attractive indication for further development in the EU by PAION as well as by its licensees.

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

Procedural Sedation Market

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 colonoscopy 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 costs and higher risks, since there is no reversal agent available for propofol in order to be able to quickly stop sedation if required. 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 prices will be paid for 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.[11] 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 expects that remimazolam, subject to FDA approval (FDA = Food and Drug Administration) 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.

PAION is currently evaluating the possibility of submitting a Marketing Authorization Application (MAA) for remimazolam in procedural sedation in **Europe** with the European Medicines Agency (EMA) based on the completed U.S. development program.

In the EU, based on its own projections for procedural sedation, PAION currently estimates an annual peak sales potential of approx. EUR 75 million. In contrast to the U.S. market which has a large freestanding ambulatory surgery healthcare infrastructure, procedural sedation in Europe

[11] Liu, H. et al. (2012): Utilization of Anesthesia Services During Outpatient Endoscopies and Colonoscopies and Associated Spending in 2003-2009, The Journal of the American Medical Association, 2012 307(11):1178-1184; Al-Awabdy, B. and Wilcox, C.M. (2013): Use of anesthesia on the rise in gastrointestinal endoscopy, World Journal of Gastrointestinal Endoscopy, January 2013 5(1): 1-5.

is mainly a hospital-based activity where anesthesiologists have the overall responsibility for the sedation of patients. This entails a high potential for synergies with the planned commercialization of remimazolam for use in general anesthesia.

General Anesthesia Market

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 aging 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. In the EU, based on its own projections for general anesthesia, PAION currently estimates an annual peak sales potential of approx. EUR 150 million to EUR 200 million.

In adults, myocardial injury during noncardiac surgery (MINS) is the most common cardiovascular complication associated with such surgery. Investigations conclude that MINS occurs in about 8% of the approximately 200 million patients yearly worldwide and leads to an increased morbidity. Approximately 10% of patients suffering such injury die within 30 days after surgery. The suspected cause of this is, inter alia, a (too) low blood pressure and a concomitant temporary undersupply of the heart muscle with oxygen during the procedure.[12] Based on the safety data available to date, remimazolam could contribute significantly to reducing this mortality rate by reducing intraoperative blood pressure drops.

[12] Khan, J. et al. (2014): Myocardial injury after noncardiac surgery, Current Opinion in Cardiology, 2014 Jul, 29(4):307-11; Abbott, T. E. F. et al. (2019): Depth of Anesthesia and Postoperative Delirium, in JAMA, 2019, 321(5):459-460.

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 bears an attractive market potential. 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.

Clinical Development

Clinical Development	
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 combined 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 Anesthesia (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. 500)**	
ICU Sedation (Japan)	
Phase II in ICU patients (49)*	
Studies in other territories	
Phase III in general anesthesia - Russia (150)	Phase I single ascending dose in China (62)
Phase III in general anesthesia - South Korea (198)	Phase I continuous infusion in China (12)
Phase II in procedural sedation - China (150)	
Phase III in procedural sedation - China (480)	
Phase IIa dose finding study - China (24)	

Patient/volunteer numbers in brackets
*) Discontinued studies, no safety concerns
**) Ongoing study

Procedural sedation (U.S. + China)

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. In China, one Phase II and one Phase III trial have also been successfully 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.

The first U.S. Phase III study was successfully completed in 2016, and the primary efficacy endpoint was achieved. 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.

The study was successfully completed in 2017, and the primary efficacy endpoint was achieved. 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 (American Society of Anesthesiologists classification) patients undergoing colonoscopy (American Society of Anesthesiologists classification) was performed which was successfully completed in 2017. 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 to start of procedure	4.0–5.0 min	17–19.5 min	16.0–19.0 min
Time from end of procedure to fully alert	3.0–7.2 min	5.0–21.3 min	7.0–15.7 min
Time to back to normal	331–404 min	572–935 min	478.5–553 min

*) 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.

In July 2018, PAION's licensee Cosmo attended a pre-NDA meeting (NDA = New Drug Application) with the FDA for remimazolam for the indication procedural sedation together with PAION delegates.

Pre-NDA meetings with the FDA represent the final step during drug development before submission of an NDA. These meetings allow companies to discuss with the FDA the appropriateness of the content of their submission package as well as the approval pathway and the preferred label.

During the pre-NDA meeting with the FDA, there was no indication that would prevent the submission of the market approval dossier as planned.

General anesthesia (Japan, EU, Russia, China + South Korea)

A total of six Phase I, three Phase II and four Phase III 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.

In order to allow using the Japanese data for filing in the EU, the same induction and maintenance doses were used in the Phase II trial performed in Germany in 2014 as part of the European development program, 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.

Subsequently, 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 has started an EU Phase III clinical trial with remimazolam for the induction and maintenance of general anesthesia in July 2018.

The randomized, single-blind, propofol-controlled, confirmatory Phase III trial is expected to enroll approx. 500 ASA III/IV patients (American Society of Anesthesiologists classification III to IV) undergoing non-emergency surgery at more than 20 European trial centers. Patient recruitment is expected to be completed by the end of 2019.

The primary objective of the trial is to demonstrate the non-inferiority of remimazolam compared to propofol for the induction and maintenance of general anesthesia during elective surgery. The key secondary objective is to show improved hemodynamic stability (avoidance of intraoperative drop of blood pressure and vasopressor usage) compared to propofol.

The trial was designed in consultation with EU key opinion leaders in general anesthesia. Based on Scientific Advice obtained from the EMA in January 2018, PAION expects that a positive

Phase III trial in combination with previously completed clinical studies in Europe and Japan should be sufficient for filing for market approval for the indication of general anesthesia in the EU.

In November 2018, PAION's licensee R-Pharm announced the successful completion of a Phase III trial in general anesthesia and PAION's licensee Hana Pharm has successfully completed patient recruitment of a Phase III trial in general anesthesia in October 2018.

ICU sedation

PAION's former licensee 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.

Pediatric development

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.

The aims of sedation and general anesthesia are the same in both adults and children: to enable diagnostic, surgical or dental procedures to be carried out safely and successfully while minimizing distress and discomfort to the patient. Advances in the diagnostics and treatment of pediatric diseases has led to an increase in the number of painful or distressing procedures for which many children need effective sedation or general anesthesia. While in adults many procedures can be undertaken with local anesthesia and verbal reassurance, this is often not possible with children and teenagers. Particularly for children, procedures are often too frightening, too painful, or need to be performed in children who are uncooperative, ill or in pain. In 2018, PAION submitted a pediatric investigation plan to the EMA. Subject to the EMA's approval for this development plan, the various trials are planned to be carried out sequentially over several years, starting with procedural sedation, followed by general anesthesia and finally ICU sedation. The clinical trials will initially be conducted with teenagers and further studies will be performed with increasingly younger children. At the same time, while at the beginning less serious diseases are included in the trials, increasingly severe diseases will be included in the trials in the later course of the development program.

Partnerships, regulatory and commercial activities

Development and commercialization collaborations with partners with local expertise or with a specific therapeutic focus with respect to remimazolam are an effective way of funding and advancing remimazolam's 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 licensees 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. In order to exploit remimazolam's full potential, it is PAION's defined target to commercialize remimazolam on its own in selected European markets immediately after a potential market approval. PAION is well positioned to find further licensees. 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. (Cosmo Pharmaceuticals), Japan (Mundipharma), China (Yichang Humanwell), Canada (Pharmascience), Russia/CIS (R-Pharm), Turkey and the MENA region (TR-Pharm) and South Korea (Hana Pharm). For all other markets outside the EU, remimazolam is available for licensing.

PAION's **Chinese** remimazolam licensee Yichang Humanwell submitted a market approval dossier to the Chinese National Medical Products Administration (NMPA) for remimazolam in the indication procedural sedation in November 2018.

PAION's **Japanese** remimazolam licensee Mundipharma submitted a market approval dossier to the Japanese Pharmaceuticals and Medical Devices Agency PMDA for remimazolam in the indication general anesthesia in December 2018.

Together with Cosmo, PAION has prepared the market approval dossier in procedural sedation in the **U.S.** to a degree that allows for filing for market approval shortly as planned.

In November 2018, PAION's **Russian** remimazolam licensee R-Pharm announced the successful completion of a Phase III trial in general anesthesia. R-Pharm currently plans to file for market approval in Russia by the end of 2019.

For **Canada**, PAION currently expects its remimazolam licensee Pharmascience to use the U.S. market approval dossier as the basis for their own filing for market approval.

PAION's remimazolam licensee TR-Pharm (**Turkey, the Middle East** and **North Africa**) plans to file for market approval in Turkey based on the U.S. or Japanese dossier.

PAION's remimazolam licensee Hana Pharm has successfully completed patient recruitment of a Phase III trial in general anesthesia in October 2018. Before filing for market approval, the production process for remimazolam needs to be established in **South Korea**. Accordingly, Hana Pharm plans to file for market approval in 2020.

For **Europe** PAION is currently evaluating the possibility of submitting a Marketing Authorization Application for remimazolam in procedural sedation with the EMA based on the completed U.S. development program. In the course of a so-called pre-submission meeting with the EMA held in February 2019, the U.S. Phase III clinical development program including key safety data and efficacy results was discussed with the EMA in regard to a potential regulatory filing in the EU.

Based on this pre-submission meeting, PAION assumes that the existing data package is sufficient to be able to submit the MAA for procedural sedation in the EU.

Pre-submission meetings with the EMA are intended to give companies the opportunity to ask the EMA process questions about a planned MAA submission for a drug, not to discuss the probability of approval. Therefore, the EMA has not provided PAION with any feedback on whether the results of the trials and the contents of the planned MAA will be sufficient to obtain regulatory approval of remimazolam.

Upfront and milestone payments (Group)			
	Total received	Maximum outstanding amount	Royalty rate
Ono, Japan (2007) (terminated in 2015)	USD 8 m	None	None
Yichang Humanwell, China (2012)	EUR 3.5 m[6]	EUR 0.5 m	10%[6]
Hana Pharm, S. Korea (2013)	EUR 1.5 m[4]	EUR 1.5 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
Pharmascience, Canada (2014)	EUR 0.4 m[1]	~ EUR 3.6 m	Tiered (starting at 15%)
Cosmo, U.S. (2016)	EUR 20 m[2]	EUR 42.5 m	20–25%[3]
Mundipharma, Japan (2017)	EUR 2 m[4]	EUR 24 m	Up to over 20%[5]
Total	EUR 36.8 m	~ EUR 83.6 m	

[1]) This amount relates to the premium received in the course of the private placement in the amount of EUR 4 million in July 2014.
[2]) 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.
[3]) Subject to adjustments under specific circumstances, but not below 15% of net sales.
[4]) Partially received after the balance sheet date
[5]) Tiered royalties starting in the low double-digits to over 20%
[6]) In case of occurrence of certain market conditions in China, PAION is obliged to pay back 50% of the milestone payments already received (partially to bet set off against royalties). In this case, royalties would drop to 5%.

Vision: Specialty Pharma Company with own sales in the EU

In order to become a leader in the anesthesia field, forward integration, particularly in the EU, is essential for PAION in the near future. For PAION, forward integration does not only imply the buildup of an own distribution for the future commercialization of remimazolam in the EU, but also the use of these structures as a platform for future products in order to develop the greatest possible synergy potential. Forward integration provides an opportunity to find partners as there are only relatively few players in this area. At the same time, this reduces the potential dependence on any chosen partner. The goal is to grow significantly in the medium to long term. Until then, the product portfolio in the field of anesthesia is planned to be enriched with innovative medicines.

3. Net assets, financial position and results of operations of PAION AG

a. Results of operations

The net result increased by KEUR 800 compared to the prior year to a net income of KEUR 654 in fiscal year 2018. This increase is particularly attributable to lower other operating expenses which decreased significantly compared to the previous year due to lower foreign exchange losses and lower expenses in connection with capital increases.

The net result is within the previous year's forecast range for 2018.

	2018 KEUR	2017 KEUR	Change in result KEUR
Revenues	1,026	1,043	-17
Other operating income	264	592	-328
Personnel expenses	-1,785	-1,725	-60
Depreciation and amortization	0	-5	5
Other operating expenses	-1,861	-3,144	1,283
Operating result	**-2,356**	**-3,239**	**883**
Financial result	3,010	3,093	-83
Net result	**654**	**-146**	**800**

Revenues decreased by KEUR 17 in the reporting period compared to the previous year and result entirely from the provision of management and other services to the subsidiaries, of which PAION UK Ltd accounted for KEUR 895 (previous year: KEUR 857) and PAION Deutschland GmbH for KEUR 131 (previous year: KEUR 186).

Other operating income decreased by KEUR 328 in the reporting period compared to the previous year and includes recharges to the subsidiaries amounting to KEUR 145 (previous year: KEUR 155), of which PAION Deutschland GmbH accounted for KEUR 75 (previous year: KEUR 73) and PAION UK Ltd for KEUR 70 (previous year: KEUR 82). Exchange rate gains were recognized in an amount of KEUR 86 (previous year: KEUR 395).

Personnel expenses increased by KEUR 60 to KEUR 1,785.

Year on year, **other operating expenses** decreased by KEUR 1,283 to KEUR 1,861 and mainly include legal and consulting fees (KEUR 763; previous year: KEUR 1,403), insurance,

contributions and fees (KEUR 233; previous year: KEUR 241), expenses in connection with Supervisory Board remuneration (KEUR 162; previous year: KEUR 141), travel expenses (KEUR 161; previous year: KEUR 146), services rendered by PAION Deutschland GmbH (KEUR 150; previous year: KEUR 173), expenses for IT hosting (KEUR 104; previous year: KEUR 106) as well as audit costs and costs for the annual report (KEUR 64; previous year: KEUR 64). In the reporting period, foreign exchange losses in the amount of KEUR 68 (previous year: KEUR 564) have been recognized. The decrease of other operating expenses in comparison to the previous year mainly results from lower foreign exchange losses and lower expenses in connection with capital increases.

Compared to the previous year, the **financial result** decreased by KEUR 83 to KEUR 3,010. The decrease mainly stems from lower interest income from affiliated companies which was generated from the loans granted to the PAION UK Group companies (KEUR 3,004; previous year: KEUR 3,073).

b. Net assets and financial position

The balance sheet total as of 31 December 2018 amounts to KEUR 132,445 and has increased by KEUR 6,177 compared to the previous year. The equity ratio is 99.4% at the current balance sheet date (previous year: 99.5%). As of 31 December 2018, cash and cash equivalents amounted to KEUR 15,048 and decreased by KEUR 8,569 compared to the previous year.

	31 Dec. 2018 KEUR	31 Dec. 2017 KEUR	Change KEUR
Fixed assets	94,761	12,768	81,993
Current assets and prepaid expenses	37,684	113,500	-75,816
Assets	**132,445**	**126,268**	**6,177**
Equity	131,607	125,579	6,028
Current liabilities	838	689	149
Shareholders' equity and liabilities	**132,445**	**126,268**	**6,177**

Fixed assets increased by KEUR 81,993 in the reporting period due to a capital increase of PAION Holdings UK Ltd against contribution in kind in the course of which the loan granted to PAION Holdings UK Ltd by PAION AG was completely (KEUR 4,737) and the loan granted to PAION UK Ltd by PAION AG was partially (KEUR 77,256) contributed to PAION Holdings UK Ltd. As of the balance sheet date, fixed assets mainly relate to the shares in PAION Holdings UK Ltd (KEUR 94,311) and the shares in PAION Deutschland GmbH (KEUR 450).

Current assets (including prepaid expenses) have decreased by KEUR 75,816 to KEUR 37,684 in fiscal year 2018. Loans granted to the subsidiaries have decreased by (net) KEUR 67,027 to KEUR 22,434 as of 31 December 2018. Thereof, a decrease of KEUR 81,993 relates to the contribution of (parts of) the loans to PAION Holdings UK Ltd in the course of a capital increase against contribution in kind, and an increase of KEUR 14,966 relates to the (net) grant of loans to PAION Holdings UK Ltd and PAION UK Ltd. The loan granted as of the balance sheet date amounting to KEUR 22,434 entirely relates to PAION UK Ltd. Cash and cash equivalents have decreased by KEUR 8,569 from KEUR 23,617 to KEUR 15,048 as of 31 December 2018.

The increase of **current liabilities** by KEUR 149 to KEUR 838 mainly results from higher accruals in the reporting period.

The change in cash and cash equivalents over the fiscal year is attributable to the following areas:

	2018 KEUR	2017 KEUR
Cash flow from operating activities	1,183	678
Cash flow from investing activities	-14,966	-17,383
Cash flow from financing activities	5,214	12,494
Change in cash and cash equivalents	**-8,569**	**-4,211**

The **cash flow from operating activities** mainly resulted from the net result of the year, corrected by cost of funds (KEUR 160) incurred in connection with the capital increase conducted in June 2018, as well as working capital changes.

The **cash flow from investing activities** entirely resulted from the (net) grant of loans to subsidiaries. In the previous year, the cash flow from investing activities also mainly resulted from the (net) grant of loans to subsidiaries.

The **cash flow from financing activities** resulted from the gross proceeds from the capital increase under exclusion of subscription rights conducted in June 2018 (KEUR 5,200), the cost of funds for this transaction (KEUR 160) as well as the exercise of stock options (KEUR 174). In the previous year, the cash flow from financing activities mainly resulted from the gross proceeds from the capital increase with subscription rights (KEUR 5,000) and the capital increase under exclusion of subscription rights (KEUR 8,034) as well as the cost of funds for these transactions (KEUR 687).

4. Net assets, financial position and results of operations of PAION Group

The Group generated a consolidated net loss of KEUR 9,939 in fiscal year 2018 (previous year: net loss of KEUR 12,093). The key items in the consolidated balance sheet as of 31 December 2018 were cash and cash equivalents (KEUR 17,227; previous year: KEUR 24,839) and equity (KEUR 20,822; previous year: KEUR 25,229).

Headcount

As of 31 December 2018, the total headcount of PAION Group was 40 employees, of whom eight worked for PAION UK Group. By comparison, the headcount as of 31 December 2017 amounted to 34 employees. As of 31 December 2018, the headcount at PAION AG totalled seven employees (previous year: seven employees).

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 1.84 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 2018, the exercise hurdle was EUR 2.66.

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 2018, the exercise hurdle was EUR 2.50.

From the Stock Option Plan 2014 approved by the Annual General Meeting on 21 May 2014, a total of 333,000 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 1.99, EUR 2.30 or EUR 2.60 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 2018, the exercise hurdle was EUR 2.24, EUR 2.75 or EUR 2.72, depending on the grant date.

From the Stock Option Plan 2016 approved by the Annual General Meeting on 25 May 2016, a total of 244,500 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 2.25 or EUR 2.60 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 2018, the exercise hurdle was EUR 2.31 or EUR 2.72, 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 2018 can be gathered from the following tables (according to German Corporate Governance Code):

Benefits granted in EUR	Dr. Wolfgang Söhngen CEO				
	2017	**2018**	**2018 (Min)**	**2018 (Max)**	
Fixed compensation	275,000	275,000	275,000	275,000	
Other remuneration	45,592	45,301	45,301	45,301	
Total	**320,592**	**320,301**	**320,301**	**320,301**	
One-year variable compensation	175,000	175,000	0	175,000	
Multi-year variable compensation					
Stock Option Plan 2014 - Grant 2018 (Waiting period 2018 to 2022) *	0	0	-	-	
Stock Option Plan 2016 - Grant 2018 (Waiting period 2018 to 2022) *	0	102,000	-	-	
Total	**495,592**	**597,301**	**320,301**	**495,301**	
Service cost	0	0	0	0	
Total remuneration	**495,592**	**597,301**	**320,301**	**495,301**	

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

Allocation in EUR	Dr. Wolfgang Söhngen CEO		
	2017	**2018**	
Fixed compensation	275,000	275,000	
Other remuneration	45,592	45,301	
Total	**320,592**	**320,301**	
One-year variable compensation	132,405	114,100	
Multi-year variable compensation			
Stock Option Plan 2008 - Grant 2008 (Waiting period 2008 to 2010)	0	50,028 *	
Total	**452,997**	**484,429**	
Service cost	0	0	
Total remuneration	**452,997**	**484,429**	

*) Dr. Söhngen exercised 41,517 stock options in the reporting period

	Abdelghani Omari CFO				Dr. Jürgen Beck CDO since 1 January 2018			
	2017	**2018**	**2018 (Min)**	**2018 (Max)**	**2017**	**2018**	**2018 (Min)**	**2018 (Max)**
	175,833	180,000	180,000	180,000	0	200,000	200,000	200,000
	15,127	15,127	15,127	15,127	0	15,127	15,127	15,127
	190,961	**195,127**	**195,127**	**195,127**	**0**	**215,127**	**215,127**	**215,127**
	90,000	90,000	0	90,000	0	70,000	0	70,000
	0	0	-	-	0	76,035	-	-
	0	102,000	-	-	0	60,965	-	-
	280,961	**387,127**	**195,127**	**285,127**	**0**	**422,127**	**215,127**	**285,127**
	0	0	0	0	0	0	0	0
	280,961	**387,127**	**195,127**	**285,127**	**0**	**422,127**	**215,127**	**285,127**

	Abdelghani Omari CFO		Dr. Jürgen Beck CDO since 1 January 2018	
	2017	**2018**	**2017**	**2018**
	175,833	180,000	0	200,000
	15,127	15,127	0	15,127
	190,961	**195,127**	**0**	**215,127**
	68,094	58,680	0	45,640
	0	0	0	0
	259,055	**253,807**	**0**	**260,767**
	0	0	0	0
	259,055	**253,807**	**0**	**260,767**

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

Management Board remuneration in fiscal year 2018 amounted to KEUR 1,290 in total (previous year: KEUR 928) and is composed as follows:

in EUR	2018	2017
Fixed remuneration	655,000	666,483
Other remuneration	75,556	60,741
Total non-performance based remuneration	**730,555**	**727,224**
Short-term variable remuneration	218,420	200,499
Total short-term remuneration	**948,975**	**927,723**
Long-term variable remuneration	341,000	0
Total long-term remuneration	**341,000**	**0**
Total remuneration	**1,289,975**	**927,723**

The increase of total remuneration compared to the previous year mainly results from the grant of stock options in the reporting period while no stock options were granted in the previous year.

The Management Board members held the following stock options as of 31 December 2018:

Status of non-exercised stock options as of 31 December 2018:		Dr. Wolfgang Söhngen	Abdelghani Omari	Dr. Jürgen Beck
Stock options 2008	No.	56,550	0	0
Stock options 2008 - fair value *	EUR	140,244	-	-
Stock options 2010	No.	162,000	80,000	0
Stock options 2010 - fair value *	EUR	270,540	133,600	-
Stock options 2014	No.	111,000	111,000	55,500
Stock options 2014 - fair value *	EUR	119,325	119,325	76,035
Stock options 2016	No.	100,000	100,000	44,500
Stock options 2016 – fair value *	EUR	102,000	102,000	60,965

*) 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, Mr. Omari and Dr. Beck are each entitled to contractual termination benefits,

which correspond to an amount of two annual fixed basic remunerations. For Dr. Beck, a claim to termination benefits in connection with a change of control can only be exerted if the change of control also entails a significant change in business strategy, in responsibilities or in regard to the company domicile.

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, 2014 and 2016, 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 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. Supervisory Board remuneration for fiscal year 2018 can be gathered from the following table:

	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	4,000	24,000
Dr. Dr. Irina Antonijevic	20,000	5,000	25,000
Dr. Hans Christoph Tanner	20,000	5,000	25,000

Supervisory Board remuneration in fiscal year 2018 amounted to KEUR 162. In the previous year the remuneration amounted to KEUR 141. The increase stems from the extension of the Supervisory Board by two members during the prior-year period.

Disclosures pursuant to section 289a (1) HGB and explanatory report

Composition of subscribed capital
As of 31 December 2018, PAION AG had a subscribed capital of EUR 63,858,143.00, divided into 63,858,143 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 shareholder 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 2018 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 22 May 2023, with the consent of the Supervisory Board, on one or more occasions, by up to EUR 30,560,023.00 in total by issuing up to 30,560,023 new no-par value bearer shares in return for cash contributions or contributions in kind (Authorized Capital 2018). 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 23 May 2018 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 21 June 2018, the Authorized Capital 2018 was used in the amount of EUR 2,600,000.00 and amounts to EUR 27,960,023.00 as of 31 December 2018.

Furthermore, subject to the consent of the Supervisory Board, the Management Board is authorized to issue on or before 22 May 2023, 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 2018 I). Conditional Capital 2018 I has not yet been used. Furthermore, the company is authorized to issue 281,093 shares (Conditional Capital 2008 I), 720,000 shares (Conditional Capital 2010 I), 740,000 shares (Conditional Capital 2014), 840,000 shares (Conditional Capital 2016) and 900,000 shares (Conditional Capital 2018 II) in connection with the Stock Option Plans 2008, 2010, 2014, 2016 and 2018.

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, 2016 and 2018 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 the reporting period, no audit was carried out by the internal auditors. 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 quarterly statements and half-year 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 quarterly statements as well as half-year and annual financial statements are published and are discussed with the Audit Committee of the Supervisory Board or 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 high risk	Very high risk
Very probable	60%-90%	Very low risk	Low risk	Increased risk	High risk	Very 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.[13]

In order to ensure timely filings for market approval of remimazolam, 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.

PAION is currently conducting an EU Phase III study in general anesthesia. 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 have been 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 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

[13] Tufts Center for the Study of Drug Development (2014): Briefing – Cost of Developing a New Drug.

may not be confirmed to the same degree in subsequent studies and primary and secondary study endpoints defined in advance cannot be achieved. 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 and the achievement of primary and secondary endpoints, a throroughly chosen study design defined in advance under consultation with external experts and/or in the course of the study potential dosage modifications and amendments to clinical trial protocols if there are indications for their necessity 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 high risk. In case of occurrence, the potential damage level could pose a threat to the continued existence of the group. The risk classification increased by two categories compared to the previous year in light of (the relevance of) the EU Phase III study in general anesthesia which is currently being conducted.

In the course of the development of remimazolam for adults, in the U.S. as well as in the EU the subsequent development for pediatric use is a requirement. Should the start or conduct of this development not be possible within the timetable proposed to EMA due to delays, there is a risk that acceptance of filing of a market approval dossier in the EU is denied by EMA at first. PAION actively works on the completion and implementation of the pediatric development plan in the EU and is in regular contact with EMA in this regard in order to minimize this risk. This is an increased 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 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. Also after filing of a market approval dossier, there is a risk that the competent authority rejects a dossier e.g. due to formal reasons and demands rework, appoints external expert committees for the evaluation of single issues and/or initially rejects dossiers demanding the conduct of further studies. This may lead to significant delays in the approval process, higher than initially planned costs (e.g. in case of the necessity to conduct additional studies) and discontinuation of further development of the product candidate (in the respective market) in the worst case. 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 and its licensees in all important markets consult the regulatory authorities informally as well as within the frame of official consultations, as e.g. in pre-NDA meetings. Moreover, PAION consults

regulatory experts. This is a high risk. In case of occurrence, the potential damage level could pose a threat to the continued existence of the group.

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 and first filings of market approval dossiers 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 can only be influenced to a minor degree. It is planned to conduct additional smaller studies which clearly emphasize the value added by remimazolam in the respective indication in the affected market in order to allow for commercialization in the respective target groups as

planned. 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 licensees will not be able to sufficiently prepare the market for launch by means of pre-marketing and market access activities as for example communication and/or exchange 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 and establishing a network of key opinion leaders. Moreover, there is regular information exchange with the U.S. licensee Cosmo and the licensees in the other regions. 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 an own commercialization in the EU) and licensees' distribution set-ups, if not existent yet, 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 is preparing implementation under consultation of external experts. Moreover, there is a regular information exchange with the U.S. licensee Cosmo and the licensees in the other regions. This is an increased risk. In case of occurrence, the potential damage level could pose a threat to the continued existence of the group.

For commercial supply of remimazolam, certain regulatory permissions and licenses need to be acquired. There is a risk that potentially required changes of processes or in the documentation at PAION cannot be implemented fast enough or that extensive inspections are undertaken by the authorities prior to the grant of such permissions leading to a delay in the supply of the commercially usable medicine for the licensees as well as for PAION itself. In order to avoid this risk, requirements and potentially necessary changes at PAION are being analyzed and implemented well in advance. This is an increased risk.

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, low to medium quantities of remimazolam have been produced in course of the clinical trials and the preparation of commercialization. Up until the start of commercialization, the so-called scale-up process still needs to be entirely completed. 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. Moreover, PAION has considered feedback from the respective regulatory authorities from formal and informal consultations in the product development program for remimazolam accordingly. 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 entirely completed until then. This could lead to a delay of studies and incur additional costs. PAION is therefore working on the timely completion of 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, not all 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.

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 licensees cannot be fulfilled if production development has not been completed yet, commercial supply agreements and purchasing infrastructures are not in place yet or if production orders cannot be submitted to the contractual manufacturers early enough. Also, PAION's own commercialization in the EU could be delayed by occurrence of these risks. In cooperation with its contractual manufacturers, PAION is working on the completion of relevant work for the

production development and, under involvement of the licensees, on the finalization of commercial supply agreements and planning of production orders. Moreover, PAION has analyzed purchasing infrastructures and is preparing implementation. This is a high risk. In case of occurrence, the potential damage level could pose a threat to the continued existence of the group.

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 licensees 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 a moderate risk. The risk classification decreased by one category compared to the previous year.

For the Chinese market, a competing remimazolam product is being developed by a competitor of PAION's Chinese licensee Yichang Humanwell. Should this product be granted market approval within a certain timeframe and should commercialization be possible without infringement of Yichang Humanwell's and PAION's existing patents, Yichang Humanwell's revenues from sales could be reduced significantly. Moreover, PAION would be obliged to pay an amount of EUR 1.75 million (partially to bet set off against royalties) to Yichang Humanwell, and the royalty rate would be halved from 10% to 5%. PAION expects the existing patent protection to avoid a successful commercialization of such competing product and would assess legal measures in cooperation with Yichang Humanwell in case of a potential market approval of this product should existing patents be infringed. This is a high risk.

ee) Risks in relation to licensees

In light of the progress of the development activities for remimazolam, increasingly bigger clinical studies are being conducted by licensees and important regulatory coordinations, meetings with the respective regulatory authorities and filings of market approval dossiers are increasingly in the focus for PAION's licensees. There is a risk that results from clinical studies, discussions with the authorities or evaluations of market approval dossiers by the authorities render the further development of remimazolam unattractive for existing licensees 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 licensees and engages in the evaluation of development plans and market approval dossiers 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 in regard to

studies as well as market approval dossiers. 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 licensees 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 further 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 Phase III study in general anesthesia which is currently being conducted 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 licensees are not met.

PAION's future ability to secure additional funding will depend on the success of its development, licensee 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 as well as (potential) pharma partners and licensees. 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. A strong rise of these currencies 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 and pound sterling. Currency risks also arise from potential

future royalties which will be payable in different currencies by licensees depending on the respective licensed market, particularly in U.S. dollars from the potential commercialization in the U.S., as well as 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, the consequences of a potential Brexit could also lead to tax payments on potential earnings expected in the future, e.g. due to controlled foreign corporation rules. 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 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. Due to a legislation change already enacted, tax credits will be significantly lower for PAION in future periods.

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 based on the current state of negotiations between the United Kingdom and the EU as well as the ongoing controversial discussion of potential (exit) scenarios within the UK. At the time of creation of this report, it is neither certain if the notified exit date end of 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 since the negotiations as well as possibilities and scenarios controversially discussed particularly within the UK have gained significant momentum since the fourth quarter of 2018. 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, trade restrictions of any kind as well as 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. Among others, free movement of employees of the PAION Group could be restrained.

Moreover, also apart from intragroup services, tax risks in particular could result from a potential Brexit, e.g. due to controlled foreign corporation rules.

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.

Clinical development of remimazolam in procedural sedation for minor medical interventions in the U.S. has already been completed and PAION's U.S. licensee Cosmo, who will be responsible for all further activities in the U.S., expects filing for market approval shortly. The start of commercialization of remimazolam in the U.S. is expected in 2020. PAION's Chinese licensee Yichang Humanwell filed for market approval in procedural sedation in China in November 2018. For Europe, PAION is currently evaluating the possibility of submitting a market approval dossier for remimazolam in procedural sedation with the EMA based on the completed U.S. development program. Based on a pre-submission meeting with the EMA, PAION assumes that the existing data package is sufficient to be able to submit the MAA for procedural sedation in the EU. Development in general anesthesia in Japan is completed and the Japanese licensee Mundipharma filed for market approval of remimazolam in general anesthesia in Japan in December 2018. PAION's Russian licensee R-Pharm currently plans to file for market approval in Russia by the end of 2019 based on the Phase III trial in general anesthesia successfully completed in November 2018. After successfully completed patient recruitment of a Phase III study in general anesthesia in October 2018, the South Korean licensee Hana Pharm plans to initially establish the production process for an own manufacture of remimazolam in South Korea and to file for market approval in general anesthesia in 2020. PAION expects that no further study in addition to the Phase III trial currently being conducted in the EU will be required for filing for market approval in general anesthesia in the EU. 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 licensees in Japan, China, Canada, Russia/CIS, Turkey, the MENA region, and South Korea financially in the form of milestone payments and royalties from launch onwards as well as in the form of additional development data. For selected European markets, an own commercialization is targeted. For all other regions, it is targeted to find licensees or distribution partners. In 2019, PAION will primarily focus on the completion of the ongoing Phase III study in general anesthesia in Europe, the support of its licensees for filings for market approvals and subsequent interactions with regulatory authorities as well as the establishment of the supply chain in order to be able to provide remimazolam for PAION's own commercial use in the EU as well as for licensees in their respective territories in time.

Overall, PAION has the chance of generating 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 filings for market approval in China and Japan in the reporting period were important milestones on the way to first market approvals for remimazolam in even more than one region and indication. Also, filing for market approval in the U.S. is expected shortly and the licensees in the other regions have made good development progress in 2018 on the way to potential filings for market approval in their licensed territories. Thus, the risk of failure of the development of remimazolam has further decreased.

The capital increase conducted in the reporting period has further reduced the required funds until filing for market approval in general anesthesia in the EU. Thus, the risk situation has improved compared to the previous year.

It is expected that the market approval dossier for procedural sedation in the U.S. will be filed shortly and that commercialization in the market could start in 2020. In Japan and China, a potential market approval could each be granted towards end of 2019 or in 2020. Moreover, further filings for market approval by licensees in their respective territories could take place in 2019. 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

There were no significant events in the period between the reporting date, 31 December 2018, and the preparation of this report.

Report on expected developments

Outlook on development and commercialization (PAION group)

PAION's focus for 2019 is on the development program in Europe, approval processes in the U.S. and other regions, manufacture of and supply chain for remimazolam. Moreover, PAION expects the development and approval activities in all territories to also further promote the other indications.

Europe

For the EU, PAION is working on the advancement of the clinical development program of remimazolam. Focus for 2019 are the conduct and completion of the ongoing Phase III study in general anesthesia as well as first development work to address the pediatric development plan stretching over several years. As a result of the consultation with EMA, PAION is currently evaluating the possibility of filing for market approval in procedural sedation in the EU based on the data from the U.S. development program.

U.S.

For the U.S., filing for market approval in procedural sedation by licensee Cosmo, which is expected shortly, has priority. With a regular course of the approval process, start of commercialization of remimazolam in the U.S. can be expected in 2020.

Rest of the World

PAION supports its licensees in the preparation and filing of approval dossiers. In China, licensee Yichang Humanwell filed for market approval in November 2018 leading to a potential market approval end of 2019 the earliest in case of a positive approval process. In Japan, licensee Mundipharma filed for market approval in December 2018; market approval could be granted end of 2019 the earliest.

PAION expects its other regional remimazolam licensees to continue their development activities and/or the preparation of market approval dossiers for remimazolam. Licensee R-Pharm plans to file for market approval in Russia by the end of 2019. Licensee TR-Pharm plans to file for market approval in Turkey based on the U.S. or Japanese dossier in the course of 2019, and in South Korea, Hana Pharm plans to file for market approval in 2020 after establishment of the production process for remimazolam.

Further activities

PAION is working on setting up the supply chain in order to be able to provide remimazolam product to the licensees timely for commercial use as well as having it available early enough for PAION's own commercialization.

Also, PAION plans small-scale pre-marketing activities for the preparation of an own commercialization subject to possible dates of filing its own market approval dossiers for remimazolam in Europe.

Financial outlook 2019 (PAION group)

PAION expects revenues of about EUR 8 million in 2019, thereof EUR 7.5 million in connection with the planned regulatory filing for remimazolam in the U.S. by Cosmo. Moreover, EUR 0.5 million are related to revenues from TR-Pharm in connection with the transfer of the Japanese filing dossier translated into English or transfer of the U.S. filing dossier.

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 between approx. EUR 13 million and approx. EUR 15 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 2 million. General administrative and selling expenses are expected to amount to between approx. EUR 4 million and approx. EUR 5 million depending on the volume of precommercial activities. Net loss is expected to amount to between approx. EUR 7 million and approx. EUR 10 million in 2019.

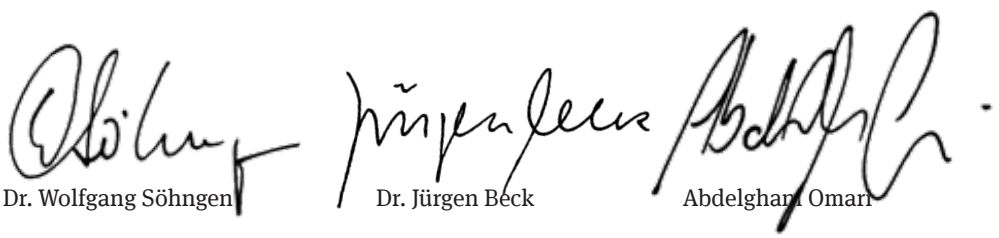
This outlook assumes that PAION and licensee activities progress as expected. In case of delays, essential cost blocks and/or revenues would shift into 2020 or subsequent periods. Plans are also based on the current status of discussions with regulatory authorities. Additional unexpected requirements by regulatory authorities could lead to higher costs than planned and to delays in approvals and revenues based thereon.

Based on current planning, cash and cash equivalents at hand, including expected tax credits from the British tax authorities on parts of research and development expenses and the expected milestone payment in connection with filing for market approval in the U.S., secure a liquidity runway until approx. mid-2020. PAION expects to require further funds of approx. EUR 10 million until filing for market approval in general anesthesia in the EU based on current planning.

Moreover, additional funds will be required in the next years for the planned own commercialization in selected European markets. The magnitude of the required funds will be dependent on the actual setup of commercialization and which European countries PAION will initially focus on. Also, there is an additional requirement for funds for the intended development of the indication ICU sedation as well as for the multi-year pediatric development plan. PAION expects that the total requirement for funds can be partially covered by potential future milestone payments and royalties.

Under consideration of the current cost structures, a net loss of approx. EUR 1 million to approx. EUR 2 million is expected for PAION AG in fiscal year 2019.

Aachen, Germany, 19 March 2019
PAION AG



Dr. Wolfgang Söhngen | Dr. Jürgen Beck | Abdelghani Omari

Financial Statements

PAION AG

Balance Sheet as of 31 December 2018

ASSETS	31 Dec. 2018 EUR	31 Dec. 2017 EUR
Fixed assets		
Financial assets		
Shares in affiliated companies	94,761,015.15	12,768,015.15
Securities	11.70	11.70
	94,761,026.85	12,768,026.85
	94,761,026.85	12,768,026.85
Current assets		
Receivables and other assets		
Receivables from affiliated companies	22,549,566.47	89,755,236.38
Other assets	32,013.96	48,700.27
	22,581,580.43	89,803,936.65
Cash on hand and bank balances	15,047,836.95	23,617,132.75
	37,629,417.38	113,421,069.40
Prepaid expenses	54,740.41	78,537.16
	132,445,184.64	**126,267,633.41**

EQUITY AND LIABILITIES	31 Dec. 2018 EUR	31 Dec. 2017 EUR
Equity		
Subscribed capital	63,858,143.00	61,120,046.00
thereof: 63,858,143 no-par value shares (prior year: 61,120,046 no-par value shares)		
Conditional capital: EUR 29,681,093.00 (prior year: EUR 28,919,190.00)		
Capital reserve	149,295,473.46	146,659,568.24
Accumulated loss	-81,546,376.56	-82,200,663.32
	131,607,239.90	125,578,950.92
Accruals		
Other accruals	545,697.38	452,223.64
Liabilities		
Trade payables	130,103.49	117,703.74
thereof due in up to one year: EUR 130,103.49 (prior year: EUR 117,703.74)		
Liabilities to affiliated companies	9,478.64	8,141.95
thereof due in up to one year: EUR 9,478.64 (prior year: EUR 8,141.95)		
Other liabilities	152,665.23	110,613.16
thereof due in up to one year: EUR 152,665.23 (prior year: EUR 110,613.16)		
thereof for taxes: EUR 92,525.89 (prior year: EUR 76,461.44)		
	292,247.36	236,458.85
	132,445,184.64	**126,267,633.41**

Income Statement for Fiscal Year 2018

	2018 EUR	2017 EUR
Revenues	1,026,159.35	1,043,479.12
Other operating income	263,851.16	592,176.85
Personnel expenses		
Wages and salaries	-1,676,315.69	-1,621,939.16
Social security	-108,376.50	-103,478.49
	-1,784,692.19	-1,725,417.65
Depreciation of intangible assets	0.00	-5,258.00
Other operating expenses	-1,860,828.10	-3,143,793.43
Other interest and similar income thereof from affiliated companies: EUR 3,003,640.97 (prior year: EUR 3,073,329.35)	3,009,796.54	3,093,098.89
Result before tax	**654,286.76**	**-145,714.22**
Other taxes	0.00	-94.66
Net result for the year	**654,286.76**	**-145,808.88**
Loss carryforward	-82,200,663.32	-82,054,854.44
Accumulated loss	**-81,546,376.56**	**-82,200,663.32**

Notes

PAION AG

Notes to the financial statements for fiscal year 2018

Preliminary remarks

The financial statements of PAION AG, Martinstr. 10–12, 52062 Aachen, Germany, HRB 12528, register court Aachen, for the fiscal year from 1 January 2018 to 31 December 2018 were prepared in accordance with the applicable provisions of the German Commercial Code (Handelsgesetzbuch, HGB) and the German Stock Corporation Act (Aktiengesetz, AktG), as amended. The balance sheet and income statement have been classified according to the provisions of Sections 266 and 275 HGB. The notes to the financial statements were prepared in accordance with the requirements of Sections 284 to 288 HGB.

PAION AG shares are admitted to trading on the Frankfurt Stock Exchange and are listed in the Prime Standard of the Regulated Market. Pursuant to Section 267 paragraph 3 sentence 2 HGB PAION AG is a large corporation, as shares issued by it are traded on an organized market within the meaning of Section 2 paragraph 11 of the German Securities Trading Act claim (Wertpapierhandelsgesetz, WpHG).

Accounting and valuation methods

1. Fixed assets are measured at acquisition cost and are subject to scheduled linear amortization. Low-value assets costing less than EUR 800 are written off in full in the year of acquisition. The lower applicable value is subject to unscheduled depreciation if required. If the reason for the unscheduled depreciation ceases to exist, the assets are written up in accordance with Section 253 (5) HGB.
2. Financial assets are recognized at the lower of acquisition cost or market value.
3. Receivables and other assets are always stated at nominal value. Receivables denominated in a foreign currency were generally converted with the average spot exchange rate at the balance sheet date. In case of a remaining term of more than one year the realization principle (Section 252 (1) No. 4 Sentence 2 HGB) and the acquisition cost principle (Section 253 (1) Sentence 1 HGB) were considered.
4. Prudent business judgement is applied to the estimation of accruals; these are recognized at an amount deemed necessary and adequate. Accruals with a remaining term of more than one year are discounted with the weighted market interest rate of the last seven years.
5. Liabilities (including those denominated in foreign currencies) are carried at the amount repayable. Liabilities denominated in a foreign currency were generally converted with the average spot exchange rate at the balance sheet date. In case of a remaining term of more than one year the realization principle (Section 252 (1) No. 4 Sentence 2 HGB) and the acquisition cost principle (Section 253 (1) Sentence 1 HGB) were considered.
6. The income statement is prepared using the cost-summary method in accordance with Section 275 (2) HGB.

Notes to the items of the balance sheet and the income statement

(I) Financial assets

The shareholdings in affiliated companies as of 31 December 2018 refer to PAION Holdings UK Ltd (KEUR 94,311) and PAION Deutschland GmbH (KEUR 450). The shares in PAION Holdings UK Ltd were increased by KEUR 81,993 in the reporting period by a capital increase against contribution in kind in the course of which the loan granted to PAION Holdings UK Ltd by PAION AG was completely (KEUR 4,737) and the loan granted to PAION UK Ltd by PAION AG was partially (KEUR 77,256) contributed to PAION Holdings UK Ltd. The composition and performance of the fixed assets is as follows:

	Historic Costs			
	1 Jan. 2018	Additions	Disposals	31 Dec. 2018
	EUR	EUR	EUR	EUR
Intangible assets				
Franchises, trademarks, patents, licenses and similar rights	60,075.05	0.00	0.00	60,075.05
	60,075.05	0.00	0.00	60,075.05
Financial assets				
Shares in affiliated companies	59,966,512.25	81,993,000.00	0.00	141,959,512.25
Securities	11.70	0.00	0.00	11.70
	59,966,523.95	81,993,000.00	0.00	141,959,523.95
	60,026,599.00	**81,993,000.00**	**0.00**	**142,019,599.00**

	Depreciation			Net Book Values	
1 Jan. 2018	Additions	Disposals	31 Dec. 2018	31 Dec. 2018	31 Dec. 2017
EUR	EUR	EUR	EUR	EUR	EUR
60,075.05	0.00	0.00	60,075.05	0.00	0.00
60,075.05	0.00	0.00	60,075.05	0.00	0.00
47,198,497.10	0.00	0.00	47,198,497.10	94,761,015.15	12,768,015.15
0.00	0.00	0.00	0.00	11.70	11.70
47,198,497.10	0.00	0.00	47,198,497.10	94,761,026.85	12,768,026.85
47,258,572.15	**0.00**	**0.00**	**47,258,572.15**	**94,761,026.85**	**12,768,026.85**

(2) Receivables from affiliated companies

The receivables from affiliated companies are comprised as follows as of 31 December 2018:

EUR	Total	of which: loans	of which: services and interest
PAION UK Ltd	22,546,538.08	22,434,000.00	112,538.08
PAION Deutschland GmbH	3,028.39	0.00	3,028.39
	22,549,566.47	**22,434,000.00**	**115,566.47**

Receivables from affiliated companies have a term of less than 12 months.

(3) Other assets

As of 31 December 2018, other assets are comprised substantially of VAT receivables (KEUR 31; previous year: KEUR 37).

(4) Equity

As of 31 December 2018, the share capital amounts to EUR 63,858,143.00 (previous year: EUR 61,120,046.00); it is divided into 63,858,143 no-par value shares (previous year: 61,120,046 shares). The increase of the share capital in the total amount of EUR 2,738,097.00 in the reporting period results from a capital increase without subscription rights conducted in June 2018 in the amount of EUR 2,600,000.00 and from the exercise of stock options in the amount of EUR 138,097.00. Details are described in the following.

By virtue of a resolution adopted by the Annual General Meeting on 23 May 2018, the Management Board was authorized to increase the share capital on or prior to 22 May 2023, with the consent of the Supervisory Board, on one or more occasions, by up to EUR 30,560,023.00 in total by issuing up to 30,560,023 new no-par value bearer shares in return for cash contributions or contributions in kind (Authorized Capital 2018). Furthermore, the Management Board was authorized to use up to EUR 6,112,004.00 of the Authorized Capital 2018 to issue new shares for cash by excluding pre-emptive rights. The still available Authorized Capital 2017 in the amount of EUR 26,273,543.00 was revoked.

On 21 June 2018, the Management Board decided with the approval of the Supervisory Board and based on the authorization of the General Meeting to issue 2,600,000 no-par value bearer shares in return for cash contribution by excluding pre-emptive rights for the existing shareholders to a French institutional investor. The new shares were issued at a price of EUR 2.00 per share. The capital increase led to gross proceeds of EUR 5.2 million. As a result, the share capital of the company was increased from EUR 61,127,526.00 by EUR 2,600,000.00 to EUR 63,727,526.00 through the issuing of 2,600,000 new shares. The capital increase was registered

in the Commercial Register on 25 June 2018. The Authorized Capital 2018 was reduced by EUR 2,600,000.00 in the course of this capital measure and amounts to EUR 27,960,023.00 as of 31 December 2018.

Furthermore, by virtue of another resolution adopted by the Annual General Meeting on 23 May 2018, subject to the consent of the Supervisory Board, the Management Board was authorized to issue on or before 22 May 2023, 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 2018 I). Furthermore, the Management Board was authorized to use up to EUR 6,112,004.00 of the Conditional Capital 2018 I for Bonds against cash by excluding pre-emptive rights. Conditional Capital 2017 in the amount of EUR 26,200,000.00 was revoked.

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, 205,250 stock options were issued to current and former Management Board members and employees of the PAION Group as of 31 December 2018. To date, 479,142 stock options from the Stock Option Plan 2008 have been exercised, thereof 138,097 in fiscal year 2018. The exercises led to cash inflows of EUR 174,002.22 in the fiscal year. As of 31 December 2018, Conditional Capital 2008 I amounts to EUR 281,093.00.

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 2018. 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, 533,885 stock options were issued to current and former Management Board members and employees of the PAION Group as of 31 December 2018. 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, 701,185 stock options were issued to Management Board members and employees of the PAION Group as of 31 December 2018. No stock options have been exercised yet.

A resolution was adopted by the Annual General Meeting on 23 May 2018 to conditionally increase the share capital of PAION AG by an aggregate of up to EUR 900,000.00 by issuing an aggregate of up to 900,000 new no-par value bearer shares (Conditional Capital 2018 II). 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 2018 exercise their options. Under the Stock Option Plan 2018, no stock options were granted yet as of 31 December 2018.

(5) Accruals

The accruals break down as follows:

	31 Dec. 2018 EUR	31 Dec. 2017 EUR
Bonuses	302,350.00	212,914.24
Outstanding invoices	95,362.23	78,500.00
Financial statements and audit	74,194.53	60,400.00
Legal advice	26,491.00	26,000.00
Others	47,299.62	74,409.40
	545,697.38	**452,223.64**

(6) Liabilities to affiliated companies

The liabilities to affiliated companies refer completely to PAION Deutschland GmbH as a result of VAT affiliation. The liabilities to affiliated companies have a term of less than 12 months.

(7) Revenues

Revenues resulted entirely from the provision of management and other services to the subsidiaries, of which PAION UK Ltd accounted for KEUR 895 (previous year: KEUR 857) and PAION Deutschland GmbH for KEUR 131 (previous year: KEUR 186).

(8) Other operating income

Other operating income includes recharges to the subsidiaries amounting to KEUR 145 (previous year: KEUR 155), of which PAION Deutschland GmbH accounted for KEUR 75 (previous year: KEUR 73) and PAION UK Ltd for KEUR 70 (previous year: KEUR 82). Exchange rate gains were recognized in an amount of KEUR 86 (previous year: KEUR 395).

(9) Other operating expenses

Other operating expenses mainly include legal and consulting fees (KEUR 763; previous year: KEUR 1,403), insurance, contributions and fees (KEUR 233; previous year: KEUR 241), expenses in connection with Supervisory Board remuneration (KEUR 162; previous year: KEUR 141), travel expenses (KEUR 161; previous year: KEUR 146), services rendered by PAION Deutschland GmbH (KEUR 150; previous year: KEUR 173), expenses for IT hosting (KEUR 104; previous year: KEUR 106) as well as audit costs and costs for the annual report (KEUR 64; previous year: KEUR 64). In the reporting period, foreign exchange losses in the amount of KEUR 68 (previous year: KEUR 564) have been recognized. The decrease of other operating expenses in comparison to the previous year mainly results from lower foreign exchange losses and lower expenses in connection with capital increases.

(10) Income attributable to other periods

In fiscal year 2018, income that is attributable to other periods amounts to KEUR 31 and results from the reimbursement of contributions.

(11) Taxes

As of 31 December 2018, the company's tax losses carried forward relating to corporate income tax amounted to about EUR 32.5 million (previous year: EUR 33.3 million) and relating to trade tax to about EUR 31.3 million (previous year: EUR 32.0 million). Based on the 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 combined German 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%.

If the current compound income tax rate was applied to the tax losses carried forward as of 31 December 2018, the resulting deferred tax assets would amount to KEUR 10,351 (previous year: KEUR 10,591).

Temporary differences between the tax base and the HGB carrying amount do not exist as of 31 December 2018 and did not exist as of the previous year's reporting date.

Other compulsory disclosures

(1) Average number of employees

In fiscal year 2018, the company had an average of seven employees (previous year: eight employees).

(2) Other financial obligations

The loan facility granted to the subsidiary PAION UK Ltd of up to KEUR 40,000 as of the balance sheet date will be granted until further notice. As of 31 December 2018, the utilization amounts to KEUR 22,434.

(3) Stock Option Plans

PAION has implemented a total of five active stock option plans in the course of which stock options can be/have been granted to Management Board members and employees of PAION AG and its subsidiaries at the time of the grant. All stock option plans include vesting periods, waiting periods and exercise hurdles. The respective exercise price is based on the average stock price during a certain period of time before the grant. Details of the individual plans can be found in the following table (the presentation of the Stock Option Plan 2018, from which no stock options have been granted yet, is omitted):

	Stock Option Plan 2008 Approved 5 May 2008
Underlying Capital	Conditional Capital 2008 I
Term of the options	10 years
Vesting period	2–4 years
Waiting period	2–4 years
Number of outstanding options for which the waiting period has expired as of 31 December 2018	205,250
Exercise condition	Cumulative stock price increase of 5% per year since grant in relation to exercise price
Exercise price *	EUR 1.84 to EUR 2.69
Weighted average exercise price *	EUR 1.89
Exercise hurdle as of 31 Dec. 2018 *	EUR 2.66 to EUR 3.88
Weighted average remaining term as of 31 Dec. 2018	1.0 years
Further grants possible? (as of 31 Dec. 2018)	No
Number of totally granted options until 31 Dec. 2018	817,550
Number of outstanding options as of 31 Dec. 2018 **	205,250
granted to employees	91,000
granted to Management Board members	114,250
Number of totally lapsed options as of 31 Dec. 2018	133,158
thereof lapsed in the reporting period	32,400
Number of totally exercised options until 31 Dec. 2018	479,142
thereof exercised in the reporting period	138,097

*) in relation to outstanding options as of 31 Dec. 2018
**) in relation to employee/Management Board member status at the time of the grant

Stock Option Plan 2010 Approved 19 May 2010	Stock Option Plan 2014 Approved 21 May 2014	Stock Option Plan 2016 Approved 25 May 2016
Conditional Capital 2010 I	Conditional Capital 2014	Conditional Capital 2016
10 years	10 years	10 years
2 years	2–4 years	2–4 years
4 years	4 years	4 years
696,626	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	Cumulative stock price increase of 5% per year since grant in relation to exercise price
EUR 2.01	EUR 1.99 to EUR 2.60	EUR 2.25 to EUR 2.60
EUR 2.01	EUR 2.21	EUR 2.34
EUR 2.50	EUR 2.24 to EUR 2.84	EUR 2.31 to EUR 2.72
5.1 years	7.0 years	9.2 years
No	No	Yes
720,000	740,000	706,500
696,626	533,885	701,185
392,876	235,572	456,685
303,750	298,313	244,500
23,374	206,115	5,315
0	0	4,361
0	0	0
0	0	0

(4) Management Board and Supervisory Board

The members of the company's Management Board are:
- Dr. Wolfgang Söhngen, CEO, Chairman (appointed until 22 November 2019)
- Abdelghani Omari, CFO (appointed until 31 August 2020)
- Dr. Jürgen Beck, CDO (since 1 January 2018) (appointed until 31 December 2019)

Management Board remuneration totalled KEUR 1,290 in fiscal year 2018. As of 31 December 2018, a total of 820,550 stock options (fair value at time of granting: EUR 1,124,034) had been issued to active Management Board members as of 31 December 2018. For more information on Management Board remuneration, please see the disclosures in the remuneration report, which is part of the management report.

All Management Board members are also Managing Directors of PAION Deutschland GmbH. Mr. Abdelghani Omari and Dr. Jürgen Beck are also Managing Directors of PAION Holdings UK Ltd and its subsidiaries. All Management Board members work full-time for the company and its subsidiaries.

As of 31 December 2018, Dr. Wolfgang Söhngen owned 1.08% (690,063 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%.

As of 31 December 2018, Dr. Jürgen Beck owned 0.02% (10,000 voting rights) of the shares in PAION AG.

Members of the Supervisory Board

The members of the Supervisory Board are:
- Dr. Jörg Spiekerkötter, Berlin/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, Boston, MA/U.S., Chairman of the Research and Development Committee; Vice President Translational Medicine and Development at Wave Life Sciences Ltd., Cambridge, MA/U.S.
  Other supervisory board memberships or similar positions:
  - 4SC AG, Planegg-Martinsried (Munich)/Germany, Member of the Supervisory Board

- Dr. Hans Christoph Tanner, Zurich/Switzerland, Member of the Supervisory Board, Head of Transactions of Cosmo Pharmaceuticals N.V., Amsterdam/The Netherlands, Head of Finance & Investor Relations 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
  - 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 of the Supervisory Board totalled KEUR 162 in fiscal year 2018. For more information on Supervisory Board remuneration, please see the disclosures in the remuneration report of the management report.

As of 31 December 2018, none of the members of the Supervisory Board owned shares in PAION AG.

(5) Shareholdings

The company owns the following direct and indirect shareholdings:

	Shares in in %	Currency	Equity as of 31 Dec. 2018 *	Result 2018 *
PAION Deutschland GmbH, Aachen	100	EUR	1,569,779.89	231,704.19
PAION Holdings UK Ltd, Cambridge/UK	100	GBP	75,967,243.96	-53,884.96
PAION UK Ltd, Cambridge/UK	100	GBP	-17,700,862.97	-8,795,735.05
TheraSci Limited, Cambridge/UK	100	GBP	0.00	0.00

*) Reporting according to local reporting standards

(6) Reportable equity investments in PAION AG pursuant to section 33 WpHG

The following notifications in respect of reportable equity investments pursuant to Section 33 (1) and (2) WpHG, which were published in accordance with the stipulations of Section 40 (1) WpHG, are relevant for assessing which shareholders held more than 3% of the shares as of 31 December 2018:

- On July 10, 2014, the College Retirement Equities Fund, New York, New York, USA has informed us according to Article 21, Section 1 of the WpHG that its voting rights in PAION AG, Aachen, Germany, have exceeded the 3% threshold of the voting rights on June 23, 2014 and on that day amounted to 3.001% (this corresponds to 925,543 voting rights).

  On July 10, 2014, TIAA-CREF Investment Management, LLC, New York, New York, USA has informed us according to Article 21, Section 1 of the WpHG that its voting rights in PAION AG, Aachen, Germany have exceeded the 3% threshold of the voting rights on June 23, 2014 and on that day amounted to 3.001% (this corresponds to 925,543 voting rights). According to Article 22, Section 1, Sentence 1, No. 6 of the WpHG, 3.001% of the voting rights (this corresponds to 925,543 voting rights) are to be attributed to TIAA-CREF Investment Management, LLC from the College Retirement Equities Fund.

- **1. Details of issuer**

  PAION AG
  Martinstr. 10-12
  52062 Aachen
  Germany

2. Reason for notification

X Acquisition/disposal of shares with voting rights
Acquisition/disposal of instruments
Change of breakdown of voting rights
Other reason:

3. Details of person subject to the notification obligation

Name:	City and country of registered office:
Cosmo Pharmaceuticals N.V.	Amsterdam, Netherlands

4. Names of shareholder(s)

holding directly 3% or more voting rights, if different from 3.
Granell Strategic Investment Fund Limited

5. Date on which threshold was crossed or reached

29 Jun 2016

6. Total positions

	% of voting rights attached to shares (total of 7.a.)	% of voting rights through instruments (total of 7.b.1 + 7.b.2)	total of both in % (7.a. + 7.b.)	total number of voting rights of issuer
Resulting situation	9.09 %	0 %	9.09 %	55736594
Previous notification	n/a %	n/a %	n/a %	/

7. Notified details of the resulting situation

a. Voting rights attached to shares (Sec.s 21, 22 WpHG)

ISIN	absolute		in %	
	direct (Sec. 21 WpHG)	indirect (Sec. 22 WpHG)	direct (Sec. 21 WpHG)	indirect (Sec. 22 WpHG)
DE000A0B65S3		5064194	%	9.09 %

Total	5064194	9.09 %

b.1. Instruments according to Sec. 25 para. 1 No. 1 WpHG

Type of instrument	Expiration or maturity date	Exercise or conversion period	Voting rights absolute	Voting rights in %
				%
		Total		%

b.2. Instruments according to Sec. 25 para. 1 No. 2 WpHG

Type of instrument	Expiration or maturity date	Exercise or conversion period	Cash or physical settlement	Voting rights absolute	Voting rights in %
					%
			Total		%

8. Information in relation to the person subject to the notification obligation

Person subject to the notification obligation is not controlled and does itself not control any other undertaking(s) holding directly or indirectly an interest in the (underlying) issuer (1.).

X Full chain of controlled undertakings starting with the ultimate controlling natural person or legal entity:

Name	% of voting rights (if at least held 3% or more)	% of voting rights through instruments (if at least held 5% or more)	Total of both (if at least held 5% or more)
Cosmo Pharmaceuticals N.V.	%	%	%
Granell Strategic Investment Fund Limited	9.09 %	0 %	9.09 %

9. In case of proxy voting according to Sec. 22 para. 3 WpHG

Date of general meeting:

Holding position after general meeting: % (equals voting rights)

According to the notifications we have received pursuant to Section 33 WpHG, the following companies or individuals held shares of more than 3% in the voting rights of PAION AG as of 31 December 2018:

- College Retirement Equities Fund (TIAA-CREF)
- Cosmo Pharmaceuticals N.V. (via Granell Strategic Investment Fund Limited)

(7) Financial statements auditor

The fees of the financial statements auditor for fiscal year 2018 are disclosed in the consolidated financial statements of PAION AG.

(8) 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 complies with all recommendations set forth in the most recent version of the German Corporate Governance Code dated 7 February 2017. In December 2018, 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/).

(9) Report on post-balance sheet date events

There were no significant events in the period between the reporting date, 31 December 2018, and the preparation of this report.

Aachen, 19 March 2019

PAION AG

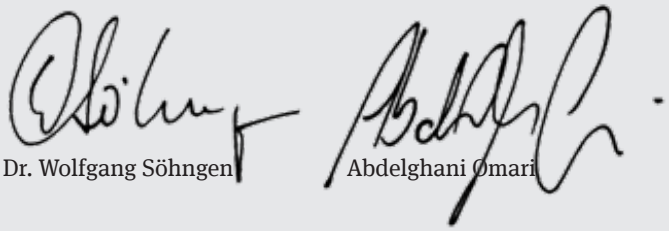
Dr. Wolfgang Söhngen Abdelghani Omari

Dr. Jürgen Beck

Responsibility Statement (Bilanzeid) in accordance with section 114(1) and (2) of the Wertpapierhandelsgesetz (WpHG – German Securities Trading Act) in conjunction with sections 264(2) sentence 3 and 289(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 financial statements give a true and fair view of the assets, liabilities, financial position and profit or loss of PAION AG, and the management report includes a fair review of the development and performance of the business and the position of PAION AG, together with a description of the principal opportunities and risks associated with the expected development of PAION AG."

Aachen, Germany, 19 March 2019
PAION AG



Dr. Wolfgang Söhngen Abdelghani Omari

Dr. Jürgen Beck

Reproduction of the auditor's report

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

"Independent auditor's report

To PAION AG,

Report on the audit of the annual financial statements and of the management report

Opinions
We have audited the annual financial statements of PAION AG, Aachen, which comprise the balance sheet as at 31 December 2018, and the income statement for the fiscal year from 1 January 2018 to 31 December 2018, and notes to the financial statements, including the recognition and measurement policies presented therein. In addition, we have audited the management report of PAION AG for the fiscal year from 1 January 2018 to 31 December 2018.

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

- the accompanying annual financial statements comply, in all material respects, with the requirements of German commercial law applicable to business corporations and give a true and fair view of the assets, liabilities and financial position of the Company as at 31 December 2018 and of its financial performance for the fiscal year from 1 January 2018 to 31 December 2018 in compliance with German legally required accounting principles, and
- the accompanying management report as a whole provides an appropriate view of the Company's position. In all material respects, this management report is consistent with the annual financial statements, complies with German legal requirements and appropriately presents the opportunities and risks of future development.

Pursuant to Sec. 322 (3) Sentence 1 HGB ["Handelsgesetzbuch": German Commercial Code], we declare that our audit has not led to any reservations relating to the legal compliance of the annual financial statements and of the management report.

Basis for the opinions
We conducted our audit of the annual financial statements and of the 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). Our responsibilities under those requirements and principles are further described in the "Auditor's responsibilities for the audit of the annual financial statements and of the management report" section of our auditor's report. We are independent of the Company 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 annual financial statements and on the management report.

Key audit matters in the audit of the annual financial statements
Key audit matters are those matters that, in our professional judgment, were of most significance in our audit of the annual financial statements for the fiscal year from 1 January 2018 to 31 December 2018. These matters were addressed in the context of our audit of the annual 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. Valuation of equity investments and valuation of loans to affiliates

1.1 Reasons why the matter was determined to be a key audit matter

Because the lead compound remimazolam has not yet been approved, the subsidiary of PAION UK Holdings Ltd., PAION UK Ltd., recorded a net loss for the year. The financing of PAION UK Ltd. is provided indirectly via PAION AG. Due to the expectation of negative results in the future, a risk exists that the loans issued to PAION UK Ltd. and the carrying value of the equity investment in this company could be impaired and that such impairment could be permanent.

The Management Board performs an annual test of the impairment of loans issued to affiliates and of the carrying value of equity investments based on an annually updated development and marketing plan for remimazolam. Furthermore, the Management Board tests for impairment of the equity investments and loans to affiliates on an ad hoc basis whenever appropriate.

The inherent uncertainties concerning the estimation and discounting of future cash flows expected from royalties for remimazolam pose a significant risk to the presentation of a true and fair view of the assets, liabilities, financial position and financial performance of the Company. In light of this and the related use of judgment, the valuation of the equity investments and of the loans issued to affiliates was a key audit matter.

1.2 Auditor's response:

We assessed the Company's process for drawing up the development and marketing plan for remimazolam as well as the principles and completeness of the Company's discounted cash flow model with a view to its adequacy for the purposes of valuing the future cash flows of PAION UK Ltd. to PAION AG. In this connection, we discussed the significant planning assumptions with the Management Board, focusing on the assessment of the expected future cash flows in the medium-term plan as well as the discount rates and growth rates used. For this purpose, we analysed the assumptions underlying the impairment test to determine whether they are in line with industry-specific market expectations.

In order to assess the cash flows, we evaluated the reliability of the planning process in the past. For this purpose, we compared the past assumptions concerning future cash flows with the actual figures. Additionally, we examined the forecast figures for future cash flows using information about the pharmaceutical market for agents for short-term sedation as well as publicly accessible information about the future industry development with the aim of determining whether they are in line with market expectations and our expectations.

With regard to the discount rate, we compared the assumptions made by the Company with data from external sources (such as bond yields and inflation rates). Another audit procedure that we performed to examine and scrutinise the recoverable amounts for remimazolam was a sensitivity analysis of the significant assumptions in order to assess any potential impairment risk in the event of a change in valuation assumptions. Furthermore, we compared the discounted present value of the future cash flows with the Group's market capitalisation.

Our audit procedures did not lead to any reservations regarding the valuation of the equity investments in and loans to affiliates.

1.3 Reference to related disclosures

With regard to the accounting bases applied to the equity investments and the valuation of loans to affiliates, refer to section (2) (note 2) and to section (3) Notes to the items of the balance sheet and the income statement 1. Financial assets in the notes to the Company's financial statements.

Other information

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

pursuant to Sec. 289f HGB, of which we received a version intended for publication before issuing our auditor's report.

Our opinions on the annual financial statements and on the 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 annual financial statements, with the 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 annual financial statements and the management report

The executive directors are responsible for the preparation of the annual financial statements that comply, in all material respects, with the requirements of German commercial law applicable to business corporations, and that the annual financial statements give a true and fair view of the assets, liabilities, financial position and financial performance of the Company in compliance with German legally required accounting principles. In addition, the executive directors are responsible for such internal control as they, in accordance with German legally required accounting principles, have determined necessary to enable the preparation of annual financial statements that are free from material misstatement, whether due to fraud or error.

In preparing the annual financial statements, the executive directors are responsible for assessing the Company'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, provided no actual or legal circumstances conflict therewith.

Furthermore, the executive directors are responsible for the preparation of the management report that, as a whole, provides an appropriate view of the Company's position and is, in all material respects, consistent with the annual 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 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 management report.

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

Auditor's responsibilities for the audit of the annual financial statements and of the management report

Our objectives are to obtain reasonable assurance about whether the annual financial statements as a whole are free from material misstatement, whether due to fraud or error, and whether the management report as a whole provides an appropriate view of the Company's position and, in all material respects, is consistent with the annual 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 annual financial statements and on the 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) 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 annual financial statements and this management report.

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

We also:

- Identify and assess the risks of material misstatement of the annual financial statements and of the 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 annual financial statements and of arrangements and measures (systems) relevant to the audit of the 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 of the Company.
- 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 Company'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 annual financial statements and in the 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 Company to cease to be able to continue as a going concern.
- Evaluate the overall presentation, structure and content of the annual financial statements, including the disclosures, and whether the annual financial statements present the underlying transactions and events in a manner that the annual financial statements give a true and fair view of the assets, liabilities, financial position and financial performance of the Company in compliance with German legally required accounting principles.
- Evaluate the consistency of the management report with the annual financial statements, its conformity with [German] law, and the view of the Company's position it provides.
- Perform audit procedures on the prospective information presented by the executive directors in the 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 annual 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 auditor by the Annual General Meeting on 23 May 2018. We were engaged by the Supervisory Board on

23 May 2018. We have been the 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 Titus Zwirner."

Cologne, 19 March 2019

Ernst & Young GmbH
Wirtschaftsprüfungsgesellschaft

Zwirner	Conrad
Wirtschaftsprüfer	Wirtschaftsprüfer
[German Public Auditor]	[German Public Auditor]

PAION AG
Martinstrasse 10–12
52062 Aachen Germany
Phone +49 241 4453-0
Fax +49 241 4453-100
info@paion.com www.paion.com