# PAION Earnings Call

## Financial Results H1 2020

Dr. Jim Phillips, CEO | Abdelghani Omari, CFO

Conference Call | 12 August 2020

PAION

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# AGENDA

1 **Corporate Overview**

2 Remimazolam

3 Financials

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# Corporate overview

PAION AG is an emerging specialty pharma company with a focus on anesthesia critical care products

Remimazolam, PAION's lead drug candidate, has multiple approvals in U.S. & Asia

PAION has commercial partners for remimazolam in the U.S., China, South Korea, Southeast Asia, Canada, Russia + CIS, Turkey, Japan and the MENA region

EUR 12.4 million cash and cash equivalents (30 June 2020)

## Supervisory Board

Dr. Jörg Spiekerkötter (Chairman)
Background: Former CFO, Schering AG, Organon

Dr. Karin Dorrepaal
Background: Former Schering AG Board Member

Dr. Dr. Irina Antonijevic
Background: Senior VP Development Triplet Therapeutics

Dr. Chris Tanner
Background: Non-Executive Director Cosmo Pharmaceuticals

Dr. Markus Leyck Dieken
Background: Managing Director Gematik

# PAION Strategy

- Bring remimazolam to market over 2020-2022
- Build a commercial capability in attractive geographies in Anesthesia & Critical Care
- Launch remimazolam & in-licence complimentary medications to grow revenue
- Reach profitability within the next 5 years as a leader in our field with fast revenue growth

# PAION Commercialization plans

- PAION continues to conduct pre-commercial activities
- The build-up of its own distribution structure in Europe is dependent on PAION's ability to add more products to its commercial portfolio
- Thus, PAION is also considering outlicensing remimazolam for commercialization in Europe
- Supply chain activities
  - PAION is building up the supply chain in order to be able to regularly provide remimazolam product to the licensees as well for PAION's potential own commercialization
  - Activities include establishing structures and processes and obtaining all necessary pharmaceutical permits and will be implemented in the second half of 2020

# Management Board

**Dr. James (Jim) Phillips, CEO**
Dr. Jim Phillips was appointed Chief Executive Officer in 2019. He is a physician who also holds an MBA from the Cass Business School in London. Dr. Phillips holds a supervisory board directorship at Herantis Pharma.
Career: Managing Director Imexvax, CEO Midatech Pharma, President of EUSA Pharma Europe in its key growth phase prior to its sales to Jazz Pharma in 2012, CEO and founder of Talisker Pharma, Chairman of Prosonix, senior executive for Johnson & Johnson and Novartis

**Abdelghani Omari, CFO**
Mr. Abdelghani Omari holds a degree in Business Administration from the University Aachen and was appointed Chief Financial Officer in 2014. He has more than 19 years experience in Finance.
Career: At KPMG he adviced international clients on accounting, post-merger integration and financial reporting and also worked several years in the audit department with a focus on the chemical industry

**Dr. Jürgen Beck, CDO**
Dr. Jürgen Beck was appointed Chief Development Officer in 2017. He is a physician and holds a diploma in business administration. Dr. Beck has over 25 years of experience in the European pharma business.
Career: Senior management positions at Synthélabo, Managing Director of Monitoring Force GmbH, Senior Vice President at Epigenomics and Vice President at InterMune International AG

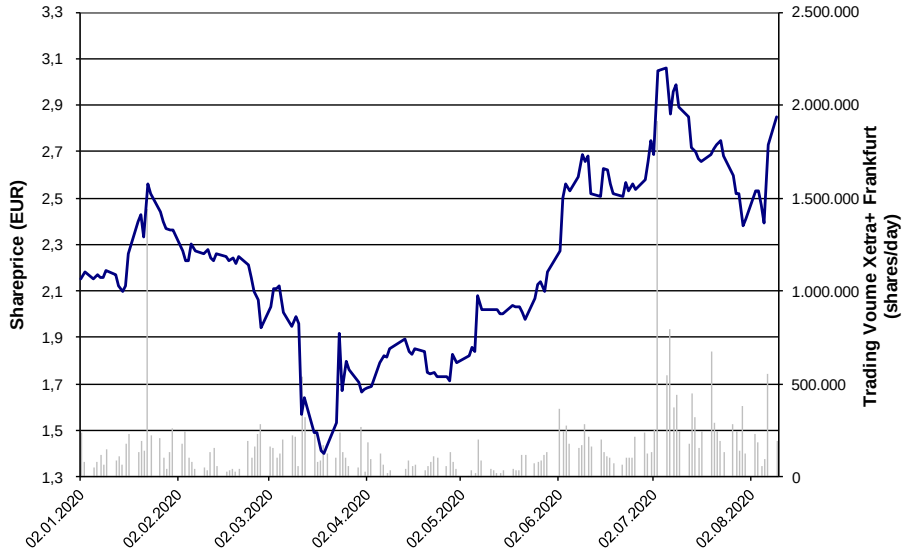
# PAION AG is listed on Frankfurt Stock Exchange

**Listed on Frankfurt Stock Exchange, Prime Standard**
(FSE: PA8)

**Market capitalization:**
cEUR200 m

**Liquidity (last six months)**
(Xetra, Tradegate & FRA stock markets):
**32 million shares traded**

## Stock Performance (2020)
(price and volume in EUR)




## Market Data

| Capitalization (as of 11 August 2020) | |
|---|---|
| Current Share Price | € 2.95 |
| FD Shares Outstanding | 66.2 million |
| Market Cap | c€ 200m |
| Mean target price of analyst reports (Edison, First Berlin, FMR) | € 4.72 |

# Short-term value drivers

# PAION has strong reserves in the current economic crisis

- Cash of approx. €12m (as of 30 June 2020)
- FDA Approval milestone of €15m from Cosmo (received in July 2020)
- R&D cash tax credits (for 2019 and 2020) of €3 to €4m
- EIB Loan facility of €20m

**TOTAL AVAILABLE CASH & RESERVE FACILITIES APPROX. €50m**

**This represents 2.5 years Cash at current spend**

**We could extend to 3 years plus**

# Covid-19 at PAION

- The pandemic has only led to minor direct effects on the PAION group to date
- All staff can nearly entirely work from home
- We have implemented virtual meetings
- On an operational level, the pandemic led to an earlier completion of patient recruitment of the EU Phase III study
  - Since a large part of the originally planned number of patients of the study had already been recruited at that time, PAION does not expect an impact on the activities planned subsequently.
- Likely Budget Impact 2020
  - No revised outlook due to the coronavirus pandemic
- Since the supply chain is only being established, there have been no direct effects of the pandemic to date

# Compassionate Use Italian Hospital

- The local Ethics Committee of the Hospital San Raffaele in Milan/Italy granted approval for the compassionate use of remimazolam for the use of sedation of five intensive care unit (ICU) patients with COVID-19 in June 2020

- PAION had been contacted by the San Raffaele Hospital as to whether remimazolam could be delivered due to a shortage of propofol and midazolam caused by the coronavirus pandemic

- PAION fulfilled the request from the hospital and supplied the material free of charge.

- Due to the currently much more relaxed situation in the hospital with regard to COVID-19 patients on the ICU, an extension to other patients is not planned for now

# Compassionate Use Belgium

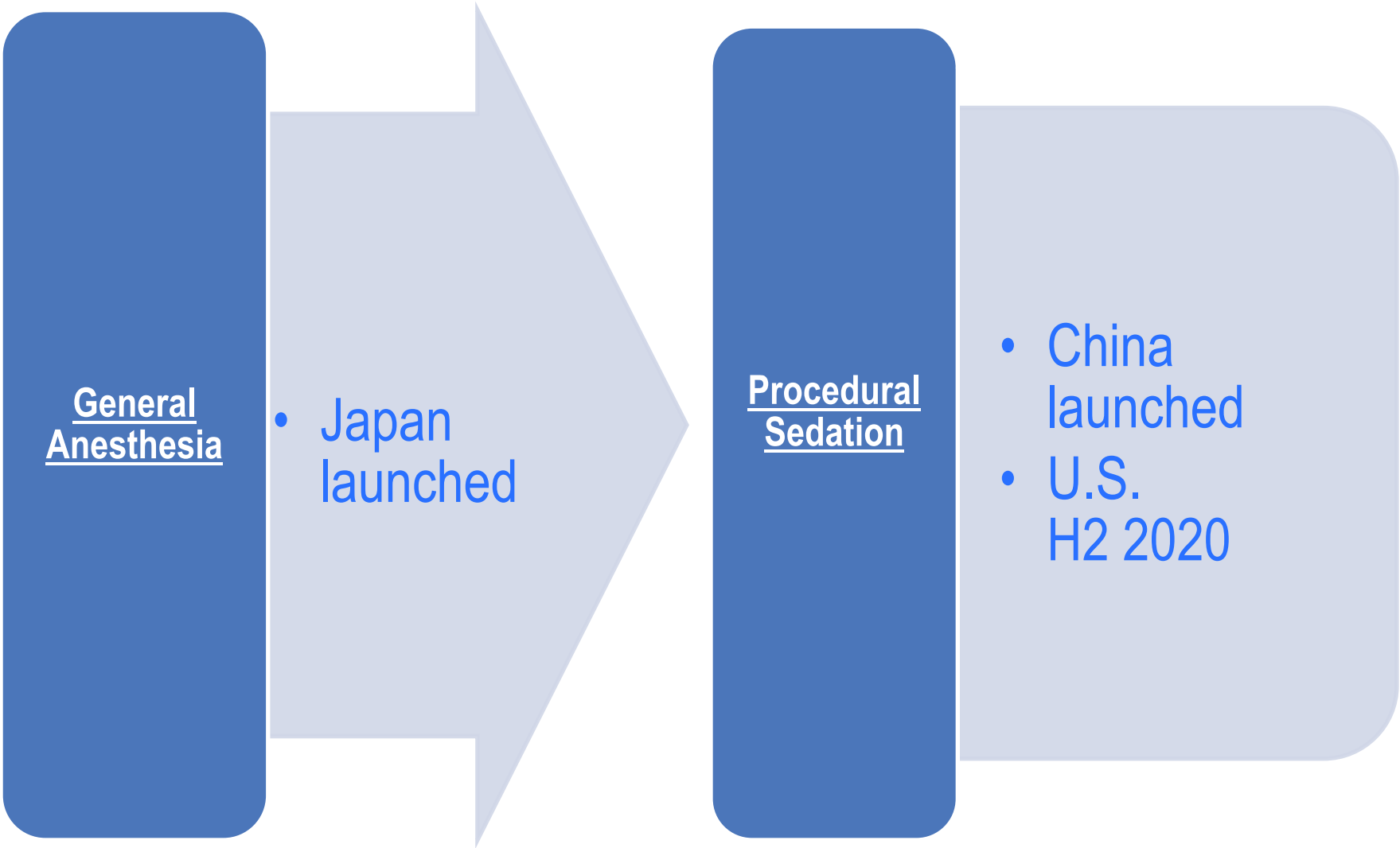
- In August 2020, the FAMHP granted approval for the compassionate use of remimazolam in Belgium

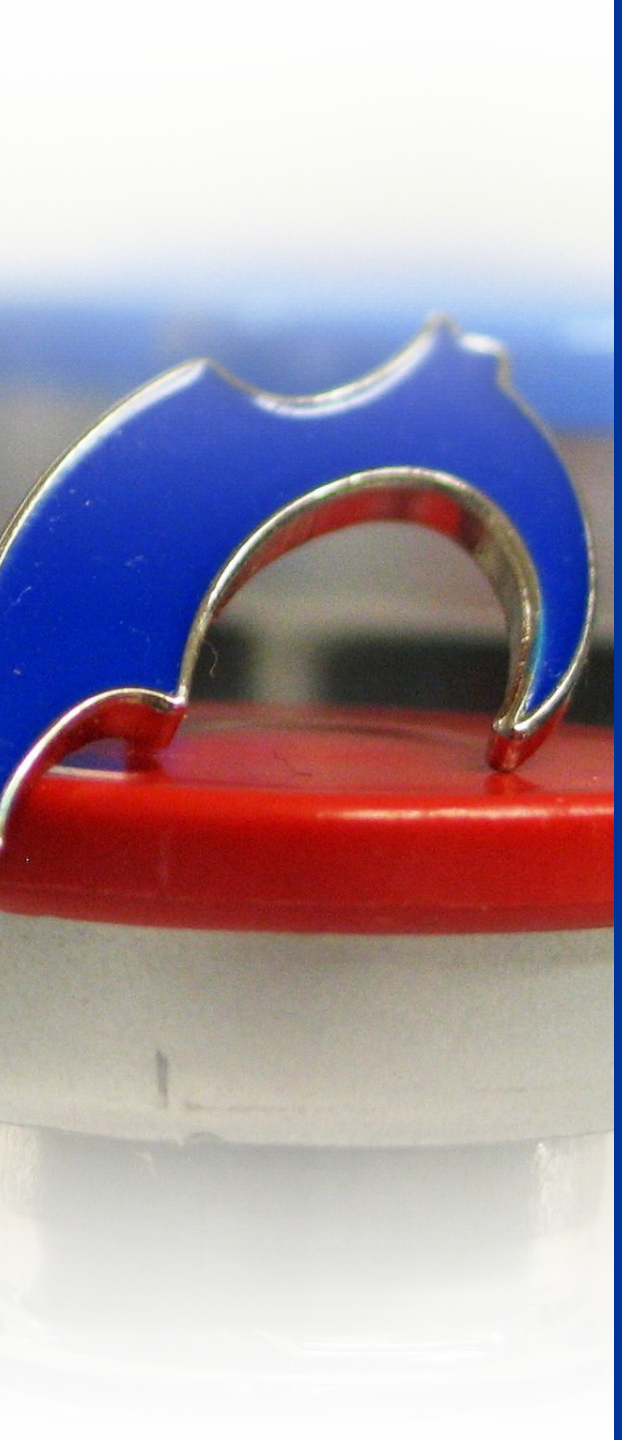
- Remimazolam can be used for
  - sedation of intensive care unit patients with COVID-19
  - as a substitute for current standard of care in general anesthesia for which there are currently shortages due to the coronavirus pandemic

- The use is limited to physicians who have experience with remimazolam

- PAION will deliver the material initially free of charge

# Launch Sequence 2020 (subject to Covid-19 Impact)





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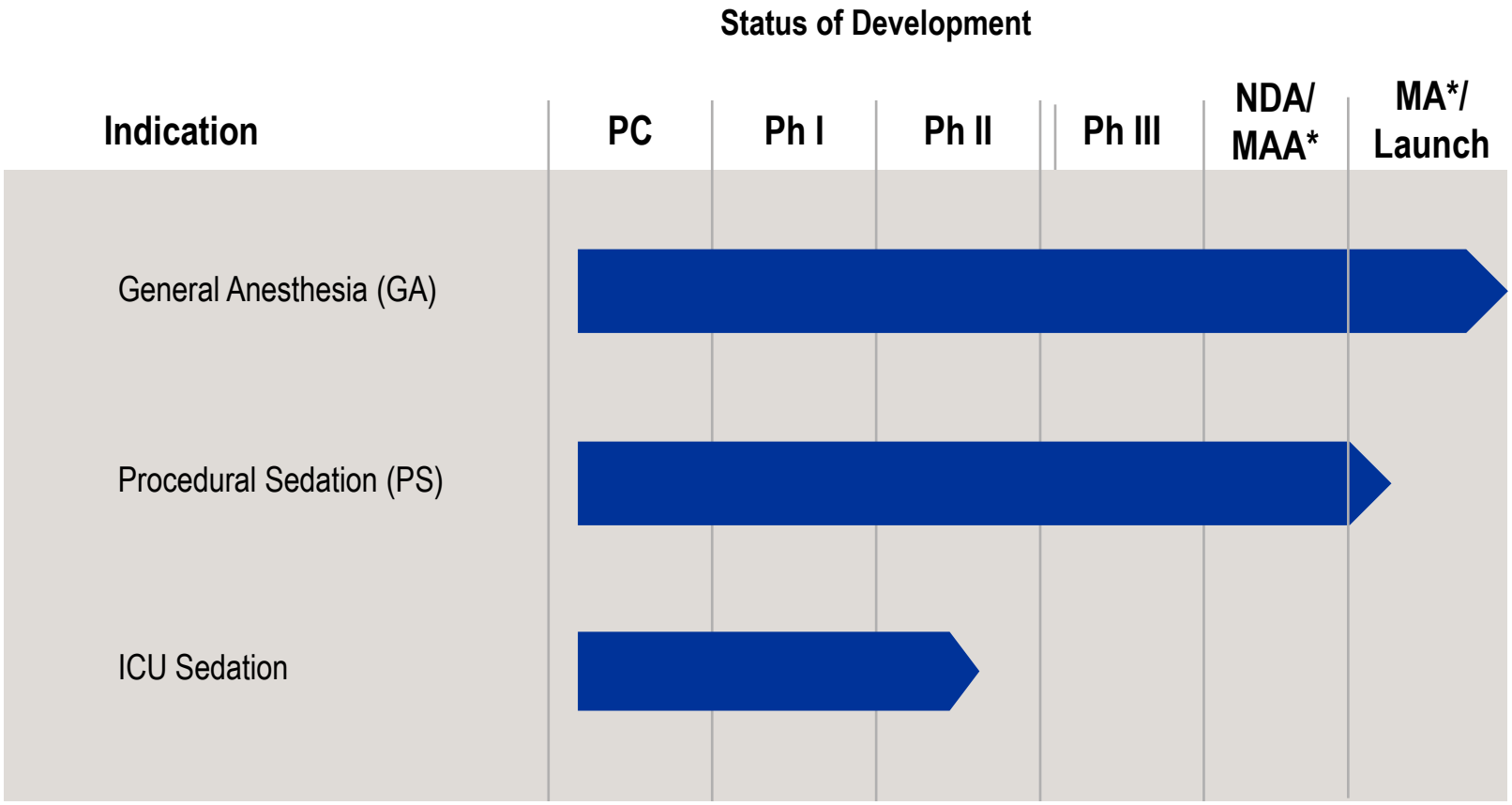
# Remimazolam - Potential in three indications




* NDA = New Drug Application; MAA = Marketing Authorization Application; MA = Market Approval

# The ideal drug would combine “the best of both worlds”*

| Propofol | Remimazolam | | Midazolam |
|---|---|---|---|
| ⊖ | ⊕ | ⊕ | ⊖ |
| • CV/Respiratory depression<br>• No reversal agent<br>• Pain on injection | • Rapid onset/offset<br>• Predictable recovery time<br>• Less resources for supervision (after procedure) | • Lower safety issues<br>• Reversal agent<br>• Less resources for supervision (during procedure) | • Variable and prolonged periods of sedation<br>• Re-sedation risk<br>• Slow onset |

→ **Remimazolam offers the opportunity to substitute both midazolam and propofol in an attractive market setting**

* said Physicians at the first ever Market Research performed in 2008 by the Company



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# Remimazolam (BYFAVO™ / Anerem® / Ruima®) – Potential to address important issues

## Need for improvement in the sedation/anesthesia space

| | |
|---|---|
| **Safety** | • Improved overall safety<br>• Avoidance of hypotension<br>• Availability of a reversal agent<br>• Improved hemodynamic stability<br>• Less requirement for vasopressors<br>• Better suited for aging patient populations |
| **Efficiency** | • Predictability of overall procedure time<br>• Improved patient throughput |
| **Patient experience** | • Amnesia of procedure with quick regaining of cognitive function<br>• "Back to normal" achieved quicker than with midazolam<br>→ improved compliance to follow-up screening<br>• Improved patient satisfaction and compliance |
| **Cost saving** | • Reduced resources for supervision |

# Remimazolam (BYFAVO™ / Anerem® / Ruima®) – Status

| | |
|---|---|
| **Class** | • First-in-class ultra-short-acting intravenous benzodiazepine sedative/anesthetic |
| **IP** | • Besylate salt – Protection until at least 2031 in the U.S.<br>• Formulation Patent – Protection until at least 2033 in the EU<br>• Dosing Patent – Protection until at least 2033 in Japan<br>• Growing IP portfolio to secure attractive period of market exclusivity in major markets |
| **Safety** | • Extensive safety and efficacy database<br>→ ~ 2,900 volunteers/patients to date |
| **Indications** | • Procedural Sedation in the U.S., EU & China<br>• General Anesthesia in the EU, Japan, Russia and South Korea<br>• Further potential in ICU sedation<br>→ Estimated market opportunity >$500 m globally for each indication alone* |
| **Results to date indicate** | • Solid efficacy and safety in studied populations<br>• Rapid onset and offset of action<br>• Appropriate depth of sedation<br>• Favorable hemodynamic stability |

* PAION estimates



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# Remimazolam – Procedural Sedation

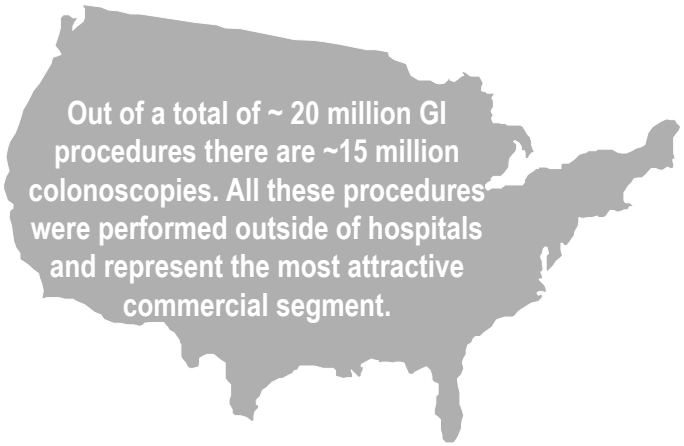
# U.S. Market Size

**Rapidly growing market, big push for colorectal cancer screening:**

- Regular and appropriate colorectal cancer screening is both recommended and covered by all major health plans including CMS
- More than 4 million patients turn 50 and are newly eligible each year, baby boomers are all “of age” for screening, i.e. > 50 years
- Potential for millions more covered lives in the U.S. as a result of the Affordable Care Act

## U.S. Market Size*

Total U.S. market for procedural sedation = 43 million procedures




26.7 million unique procedure claims for colonoscopy and endoscopy in 2015

Source: *I DATA Market Report on US Gastrointestinal Endoscopic Device Market - 2016*

Source: *Ambulatory Surgery in the United States, 2006, National Health Statistics Reports Number 11, U.S. Department of Health and Human Services* and PAION projections based on *Symphony Health Solutions (2013), Colonoscopy: Scoping & Mapping*)

Various data sources indicate that between 20-27% of procedures are done in hospitals. 2006 CDC/NCHS, National survey of Ambuatory Surgery(NSAS) and National Hospital Discharge Survey (NHDS) (27%). Qualitative market research by Kennedy associates for PAION Inc. 2015 (20%).

* Based on primary market research performed by PAION

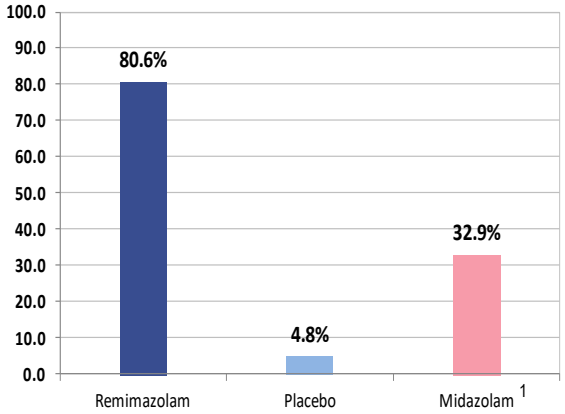
# Remimazolam: Clinical development program successfully completed in Procedural Sedation in the U.S. and China

## Three U.S. trials with positive results*

Phase III trial in Procedural Sedation in patients undergoing bronchoscopy (n = 446)

**Phase III bronchoscopy (ASA I–III)**

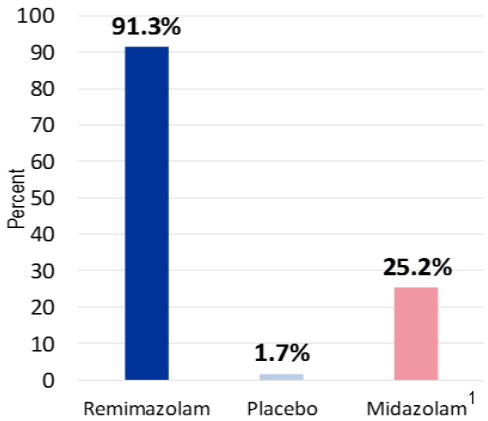
Success of procedure




Phase III trial in Procedural Sedation in patients undergoing colonoscopy (n = 461)

**Phase III colonoscopy (mostly ASA I–III)**

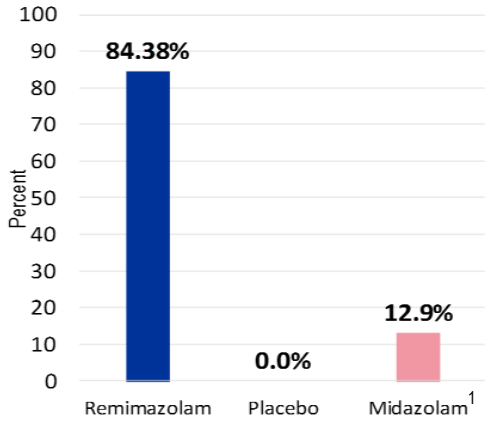
Success of procedure




Safety study in ASA III/IV (high-risk) patients undergoing colonoscopy (n = 79)

**ASA III/IV patients**

Success of procedure




1. Open label

* Phase III trials performed by PAION

# U.S. pivotal Phase III study in colonoscopy: Supports business case (ability to treat more patients)

| Time from start of medication to start of procedure | minutes |
|---|---|
| Remimazolam – 5.0/2.5 mg | **4.0** |
| Midazolam – 1.75/1.0 mg (1.0/0.5 mg in the elderly and debilitated) | 19.0 |

| Time from end of procedure to fully alert | minutes |
|---|---|
| Remimazolam – 5.0/2.5 mg | **6.0** |
| Midazolam – 1.75/1.0 mg | 13.0 |

**With an average reduction of 22 min/procedure and an average number of procedures of 10/day/doctor with midazolam, centers could increase throughput significantly**

# Remimazolam – Procedural Sedation EU

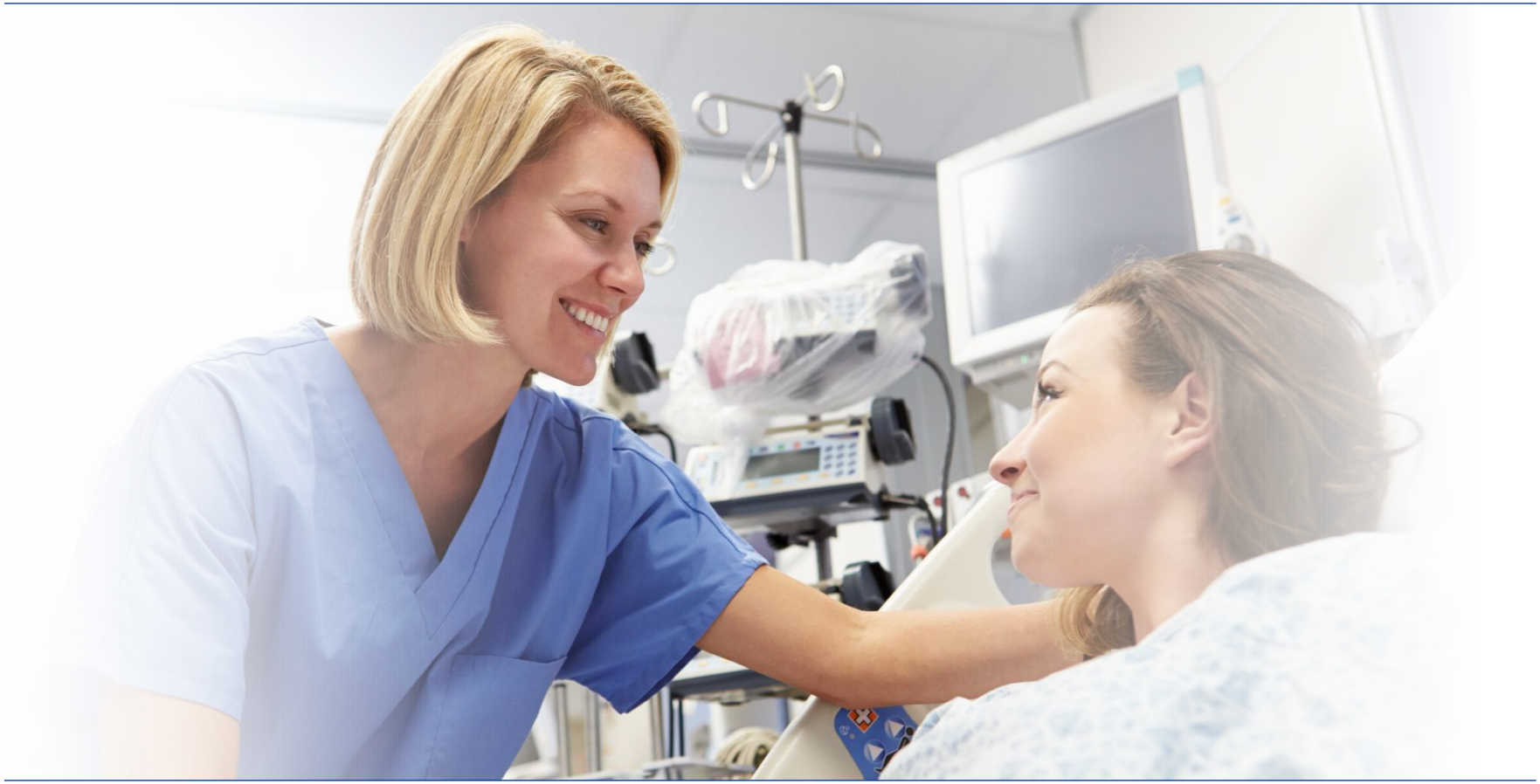
- PAION submitted an MAA based on the completed U.S. development program in November 2019

- Commercialization of remimazolam in Europe

  - Build-up of an own distribution structure in Europe is dependent on the possibility of extending the portfolio by additional products

  - PAION also considers the option to outlicense remimazolam for Europe as an alternative to building up an own distribution structure

# Remimazolam – General Anesthesia



# General Anesthesia – Room for improvement

- Little innovation in anesthetic drug development in recent years
- Aging population with increasing levels of co-morbidity → complication rates associated with General Anesthesia/surgery are increasing
- Low awareness concerning post-operative complications & mortality related to intra-operative hypotension events
  - Intra-operative hypotension as strong predictor of myocardial necrosis leading to higher 1-year post–surgical mortality[1–4]
  - Even short durations of intra-operative hypotension associated with acute kidney, myocardial injury, cardiac complications and 30-day mortality[4]
  - Connection between intra-operative hypotension and post-operative cognitive dysfunction[5]

→

- With remimazolam, there is a significantly lower incidence of hypotension in surgical patients undergoing General Anesthesia compared to propofol[6]
- Opportunity for remimazolam to impact patient care and outcomes in General Anesthesia

1. Brady _Anesth_2013_119_495-7 2.Bjiker_Anesthesiology_2009; 111:1217–26 3. Monk_Anesth Analg 2005; 100:4–10 4. Walsh_Anesth_2013_119_507–15 5. Slide 28 and 29 6. ONO study report _Data on file



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# Perioperative Myocardial Injury is Common, Silent and Deadly

- 8 million adults with MINS worldwide
- 93% without symptoms
- 4% mortality at 30d
- 8.5% have myocardial infarction, cardiac arrest or death in 30d

Source: Vascular Events In Noncardiac Surgery Patients Cohort Evaluation Study

# Intraoperative Hypotension (IOH) is root cause for MINS

*JAMA*. 2019;321(5):459-460. doi:10.1001/jama.2019.0164 (Editorial on the ENGAGES trial)

## Depth of Anesthesia and Postoperative Delirium

Thomas E. F. Abbott, PhD, MRCP[1]; Rupert M. Pearse, MD, FRCA[1]

The principal finding of this trial was that the incidence of postoperative delirium was not significantly different between groups, occurring in 157 of 604 patients (26%) in the EEG-guided group compared with 140 of 609 patients (23%) in the usual care group. However, the dose of anesthetic agent delivered (minimum alveolar concentration) was lower in the EEG-guided group (0.69) compared with the usual care group (0.80). An unexpected finding was that 30-day mortality was also lower in the EEG-guided group (0.7% vs 3.1%).

On one hand, proposed applications for the use of EEG-guided anesthesia for prevention of unintentional awareness under anesthesia, and perhaps prevention of delirium, have not been supported. On the other hand, a reduction in hypotension-related myocardial injury would likely save many lives. The choice of anesthetic dose remains critically important in the context of an aging surgical patient population, and the role of good-quality, safe anesthesia is as important as ever.



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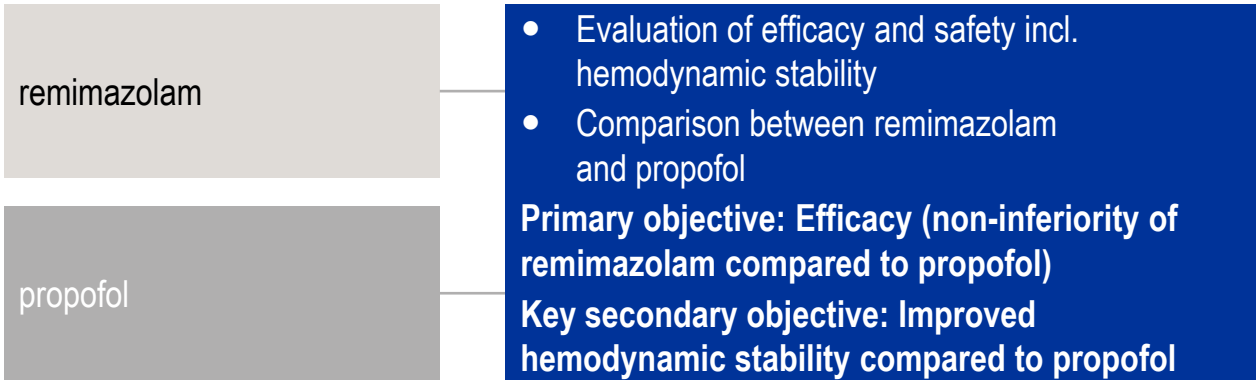
# EU-Phase III: General Anesthesia (ASA III/IV)

- EU Phase III study (N 424)
  - Multicenter, randomized and active-controlled European (EU) Phase III trial in 424patients undergoing elective surgery
  - Countries: Germany, France, Italy, Switzerland, The Netherlands, UK, Belgium
  - Due to the coronavirus pandemic, patient recruitment was completed in April 2020 with 424 patients enrolled, as agreed to by the Data Monitoring Committee
  - Topline data of the trial are expected in the second half of 2020



# General Anesthesia EU: Next steps

- Due to the coronavirus pandemic, patient recruitment was completed in April 2020 with 424 patients enrolled, as agreed to by the Data Monitoring Committee

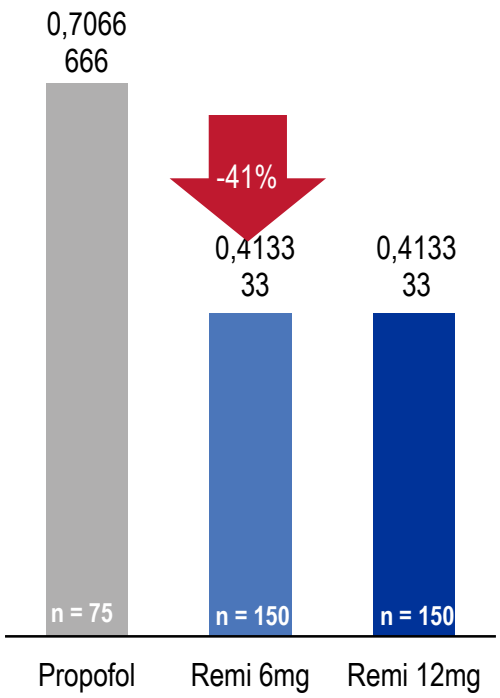
- Following approval in procedural sedation, an extension of the dossier to also include general anesthesia is planned. This would allow for an abbreviated application for general anesthesia that is generally processed faster

# Remimazolam clinical data (General Anesthesia – ASA I/II): Phase IIb/III pivotal trial: post hoc analyses

## In Hypotension

Patients with MAP < **60** mm Hg
First hour after intubation

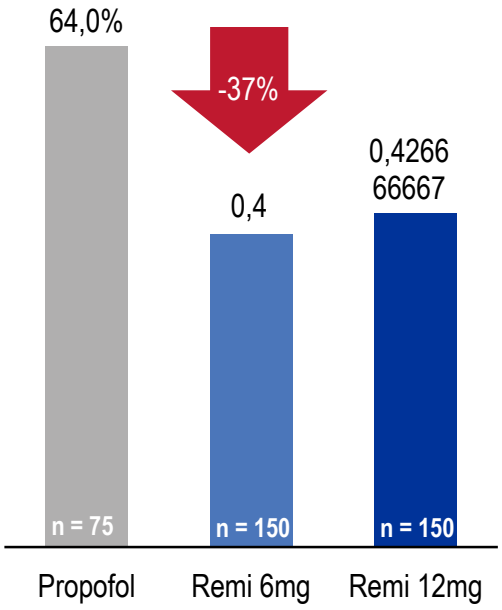
**NNT = 3.4**




## Need for Vasopressors

Share of patients with any vasopressor entire study

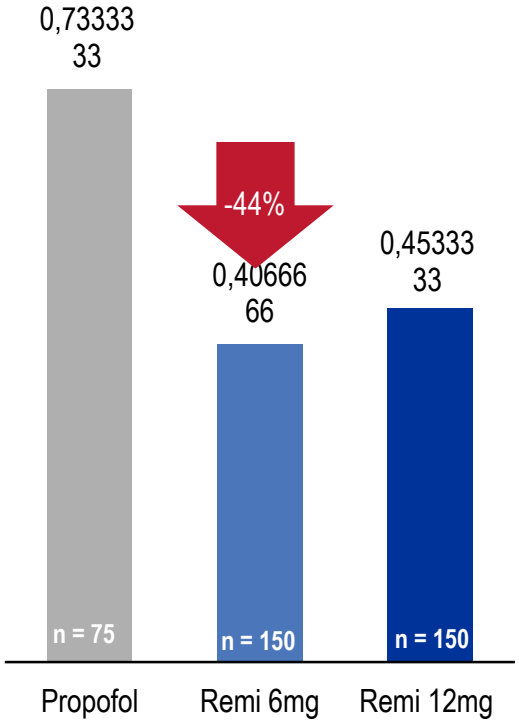
**NNT = 4.2**



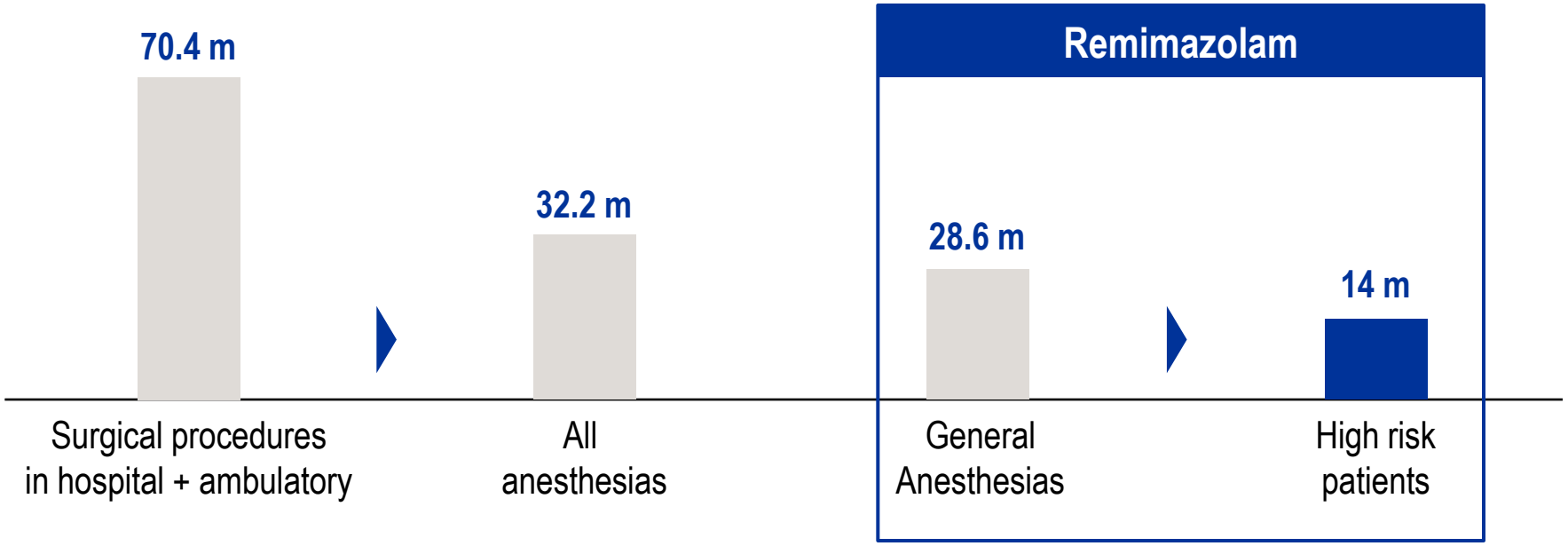

## Too deep sedation

Share of patients with BIS score below **40** until 1 h after intubation

**NNT = 3.1**



# EU: Remimazolam's launch target population[1] – 14 million high risk patients (e.g. ASA III/IV, co-morbidities)




- Patient demographics continue to evolve driven by the aging population and the differences between the functional or physical ages of patients compared to actual age
- General Anesthesia is more frequently offered to elderly patients than years ago but the choice is an individual one depending on the type of surgery, the underlying disease and assessment of the general physical health of the patient, including co-morbidities

1. Modeled data combining 2010 and 2012 national and regional statistics

# PAION's commercial partners

## U.S. – Acacia

- **Lead indication: Procedural Sedation**
- Market approval received in July 2020
- Acacia plans to launch remimazolam in H2 2020

## Japan – Mundipharma

- **Lead indication: General Anesthesia**
- Market approval received in January 2020
- Mundipharma successfully launched remimazolam in mid-2020 with first commercial product sales

## China – Yichang Humanwell

- Indications General Anesthesia + Procedural Sedation
- Yichang Humanwell received market approval in Procedural Sedation in July 2020
- Yichang Humanwell recently launched remimazolam

## South Korea + Southeast Asia – Hana Pharm

- **Lead indication: General Anesthesia**
- Hana Pharm filed for market approval in December 2019; market approval expected in H2 2020
- Extended license territory by adding Southeast Asia in January 2020

## Canada – Pharmascience

- **Lead indication: Procedural Sedation**
- PAION expects Pharmascience to use the U.S. market approval dossier as the basis for their own filing for market approval of remimazolam

## R-Pharm (Russia, Turkey, MENA Region)

- R-Pharm successfully completed a Phase III trial in General Anesthesia in November 2018
- R-Pharm is currently preparing first market approval dossiers for the licensed territories

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# EIB Financing Agreement / Yorkville convertible notes

## EIB Financing Agreement:

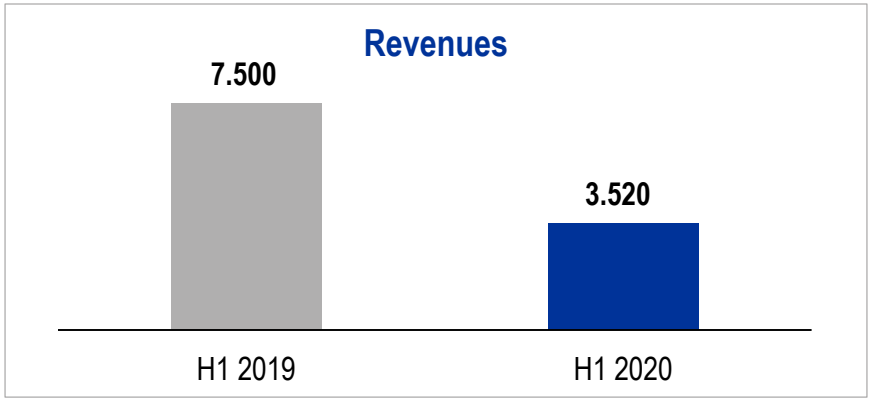
- Unsecured loan of up to EUR 20 million
- Can be drawn down in a total of three tranches based on certain conditions as e.g. the achievement of operational milestones
- Available until June 2021
- The first tranche of the loan is already available and the two further tranches could become available in 2020
- PAION has not drawn down the loan yet

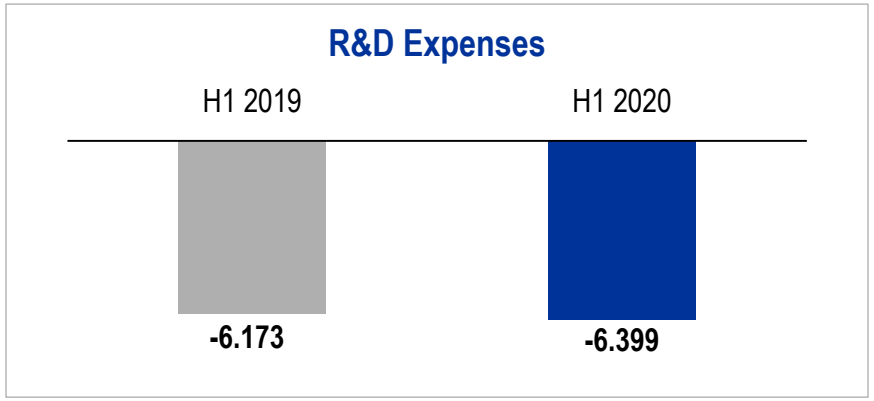
## Yorkville Growth Financing:

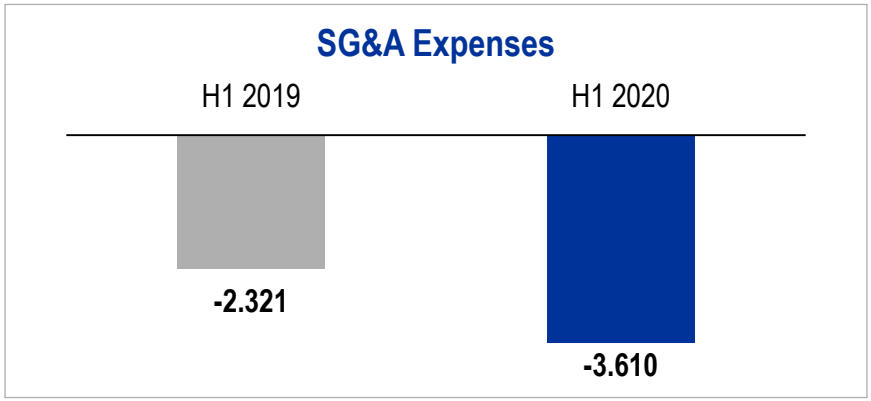
- Unsecured convertible notes in a total nominal amount of up to EUR 15 million
- The first tranche with a nominal amount of EUR 5 million was issued in September 2019
  - The first tranche of convertible notes has been converted entirely into a total of 2,363,350 new PAION shares until 8 July 2020
- A further issue of convertible notes under this agreement is not planned

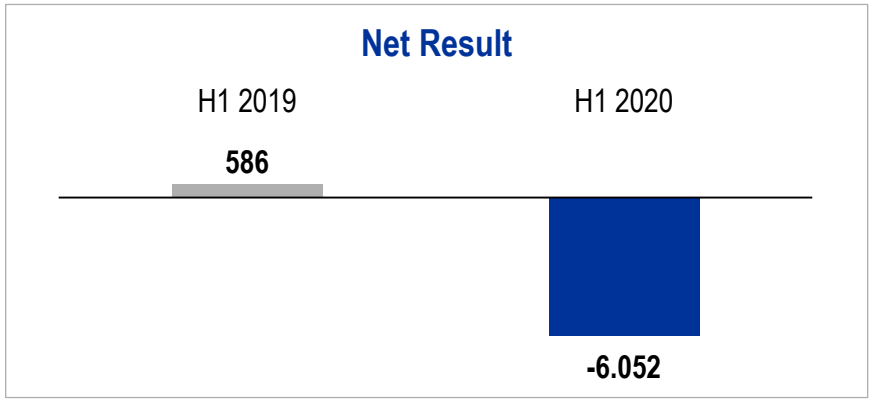
# Consolidated statement of comprehensive income

## In accordance with IFRS (all figures in EUR k)



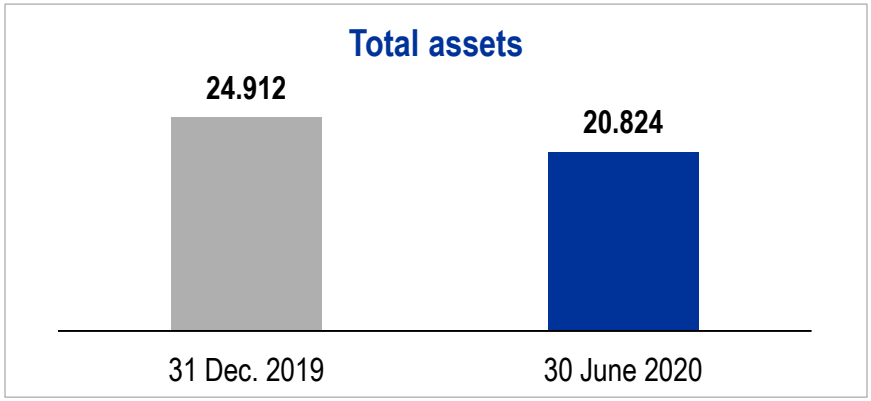



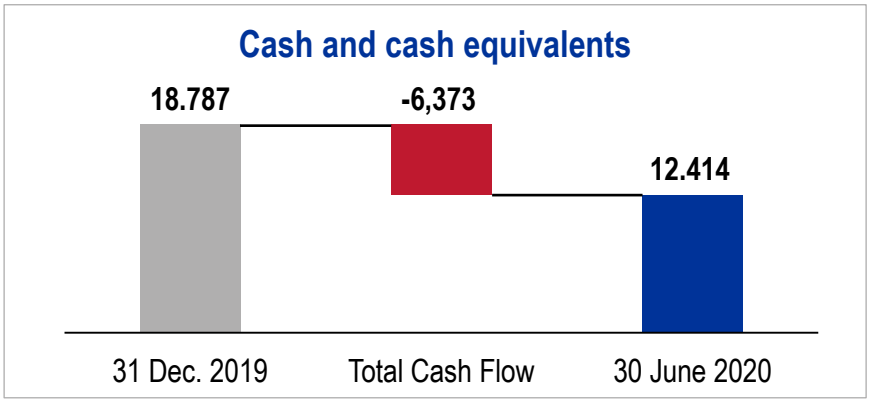



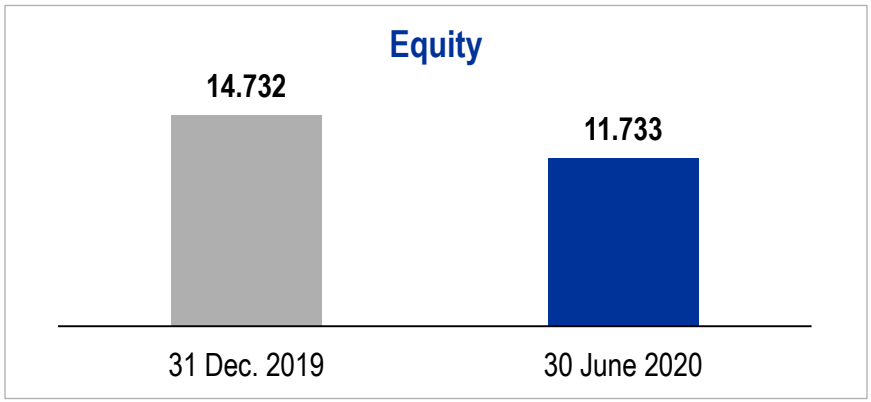

- R&D expenses mainly relate to the EU Phase III study in general anesthesia for which the data analysis is currently ongoing
- SG&A expenses increased particularly due to pre-commercial activities and build-up of a supply chain

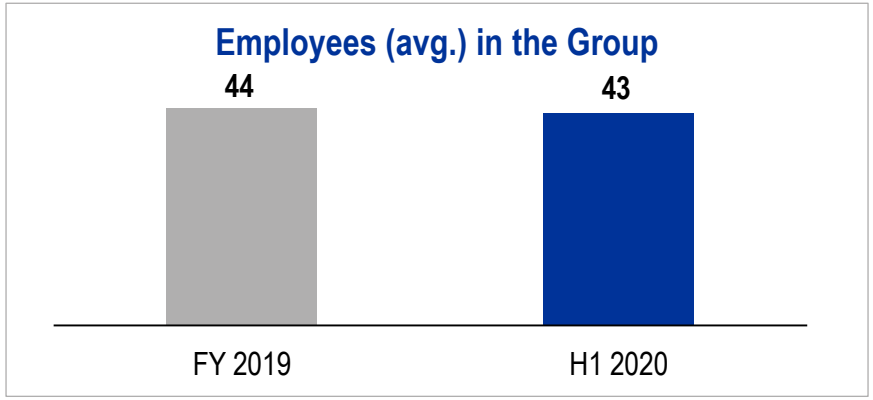
# Consolidated balance sheet and employees

## In accordance with IFRS (all figures in EUR k if not otherwise noted)




→ Equity ratio as of 30 June 2020 was 56.3%

# Financial Outlook 2020

| | | Actual FY 2019 EUR million | Plan FY 2020 EUR million | Comments |
|---|---|---|---|---|
| Revenues | | € 8.0m | **~ € 20m** | EUR 15m from market approval in the U.S.; further revenues from market approvals in Japan & China, license extension with Hana Pharm and in connection with potential market approval in South Korea |
| Expenses | R&D | € 13.1m | **~ € 10m – ~ € 12m** | Significant R&D expenses due to continuation of development program of remimazolam including EU Phase III study |
| | SG&A | € 5.0m | **~ € 7m – ~ € 9m** | SG&A expenses increase due to pre-commercial activities and build-up of supply chain |
| Tax credits | | € 2.4m | **~ € 1m – ~ € 1.5m** | Tax credits on portion of R&D expenses from UK tax authorities |
| Net result | | € -7.0m | **~ € 0.5m – ~ € 4m** | Positive net result expected |

## Cash Runway

→ Cash reach is at least into the second half of 2021 based on current planning


# Q&A

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