

# PAION HI#2018

Consolidated Financial Interim Report for the First Half-Year 2018

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2018

PAION AG

## About PAION AG

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

PAION is headquartered in Aachen (Germany) with an additional site in Cambridge (United Kingdom).

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

## Key Figures

(all figures in KEUR unless otherwise noted)	Q2 2018	Q2 2017	H1 2018	H1 2017
Revenues	260	2,032	517	4,083
Research and development expenses	-3,184	-5,851	-6,544	-9,930
General administrative and selling expenses	-966	-980	-1,761	-1,983
Result for the period	-3,118	-3,553	-6,243	-5,771
Earnings per share in EUR for the period (basic)	-0.05	-0.06	-0.10	-0.10
Earnings per share in EUR for the period (diluted)	-0.05	-0.06	-0.10	-0.10

	H1 2018	H1 2017
Cash flows from operating activities	-6,626	-7,634
Cash flows from investing activities	-12	-17
Cash flows from financing activities	5,067	4,678
Change in cash and cash equivalents	-1,572	-2,991
Average number of group employees	38	31

	30-06-2018	31-12-2017
Intangible assets	2,340	2,415
Cash and cash equivalents	23,267	24,839
Equity	24,192	25,229
Current liabilities	7,232	6,656
Balance sheet total	31,424	31,885

# Interim Group Management Report for the First Half-Year 2018

## The First Six Months at a Glance

### March

PAION's license partner Hana Pharm starts a Phase III trial with remimazolam in general anesthesia in South Korea

### May

PAION's license partner R-Pharm successfully completes patient recruitment of a Phase III trial with remimazolam in general anesthesia in Russia

### June

PAION raises gross proceeds of EUR 5.2 million via private placement

## Update on development activities and Outlook

### U.S.

Following the successful completion of the U.S. clinical development program for remimazolam in procedural sedation in 2017, in the first half of 2018, PAION focused on the work to complete the data package and documentation necessary to enable the U.S. license partner Cosmo Pharmaceuticals (Cosmo) to prepare the market approval dossier and to submit for regulatory approval as planned in the fourth quarter of 2018/first quarter of 2019.

### EU

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

The randomized, single-blind, propofol-controlled, confirmatory Phase III trial is expected to enroll approximately 500 ASA III/IV patients (American Society of Anesthesiologists classification III to IV) undergoing a planned surgery at more than 20 European trial centers. Patient recruitment is expected to be completed in 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 European Medicines Agency (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.

### Partner activities in other territories

PAION's license partners are extending the data base with clinical studies and are preparing the future filings of remimazolam in their respective territories through regulatory interactions.

In May 2018, PAION's license partner for Russia, R-Pharm, announced the completion of patient recruitment of a Phase III study with remimazolam in general anesthesia in Russia. R-Pharm currently plans filing for market approval end of 2018.

In December 2017, PAION entered into a remimazolam license agreement for Japan with Mundipharma. Based on the positive pre-NDA meeting (NDA = New Drug Application) with the Japanese regulatory authority, PAION had started preparations for a market approval dossier for remimazolam. Mundipharma has taken over this work with PAION's support. Mundipharma plans to file for market approval in 2018.

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

The current development program of PAION's Chinese license partner Yichang Humanwell with remimazolam amongst others includes a Phase II study in general anesthesia and a Phase III study in procedural sedation in China.

### **Funding activities**

In June 2018, PAION raised gross proceeds of EUR 5.2 million in a capital increase under exclusion of subscription rights. PAION will use the proceeds of the transaction to prepare the necessary work for the submission of the EU market approval dossier for remimazolam.

## **Financial Overview**

In the first half-year 2018, revenues amounting to EUR 0.5 million (prior-year period: EUR 4.1 million) were generated particularly in connection with the remimazolam license agreement for Japan entered into with Mundipharma in the prior year. Research and development expenses amounted to EUR 6.5 million and decreased by EUR 3.4 million compared to the first half-year 2017 mainly due to lower costs for Phase III and Phase I studies. General administrative and selling expenses decreased by EUR 0.2 million compared to the prior-year period. In total, a net loss of EUR 6.2 million has been incurred in the first half-year 2018 compared to a net loss of EUR 5.8 million in the prior-year period.

Cash and cash equivalents decreased by EUR 1.6 million in the first half-year 2018 compared to 31 December 2017 and amounted to EUR 23.3 million as of 30 June 2018. Based on current plans, PAION believes that cash and cash equivalents enable PAION to complete all activities for preparation of the filing dossier in procedural sedation in the U.S. PAION expects to receive payments from its license partners, subject to the achievement of certain regulatory milestones, and, once remimazolam is approved, royalties on net sales.

For the ongoing EU Phase III study, no further funding is required based on current planning. Cash and cash equivalents, including expected tax credits from the British tax authorities on parts of research and development expenses and expected potential milestone payments in connection with filings for market approval in the U.S. and Japan, secure the conduct of the Phase III study in the EU based on current cost planning. Overall, this ensures a cash reach until the end of 2019. Until filing for market approval in the EU, further funds of approx. EUR 10 million are required based on current planning. This funding requirement may partly be covered by potential further milestone payments from existing license agreements.

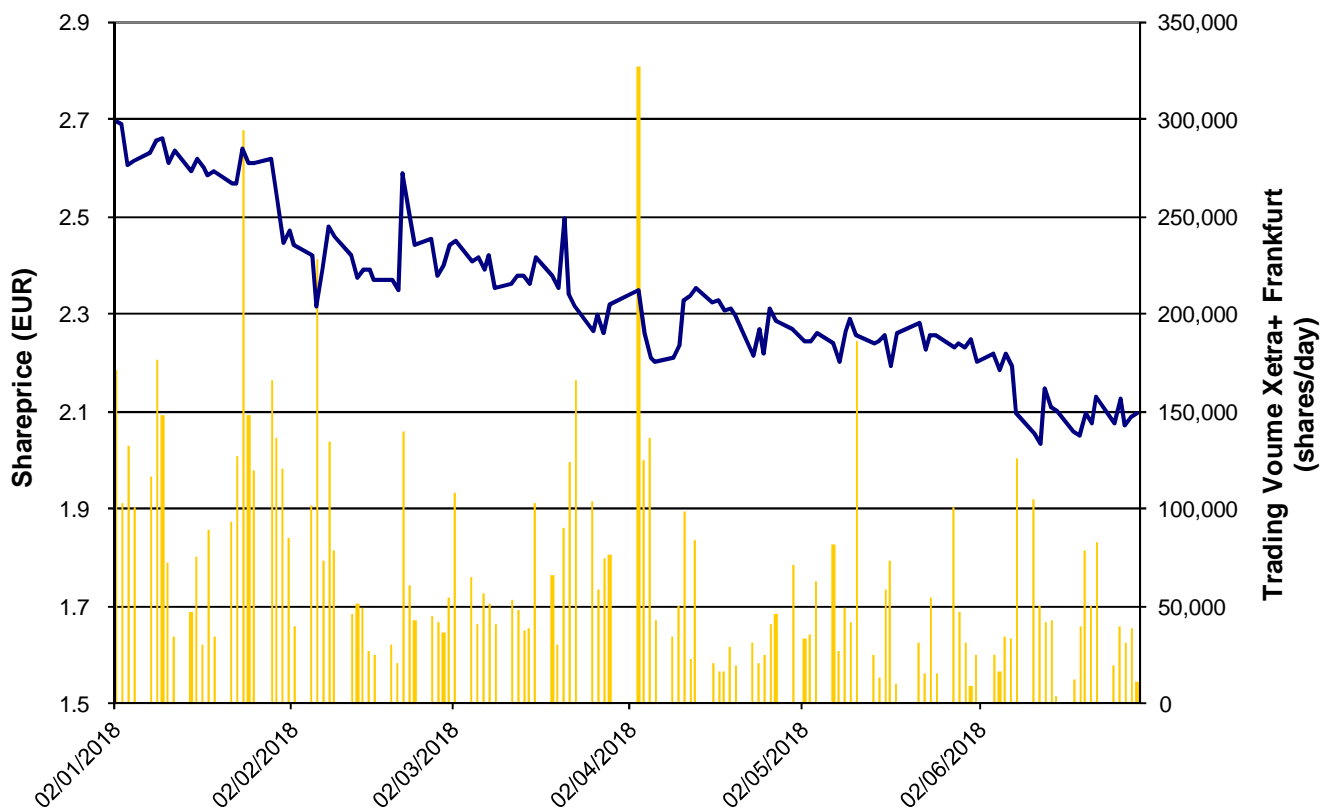
## Capital Market Environment and PAION Share Performance

The development of the German capital markets in the first half of 2018 was mainly impacted by continuously low interest rates, the Quantitative Easing of the European Central Bank, U.S. monetary policy and the threat of global trade wars. The DAXsubsector Biotechnology Index increased by 23% and the NASDAQ Biotechnology Index also trended slightly higher (+0.3%) in the first six months of 2018.

The PAION share price started the year 2018 with a closing price of EUR 2.70 (Xetra) which already marked the peak share price in the first half-year 2018 on 2 January 2018 based on Xetra closing prices. On 12 June 2018, the lowest price in the first half-year 2018 was marked at EUR 2.04 (Xetra). The closing price on 29 June 2018 was EUR 2.10 (Xetra). This corresponds to a decrease of approx. 23% compared to the closing price on 29 December 2017 (EUR 2.71; Xetra).

The average daily trading volume (Xetra and Frankfurt Stock Exchange) amounted to 68,328 shares during the first half of 2018 (in the year 2017: 193,073 shares). Thereby, 8.5 million shares were traded during the first half of 2018 (in the year 2017: 49 million shares).

### Development of the PAION Share Price and Volume (Xetra) in the First Half-Year 2018



## Overview of Research and Development Activities

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

### Remimazolam

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

PAION has completed clinical development of remimazolam for procedural sedation in the U.S. Currently, an integrated overall analysis of all clinical studies with remimazolam is being conducted in preparation of Cosmo's filing for market approval. After completion of the development for procedural sedation, Cosmo is responsible for any further development activities in the U.S. The U.S. license partner currently plans to file for market approval in procedural sedation in the fourth quarter 2018/first quarter 2019. A full clinical development program for general anesthesia was completed in Japan, and the remimazolam license partner for this region, Mundipharma, is planning filing for market approval in this indication in Japan in 2018. In Europe, a Phase III study in general anesthesia was started in July 2018 which can be expected to be the only necessary outstanding trial for filing for market approval in the EU based on the Scientific Advice obtained from the EMA in January 2018.

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

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

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

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

The growth of the procedural sedation market in the U.S. has been driven for many years by the increase in medical interventions requiring procedural sedation, such as colonoscopies, as well as an increase in general demand for preventive screenings. According to iData Research, which examines historical trends and creates procedure forecasts in the U.S. drawing from an extensive collection of national- and state-level procedure databases, 26.7 million colonoscopy and endoscopy claims were reported in 2015 in the U.S., and the number

is expected to grow at an average rate of 2.6% annually through 2020. PAION estimates that 75% of the colonoscopies and endoscopies claimed were conducted in an out-patient setting.

Regular 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 cost. For midazolam, these side effects are less pronounced and have a different relevance, since an undesirably deep sedation can be reversed with flumazenil. Midazolam has a slower onset and a longer duration of action which can impact patient throughput and overall efficiency.

In the U.S. increased enrollment and screenings are expected to result in a performance-based payment system that will seek to better align payments with high quality of care measures. This would imply that cost-efficient medicines with clinical value will be used more extensively and that continued premium will be placed on innovative medicines with strong clinical profile. Thus, PAION believes that concerns related to the overall cost of procedures, driven by the need for anesthesia professionals monitoring during procedures using agents such as propofol, will impact the choice of drug products for procedural sedation. Costs related to anesthesia services in gastrointestinal endoscopy procedures alone were estimated at USD 1.3 billion in 2009.<sup>1</sup> Accordingly, PAION expects reimbursement regimes under national and commercial healthcare systems, such as Medicare, which differentiate the amounts reimbursed to physicians and/or patients depending on whether an anesthesia professional’s service is used, may also positively impact the demand for products that do not require monitoring by an anesthesia professional.

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

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<sup>1</sup> 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 C.M. Wilcox (2013), Use of anesthesia on the rise in gastrointestinal endoscopy, World Journal of Gastrointestinal Endoscopy, January 2013 5(1): 1-5.

Provided that it could be administered under the supervision of a proceduralist, remimazolam would be able to offer a competitive alternative to midazolam. This is based on its enhanced efficiency profile compared to midazolam.

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

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

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

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

#### Intensive care unit (ICU) sedation

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

Internationally renowned anesthesiologists have repeatedly confirmed to PAION that ICU sedation 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. Development for ICU sedation requires additional funds.

Another field of high clinical need is pediatric use, which is a development requirement for both the EU and U.S. after the respective first approval.

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 IIb Multiple bolus in colonoscopy (161) Phase III in colonoscopy (461) Phase III ASA III/IV in colonoscopy (79) Phase III in bronchoscopy (446)	Phase I Single bolus in healthy volunteers (81) Phase Ib Multiple bolus in volunteers undergoing colonoscopy (51) Phase I Renal Impairment (22) Phase I Thorough QT (54) Phase I Abuse Liability <ul style="list-style-type: none"> <li>• Intravenous administration (40)</li> <li>• Oral bioavailability (14)</li> <li>• Oral administration in combination with alcohol (20)</li> <li>• Intranasal administration (12)</li> </ul>
General Anesthesia (Japan)- completed	
Phase II Induction and maintenance of anesthesia in general surgery (85) Phase II/III Induction and maintenance of anesthesia in general surgery (375) Phase III in ASA III or higher surgical patients (62)	Phase I Bolus in healthy volunteers (42) Phase Ib Infusion in healthy volunteers (10) Phase I Hepatic impairment (U.S.) (20)
General Anesthesia (EU)	
Phase II in cardiac surgery patients (90) Phase III in cardiac surgery patients (23)* Phase III in general surgery (approx. 500)**	Phase I PK/PD modeling study (EEG) in healthy volunteers (20)
ICU Sedation (Japan)	
Phase II in ICU patients (49)*	

Patient/volunteer numbers in brackets

\* Discontinued studies, no safety concerns

\*\* Ongoing study

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

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

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

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

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

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

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

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

Patient satisfaction was similar in all arms of the study.

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

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

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

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

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

As part of the U.S. development program, also a safety study in ASA III/IV patients undergoing colonoscopy (American Society of Anesthesiologists classification) was performed. In December 2016, successful completion of patient recruitment was announced, and in March 2017, PAION announced positive headline data from the U.S. clinical safety trial of remimazolam in ASA III/IV patients (American Society of Anesthesiologists classification) undergoing colonoscopy. The trial enrolled 79 patients and was designed to evaluate the efficacy and safety of remimazolam compared to placebo (with midazolam 'rescue' sedation) in patients undergoing proceduralist-supervised sedation for colonoscopy. This study also included an open-label arm in which midazolam was dosed according to U.S. label. The trial confirmed remimazolam's safety profile and tolerability shown in all previous studies in a more vulnerable patient population. Overall, remimazolam demonstrated good respiratory and cardiovascular stability as compared to placebo with midazolam rescue. No adverse events of concern were observed in either group. In addition, the efficacy and efficiency improvements were comparable to the two positive pivotal U.S. Phase III trials in colonoscopy and bronchoscopy patients. Success of the procedure (including no requirement for rescue medication and the application of not more than five doses in any 15-minute interval) was achieved in 84.4% of patients in the remimazolam arm and 0% in the placebo arm. Other relevant endpoints showed a median time from start of medication to start of procedure of 5.0 minutes for remimazolam (placebo: 18.5 minutes) and a median time from end of procedure to return to full alertness of 3.0 minutes (placebo: 5.0 minutes). By comparison, procedural success was achieved in 12.9% of the midazolam patients. Midazolam patients showed a median time from start of medication to start of procedure of 19.0 minutes and a median time from end of procedure to return to full alertness of 7.0 minutes.

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

	<b>Remimazolam</b>	<b>Placebo</b>	<b>Midazolam (Open Label) *</b>
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 license partner Cosmo, attended a pre-NDA meeting 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. In preparation for the meeting, the FDA had received a summary of the application documentation as well as a set of questions, along with company positions and explanatory background.

During the meeting, the main questions raised for discussion following the preliminary assessment of remimazolam by the FDA were clarified. This will allow the process to proceed as planned to file for approval in the fourth quarter 2018/first quarter 2019.

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

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

The Japanese program started with a comparative Phase I study building on PAION's first human trial and showed an identical pharmacokinetic and pharmacodynamic profile. The next step was a continuous infusion Phase I study to define induction and maintenance doses for anesthesia. The doses for induction and maintenance identified as safe and effective in the Phase II study subsequently conducted were then used in the

Japanese Phase III studies, which confirmed remimazolam's efficacy and safety as a general anesthetic and its favorable hemodynamic profile compared to propofol.

A pre-NDA meeting with the Japanese Pharmaceuticals and Medical Devices Agency ("PMDA") took place in January 2016. The PMDA stated that the non-clinical and clinical data package of remimazolam were regarded as complete for filing in the indication "Induction and maintenance of general anesthesia" in Japan. The PMDA had already confirmed earlier that both the raw materials produced by PAION in Europe as well as the finished formulation of remimazolam fulfill the requirements for filing in Japan. Based on the positive feedback by the Japanese authority, PAION has started preparations for a market approval dossier for remimazolam. In course of the license agreement for remimazolam in Japan entered into in December 2017, Mundipharma has now taken over these tasks with PAION's support and plans to file for market approval in 2018.

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

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

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

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 in 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 European Medicines Agency (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.

#### ICU sedation

PAION's former partner in Japan, Ono, independently initiated a Phase II trial for sedation in intensive care units (ICUs). Higher than by Ono expected plasma concentrations of remimazolam were observed in isolated cases after long-term treatment as is known from similar substances, and Ono discontinued this exploratory trial in 2013. Patients were sedated successfully and no significant unexpected adverse events were reported.

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

#### Partnerships

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

a commercially viable alternative in a global healthcare environment characterized by increasing cost consciousness.

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

PAION's license partners are extending the data base with clinical studies and are preparing the future filings of remimazolam in their respective territories through regulatory interactions.

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

In May 2018, PAION's license partner for Russia, R-Pharm, announced the completion of patient recruitment of a Phase III study with remimazolam in general anesthesia in Russia. R-Pharm currently plans filing for market approval end of 2018.

In December 2017, PAION entered into a remimazolam license agreement with Mundipharma in course of which PAION has granted Mundipharma an exclusive license for the development and commercialization of remimazolam in Japan. Under the terms of the agreement, Mundipharma has the right and obligation to further develop remimazolam in all indications in Japan with PAION's support. Mundipharma will bear all cost for market authorization and distribution. Based on the positive pre-NDA meeting with the Japanese authority, PAION had started preparations for a market approval dossier for remimazolam. Mundipharma has taken over these tasks with PAION's support. Mundipharma currently plans filing for market approval in Japan in 2018.

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

The current development program of PAION's Chinese license partner Yichang Humanwell with remimazolam amongst others includes a Phase II study in general anesthesia and a Phase III study in procedural sedation in China.

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 m	EUR 4 m	10%
Hana Pharm, S. Korea (2013)	EUR 1 m	EUR 2 m	10%
R-Pharm, CIS (2013)	EUR 1 m	EUR 3 m	Low double-digit
(T)R-Pharm, Turkey (2013)	EUR 1 m	EUR 3 m	Low double-digit
(T)R-Pharm, MENA (2014)	EUR 1.5 m	EUR 5.5 m	Low double-digit
Pendopharm, Canada (2014)	EUR 0.4 m*	~ EUR 3.7 m	Tiered (starting at 15%)
Cosmo, U.S. (2016)	EUR 20 m**	EUR 42.5 m	20%–25%***
Mundipharma, Japan (2017)	EUR 1 m	EUR 25 m	Up to over 20%****
<b>Total</b>	<b>EUR 34.8 m</b>	<b>~ EUR 88.7 m</b>	

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

\*\* Comprising EUR 10 million received via private placement in June 2016 and via capital increase with subscription rights conducted in February 2017 as well as the received upfront payment in the amount of EUR 10 million.

\*\*\* Subject to adjustments under specific circumstances, but not below 15% of net sales.

\*\*\*\* Tiered royalties starting in the low double-digits to over 20%



## Net Assets, Financial Position, and Results of Operations

### Results of Operations

	Q2 2018	Q2 2017	H1 2018	H1 2017
	KEUR	KEUR	KEUR	KEUR
Revenues	260	2,032	517	4,083
Gross profit	260	2,032	517	4,083
Research and development expenses	-3,184	-5,851	-6,544	-9,930
General administrative and selling expenses	-966	-980	-1,761	-1,983
Other income (expenses)	30	22	52	9
Operating expenses	-4,120	-6,809	-8,253	-11,904
Operating result	-3,860	-4,777	-7,736	-7,821
Financial result	2	3	4	7
Income taxes	740	1,221	1,489	2,043
Net result for the period	-3,118	-3,553	-6,243	-5,771

**Revenues** in the first half-year 2018 amounted to KEUR 517 compared to KEUR 4,083 in the prior-year period and mainly resulted from the upfront payment of KEUR 1,000 received from Mundipharma in January 2018 under the remimazolam license agreement for Japan entered into in 2017. Revenues in the prior-year period primarily resulted from the license agreement with U.S. license partner Cosmo.

**Research and development expenses** amounted to KEUR 6,544 in the first half-year 2018 and mainly related to expenses in connection with the preparation of the EU Phase III trial in general anesthesia started in July 2018, the validation of commercial scale production as well as preparatory activities for filing for market approval for remimazolam. The decrease of KEUR 3,386 compared to the prior-year period is mainly due to lower costs for Phase III and Phase I studies which had been incurred to a significant extent in the first half-year 2017, particularly in connection with the U.S. development program.

**General administrative and selling expenses** decreased by KEUR 222 to KEUR 1,761 in the first half-year 2018 compared to the prior-year period. General administrative expenses decreased by KEUR 54 to KEUR 1,605 and selling expenses decreased by KEUR 168 to KEUR 156.

**Income taxes** amounted to KEUR 1,489 in the first half-year 2018 (prior-year period: KEUR 2,043) and relate to tax claims for reimbursement of parts of the research and development costs from the British tax authorities. The decrease is primarily attributable to lower research and development costs.

The **net loss** for the first half-year 2018 amounted to KEUR 6,243 compared to a net loss of KEUR 5,771 in the prior-year period. This means an increase of the net loss in the

amount of KEUR 472 compared to the first half-year 2017 which is mainly attributable to lower revenues and lower research and development expenses than in the prior-year period.

## Net Assets

	30-06-2018	31-12-2017	Change
	KEUR	KEUR	KEUR
Non-current assets	2,434	2,528	-94
Current assets	28,990	29,357	-367
Total Assets	31,424	31,885	-461
Equity	24,192	25,229	-1,037
Current liabilities	7,232	6,656	576
Total Equity and liabilities	31,424	31,885	-461

**Non-current assets** mainly comprise the development project remimazolam (KEUR 2,276).

**Current assets** consist of cash and cash equivalents (KEUR 23,267) as well as prepaid expenses and other assets (KEUR 5,723). The reduction of KEUR 367 is mainly attributable to a decrease of cash and cash equivalents by KEUR 1,572 and of prepaid expenses relating to research and development services for remimazolam by KEUR 291 as well as an increase of tax claims for reimbursement of parts of the research and development costs from the British tax authorities by KEUR 1,498.

The decrease in **equity** of KEUR 1,037 compared to 31 December 2017 mainly results from the net loss of the first half-year 2018 in the amount of KEUR 6,243 on the one hand and from net proceeds from the capital increase conducted in June 2018 in the amount of KEUR 5,042 on the other hand. As of 30 June 2018, the equity ratio was 77.0% (31 December 2017: 79.1%).

**Current liabilities** increased by KEUR 576 compared to 31 December 2017 mainly due to an increase of deferred income relating to the remainder of the upfront payment of KEUR 1,000 received from Mundipharma in January 2018 not recognized as revenue yet.

## Financial Position

Compared to 31 December 2017, **cash and cash equivalents** decreased by KEUR 1,572 to KEUR 23,267 at the end of the current reporting period. The change in cash and cash equivalents stems from the following areas:

	H1 2018 KEUR	H1 2017 KEUR
Cash flows from operating activities	-6,626	-7,634
Cash flows from investing activities	-12	-17
Cash flows from financing activities	5,067	4,678
Effects of exchange rate changes	-1	-18
Change in cash and cash equivalents	-1,572	-2,991

The **cash flows from operating activities** in the first half-year 2018 were KEUR -6,626. These primarily result from the net loss (KEUR 6,243) and changes in the working capital, adjusted for the current tax credit claim towards the British tax authorities which has not had a cash effect yet as well as adjusted for the part of the upfront payment of KEUR 1,000 received from Mundipharma in January 2018 which has had a cash effect already but has not been recognized as revenues yet.

The **cash flows from financing activities** of KEUR 5,067 in the first half-year 2018 mainly relate to the net proceeds of the capital increase conducted in June 2018 (KEUR 5,042).

## Personnel Development

On average, PAION employed 38 employees in the first six months of 2018 (fiscal year 2017: 33 employees). As of 30 June 2018, the headcount was 40.

## Changes in the Management Board

Dr. Jürgen Beck was appointed member of the Management Board and Chief Development Officer effective 01 January 2018.

## Risks and Opportunities

Material risks and opportunities relating to future development are presented in detail in the group management report for fiscal year 2017 and have not changed significantly in the first half-year of 2018.

## Significant Events Occurring After the Balance Sheet Date

There were no significant events in the period between the reporting date, 30 June 2018, and the preparation of this report.

## Report on expected developments

### Outlook on Development and Commercialization Activities

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

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

PAION expects its other regional remimazolam partners to continue their development activities towards filing. PAION's partner Mundipharma plans to file for market approval in Japan in 2018. PAION's partner R-Pharm currently plans to file for market approval end of 2018. The current development program of PAION's Chinese license partner Yichang Humanwell with remimazolam amongst others includes a Phase II study in general anesthesia and a Phase III study in procedural sedation in China. PAION's partner Hana Pharm is currently conducting a Phase III study with remimazolam in general anesthesia in South Korea. The partners Pharmascience, Hana Pharm and TR-Pharm plan to file for market approval in their respective territories based on the U.S. or Japanese dossier.

### Financial outlook

PAION expects revenues of about EUR 3 million in 2018, thereof EUR 2 million in connection with the planned regulatory filing for remimazolam in Japan by Mundipharma. Moreover, approx. EUR 1 million are related to the upfront payment received from Mundipharma in January 2018 in course of the remimazolam license agreement for Japan. In case of regulatory filing in the U.S. in the fourth quarter 2018, revenues would increase by EUR 7.5 million in 2018.

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 15 million and approx. EUR 17 million, depending on the progress of development. Income from tax credits on parts of research and development expenses from British tax authorities is expected to amount to approx. EUR 3 million. General administrative and selling expenses are expected to amount to between approx. EUR 3.5 million and approx. EUR 4 million. Net loss is expected to amount to between approx. EUR 12.5 million and approx. EUR 15 million in 2018. Should filing for market approval in Japan be delayed to 2019, revenues and net result would decrease by EUR 2 million.

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

Based on current plans, PAION believes that cash and cash equivalents of EUR 23.3 million as of 30 June 2018 enable PAION to complete all activities for preparation of the filing dossier in procedural sedation in the U.S. PAION expects to receive payments from its license partners, subject to the achievement of certain regulatory milestones, and, once remimazolam is approved, royalties on net sales.

For the ongoing EU Phase III study, no further funding is required based on current planning. Cash and cash equivalents, including expected tax credits from the British tax authorities on parts of research and development expenses and expected potential milestone payments in connection with filings for market approval in the U.S. and Japan, secure the conduct of the Phase III study in the EU based on current cost planning. Overall, this ensures a cash reach until the end of 2019. Until filing for market approval in the EU, further funds of approx. EUR 10 million are required based on current planning. This funding requirement may partly be covered by potential further milestone payments from existing license agreements.

Aachen, Germany, 08 August 2018

PAION AG



Dr. Wolfgang Söhngen



Dr. Jürgen Beck



Abdelghani Omari

## Condensed Consolidated Interim Financial Statements

### Consolidated Balance Sheet

ASSETS	30 June 2018	31 Dec. 2017
	EUR	EUR
<b>Non-current assets</b>		
Intangible assets	2,340,215.02	2,414,870.55
Equipment	93,343.49	113,682.01
Other assets	13.96	13.95
	<b>2,433,572.47</b>	<b>2,528,566.51</b>
<b>Current assets</b>		
Trade receivables	0.00	37,433.15
Prepaid expenses and other assets	5,723,160.09	4,480,716.05
Cash and cash equivalents	23,267,050.78	24,838,652.24
	<b>28,990,210.87</b>	<b>29,356,801.44</b>
<b>Total assets</b>	<b>31,423,783.34</b>	<b>31,885,367.95</b>

EQUITY AND LIABILITIES	30 June 2018	31 Dec. 2017
	EUR	EUR
Equity		
Share capital	63,739,486.00	61,120,046.00
Capital reserve	138,459,479.64	135,854,744.31
Translation reserve	-648,209.88	-630,192.60
Loss carryforward	-171,115,423.14	-159,021,995.85
Result for the period	-6,243,049.40	-12,093,427.29
	<b>24,192,283.22</b>	<b>25,229,174.57</b>
Current liabilities		
Trade payables	5,923,912.64	5,920,968.99
Provisions	487,882.42	390,855.94
Other current liabilities	336,300.25	325,453.79
Deferred income	483,404.81	18,914.66
	<b>7,231,500.12</b>	<b>6,656,193.38</b>
<b>Total equity and liabilities</b>	<b>31,423,783.34</b>	<b>31,885,367.95</b>

## Consolidated Statement of Comprehensive Income

EUR	1 April – 30 June 2018	1 April – 30 June 2017	1 January – 30 June 2018	1 January – 30 June 2017
Revenues	259,784.71	2,031,955.50	517,168.28	4,082,785.14
Gross profit	259,784.71	2,031,955.50	517,168.28	4,082,785.14
Research and development expenses	-3,184,505.66	-5,851,292.97	-6,544,355.73	-9,930,304.60
General administrative and selling expenses	-965,421.53	-979,822.20	-1,760,642.32	-1,982,800.39
Other income (expenses), net	30,441.96	22,840.97	52,353.11	9,621.05
Operating expenses	-4,119,485.23	-6,808,274.20	-8,252,644.94	-11,903,483.94
Operating result	-3,859,700.52	-4,776,318.70	-7,735,476.66	-7,820,698.80
Financial income	1,832.79	2,645.02	3,609.82	7,026.90
Financial result	1,832.79	2,645.02	3,609.82	7,026.90
Result for the period before taxes	-3,857,867.73	-4,773,673.68	-7,731,866.84	-7,813,671.90
Income taxes	739,679.90	1,220,982.10	1,488,817.44	2,042,739.95
Result for the period	-3,118,187.83	-3,552,691.58	-6,243,049.40	-5,770,931.95
of which attributable to other shareholders	0.00	0.00	0.00	0.00
of which attributable to shareholders of PAION	-3,118,187.83	-3,552,691.58	-6,243,049.40	-5,770,931.95
Foreign currency translation	-11,429.13	-197,330.36	-18,017.28	-211,355.20
Total income and expense recognized directly in equity that will be reclassified to profit or loss when specific conditions are met	-11,429.13	-197,330.36	-18,017.28	-211,355.20
Other comprehensive income	-11,429.13	-197,330.36	-18,017.28	-211,355.20
Total comprehensive income	-3,129,616.96	-3,750,021.94	-6,261,066.68	-5,982,287.15
of which attributable to other shareholders	0.00	0.00	0.00	0.00
of which attributable to shareholders of PAION	-3,129,616.96	-3,750,021.94	-6,261,066.68	-5,982,287.15
Earnings per share (basic)	-0.05	-0.06	-0.10	-0.10
Earnings per share (diluted)	-0.05	-0.06	-0.10	-0.10



## Consolidated Cash Flow Statement

EUR	1 January – 30 June 2018	1 January – 30 June 2017
<b>Cash flows from operating activities:</b>		
Result for the period	-6,243,049.40	-5,770,931.95
<b>Reconciliation of net result for the period to cash flows from operating activities:</b>		
Income taxes	-1,488,817.44	-2,042,739.95
Amortization/depreciation and non-cash changes of fixed assets	107,158.87	195,932.29
Loss/Profits from the disposal of non-current assets	0.00	1,167.78
Interest expenses and interest income	-3,609.82	-7,026.90
Release of deferred income	-504,827.40	-3,870,104.47
Expenses from stock option plans	157,461.87	58,520.87
<b>Change in assets and liabilities which are not attributable to investing or financing activities:</b>		
Trade receivables	37,433.15	0.00
Prepaid expenses and other assets	246,138.52	-10,866.64
Trade payables	2,943.65	-152,547.21
Provisions	97,026.48	-94,507.89
Other current liabilities	10,846.46	-79,669.87
Deferred income	969,317.55	-253,799.16
Non-cash exchange losses/gains	-18,183.45	-194,136.44
	<b>-6,630,160.96</b>	<b>-12,220,709.54</b>
Paid income taxes	0.00	-19,696.15
Tax payments received	0.00	4,596,583.91
Interest received	3,844.70	9,472.62
<b>Cash flows from operating activities</b>	<b>-6,626,316.26</b>	<b>-7,634,349.16</b>
<b>Cash flows from investing activities:</b>		
Cash paid for investments in intangible assets and equipment	-12,164.83	-17,346.17
<b>Cash flows from investing activities</b>	<b>-12,164.83</b>	<b>-17,346.17</b>
<b>Cash flows from financing activities:</b>		
Capital increase	2,619,440.00	2,499,497.00
Contributions to the capital reserve	2,605,054.40	2,587,574.29
Payments in connection with raising capital	-157,780.94	-409,120.99
<b>Cash flows from financing activities</b>	<b>5,066,713.46</b>	<b>4,677,950.30</b>
Change in cash and cash equivalents	-1,571,767.63	-2,973,745.03
Effect of exchange rate changes on cash	166.17	-17,218.79
Cash and cash equivalents at beginning of the period	24,838,652.24	30,111,355.87
<b>Cash and cash equivalents at end of the period</b>	<b>23,267,050.78</b>	<b>27,120,392.05</b>
<b>Composition of cash and cash equivalents at the end of the period:</b>		
Cash and cash equivalents	23,267,050.78	27,120,392.05

## Consolidated Statement of Changes in Equity

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	-211,355.20	-5,770,931.95	-5,982,287.15
Issue of shares	2,499,497.00	0.00	0.00	0.00	2,499,497.00
Contribution to the capital reserve	0.00	2,587,574.29	0.00	0.00	2,587,574.29
Cost of raising capital	0.00	-409,120.99	0.00	0.00	-409,120.99
Additional contribution to the capital reserve due to the issue of options	0.00	58,520.87	0.00	0.00	58,520.87
30 June 2017	58,256,591.00	130,785,776.74	-552,132.57	-164,792,927.80	23,697,307.37
Total comprehensive income	0.00	0.00	-68,286.69	-6,322,495.34	-6,390,782.03
Issue of shares	2,863,455.00	0.00	0.00	0.00	2,863,455.00
Contribution to the capital reserve	0.00	5,230,969.87	0.00	0.00	5,230,969.87
Cost of raising capital	0.00	-277,956.15	0.00	0.00	-277,956.15
Additional contribution to the capital reserve due to the issue of options	0.00	115,953.85	0.00	0.00	115,953.85
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	-18,017.28	-6,243,049.40	-6,261,066.68
Issue of shares	2,619,440.00	0.00	0.00	0.00	2,619,440.00
Contribution to the capital reserve	0.00	2,605,054.40	0.00	0.00	2,605,054.40
Cost of raising capital	0.00	-157,780.94	0.00	0.00	-157,780.94
Additional contribution to the capital reserve due to the issue of options	0.00	157,461.87	0.00	0.00	157,461.87
30 June 2018	63,739,486.00	138,459,479.64	-648,209.88	-177,358,472.54	24,192,283.22

## Selected Explanatory Notes to the Consolidated Interim Financial Statements as of 30 June 2018

### General

The half-year financial report of PAION AG includes interim consolidated financial statements and an interim group management report in accordance with the provisions of Sec. 115 (2) WpHG [“Wertpapierhandelsgesetz”: German Securities Trading Act] in conjunction with Sec. 117 WpHG as well as a statement of the management board according to Secs. 264 (2) sentence 3 and 289 (1) sentence 5 HGB [“Handelsgesetzbuch”: German Commercial Code]. The consolidated financial statements were prepared in accordance with the provisions of the International Financial Reporting Standards (IFRSs) for interim financial reporting. The interim group management report was prepared in accordance with the relevant provisions of the German Securities Trading Act.

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

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

### Basis of Accounting

The interim consolidated financial statements have been prepared in accordance with Sec. 315e (1) HGB [“Handelsgesetzbuch”: German Commercial Code] and IFRSs, as adopted by the EU, and the interpretations of the International Financial Reporting Interpretations Committee (IFRIC). The consolidation principles and accounting policies adopted in the preparation of the interim condensed consolidated financial statements are consistent with those followed in the preparation of the Group’s annual consolidated financial statements for the year ended 31 December 2017, except for the adoption of

the following new or revised standards effective for the current reporting period:

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

The application of these new and/or revised standards may, in some cases, result in additional disclosure obligations in future consolidated financial statements. All disclosure obligations in interim consolidated financial statements resulting from first-time adoption of new standards in the current reporting period have been met accordingly. The amendments did not have any effects on the Group’s net assets, financial position and results of operations.

First-time adoption of IFRS 9 has not led to the identification of default risks.

In the course of first-time adoption of IFRS 15, the cumulative effect method was applied leading to no transition effects.

The provisions of IAS 34, “Interim Financial Reporting”, have been applied. The interim financial statements as of 30 June 2018 should be read in conjunction with the consolidated financial statements as of 31 December 2017.

The preparation of interim consolidated financial statements in accordance with IFRSs requires management to make estimates and assumptions which

have an effect on the amount of recognised assets and liabilities, income and expenses and contingent liabilities. Actual amounts may differ from these estimates.

The interim consolidated financial statements do not contain any segment information as no material reportable segments could be identified.

## Foreign Currency Translation

The consolidated financial statements are shown in Euro, 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 and Pound Sterling for the UK-based companies. All items on the respective financial statements of each company are initially converted to the functional currency at the exchange rate applicable on the transaction date. Monetary assets and liabilities denominated in a foreign currency are translated into the functional currency on the reporting date at the exchange rate applicable on that date. All ensuing currency differences are recognised 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 recognised in equity.

The assets and liabilities of the foreign companies are translated into Euro on the balance sheet reporting date at the exchange rate applicable on that date. 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. The resulting currency differences are accounted for separately within equity.

## Equity

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 30 June 2018.

## Stock options

On 18 January 2018, 55,500 stock options were granted from Stock Option Plan 2014. From Stock Option Plan 2016, 45,500 stock options were granted on 18 January and 449,500 stock options were granted on 23 June 2018.

In connection with the stock options granted from Stock Option Plan 2014 in 2015, 2016 and 2018 and in connection with the stock options granted from Stock Option Plan 2016 in 2017 and 2018, personnel expenses in the amount of KEUR 157 were recognized in the first half-year 2018.

In the first half-year 2018, 19,440 stock options were exercised from the Stock Option Plan 2008. This led to cash inflows of KEUR 25. The new shares have not been recorded in the commercial register so far.

## Tax Effects on Other Comprehensive Income

In the reporting period the Other Comprehensive Income (foreign currency translation of foreign subsidiaries) did not have any tax effects.

## Fair value of financial assets and liabilities

As of 30 June 2018 and as of 31 December 2017, the fair value of financial assets and liabilities was identical to the respective book value.

in KEUR	Book value		Fair Value		
	30 June 2018	31 Dec. 2017	30 June 2018	31 Dec. 2017	
<b>Financial assets</b>					
Cash and cash equivalents	(1)	23,267	24,839	23,267	24,839
Trade receivables	(1)	0	37	0	37
Other assets	(1)	54	7	54	7
<b>Financial liabilities</b>					
Provisions	(2),(3)	488	391	488	391
Trade payables	(2),(3)	5,924	5,921	5,924	5,921
Other liabilities	(2),(3)	218	154	218	154

Measurement category according to IAS 39:

- (1) Loans and receivables
- (2) Liabilities recognised at amortised cost
- (3) Lead to cash outflows

The determination of the fair values of these financial instruments was based on unobservable input factors (Level 3 inputs according to IFRS 13). In the first half-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.

## Related Parties

The relationships with related parties have not changed in comparison to those applied in the consolidated financial statements as of 31 December 2017.

**Declaration of the Management Board  
pursuant Secs. 264 para. 2 sentence 3 and  
289 para.1 sentence 5 HGB [German  
Commercial Code]**

“To the best of our knowledge and in accordance with the applicable reporting principles for interim financial reporting, the consolidated interim financial statements give a true and fair view of the assets, liabilities, financial position and profit or loss of the group, and the interim management report of the group 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 for the remaining months of the financial year.”

Aachen, Germany, 08 August 2018

PAION AG



Dr. Wolfgang Söhngen



Abdelghani Omari



Dr. Jürgen Beck

# Review Report

## To PAION AG, Aachen:

We have reviewed the condensed consolidated interim financial statements - comprising the condensed statement of financial position, the condensed statement of comprehensive income, the condensed statement of cash flows, the condensed statement of changes in equity and selected explanatory notes - together with the interim group management report of PAION AG, Aachen, for the period from January 1 to June 30, 2018, part of the six-monthly financial report pursuant to § (Article) 115 WpHG ("Wertpapierhandelsgesetz": German Securities Trading Act). The preparation of the condensed consolidated interim financial statements in accordance with the IFRS applicable to interim financial reporting as adopted by the EU and of the interim group management report in accordance with the provisions of the German Securities Trading Act applicable to interim group management reports is the responsibility of the parent Company's Board of Managing Directors. Our responsibility is to issue a review report on the condensed consolidated interim financial statements and on the interim group management report based on our review.

We conducted our review of the condensed consolidated interim financial statements and the interim group management report in accordance with German generally accepted standards for the review of financial statements promulgated by the Institut der Wirtschaftsprüfer (Institute of Public Auditors in Germany) (IDW) and additionally in accordance with the International Standard on Review Engagements "Review of Interim Financial Information Performed by the Independent Auditor of the Entity" (ISRE 2410). Those standard require that we plan and perform the review so that we can preclude through critical evaluation, with moderate assurance, that the condensed consolidated interim financial statements have not been prepared, in all material respects, in accordance with the IFRS applicable to interim financial reporting as adopted by the EU and that the interim group management report has not been prepared, in all material respects, in accordance with the provisions of the German Securities Trading Act applicable to interim group management reports. A review is limited primarily to inquiries of company personnel and analytical procedures and thus provides less assurance than an audit. Since, in accordance with our engagement, we have not performed a financial statement audit, we cannot express an audit opinion.

Based on our review, no matters have come to our attention that cause us to presume that the condensed consolidated interim financial statements have not been prepared, in all material respects, in accordance with the IFRS applicable to interim financial reporting as adopted by the EU nor that the interim group management report has not been prepared, in all material respects, in accordance with the provisions of the German Securities Trading Act applicable to interim group management reports.

Cologne, Germany, August 8, 2018

Ernst & Young GmbH

Wirtschaftsprüfungsgesellschaft

(s) Zwirner

(s) Conrad

Wirtschaftsprüfer

Wirtschaftsprüfer

[German Public Auditor] [German Public Auditor]

## Information on PAION Shares

Market segment	Regulated market – Prime Standard Frankfurt Stock Exchange
Ticker symbol	PA8
Reuters symbol	PA8G.DE (Xetra)
Bloomberg	PA8 GY (Xetra)
ISIN	DE000A0B65S3
First day of trading	11 February 2005
Designated sponsor	Oddo Seydler, Baader Bank AG

Key figures	H1 2018	2017
Numbers of shares at the end of the period	63,739,486	61,120,046
Average daily trading volume (Xetra, FSE)	68,328	193,073
Year high (Xetra closing price)	EUR 2.70 (02 Jan 2018)	EUR 3.30 (26 Jun 2017)
Year low (Xetra closing price)	EUR 2,04 (12 Jun 2018)	EUR 2.15 (22 Mar 2017)
Share price at the end of the period	EUR 2.10	EUR 2.71
Market capitalization at the end of the period (Xetra)	EUR 133 m	EUR 166 m

## Corporate Calendar

22 March 2018	Publication of the financial results 2017
09 May 2018	Publication of the financial results of the first quarter 2018
23 May 2018	Annual General Meeting, Aachen
08 August 2018	Publication of the financial results of the second quarter and the first half-year 2018
07 November 2018	Publication of the financial results of the third quarter and the first nine months of 2018



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