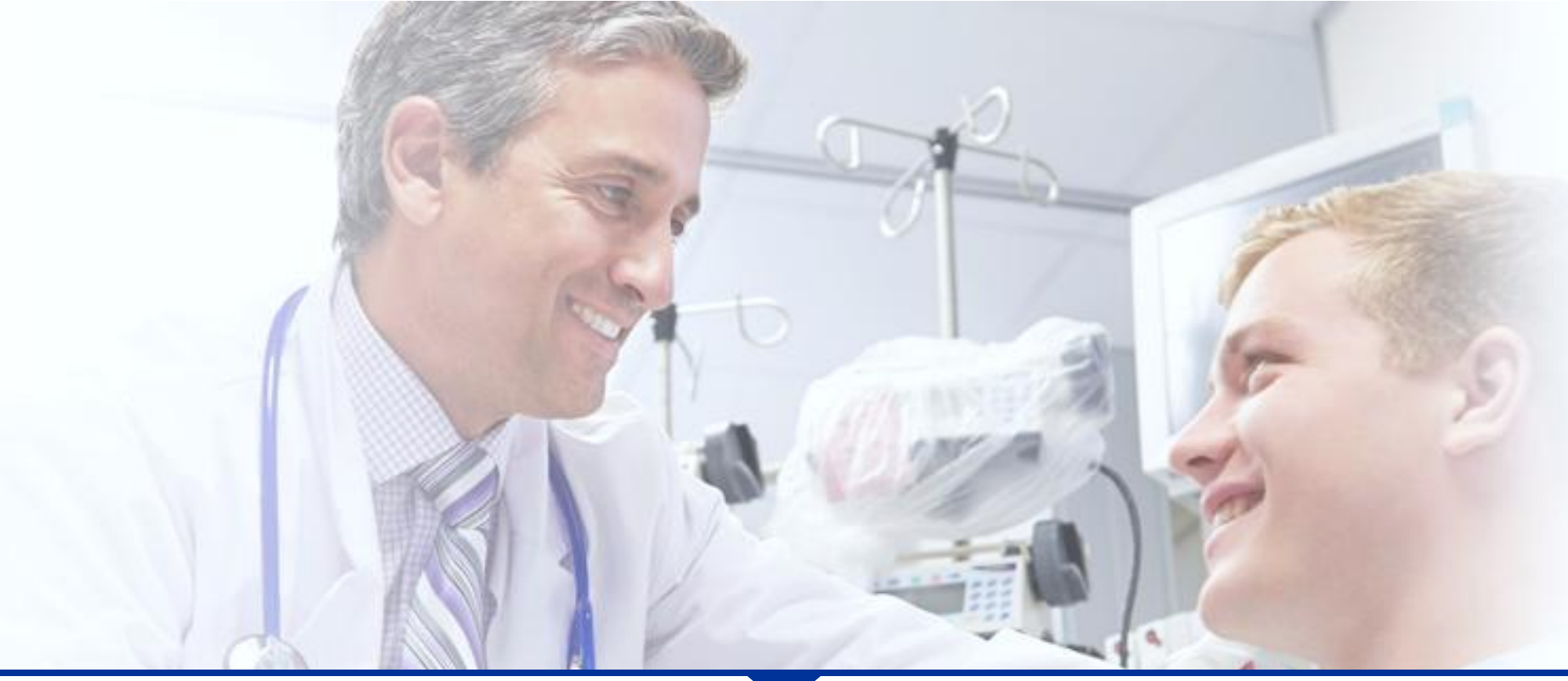

Q3 2018 FINANCIAL RESULTS AND BUSINESS UPDATE

Dr. Wolfgang Söhngen, CEO | Abdelghani Omari, CFO

Conference Call | 7 November 2018

PAION

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AGENDA

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Corporate overview

PAION AG is a specialty pharma company with a focus on anesthesia products

Remimazolam, PAION's lead drug candidate, is in final stage of clinical development

Eight regional partnerships for remimazolam in the U.S., China, South Korea, Canada, Russia (CIS), Turkey, Japan and MENA region

Headcount of 39 (avg. Q1-Q318), HQ in Aachen, Germany: PAION AG with a subsidiary in Cambridge (UK)

EUR 19.8 million cash and cash equivalents (end of Q3 2018)

Market capitalization: EUR ~ 150 m

Supervisory Board

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

Dr. Karin Dorrepaal
Background: Former Schering AG Board Member

John Dawson
Background: CEO Oxford BioMedica

Dr. Dr. Irina Antonijevic
Background: VP Translational Medicine Wave Life Sciences

Dr. Chris Tanner
Background: Head of Transactions Cosmo Pharmaceuticals

Management

Dr. Wolfgang Söhngen
Title: CEO, Founder

Abdelghani Omari
Title: CFO

Dr. Jürgen Beck
Title: CDO

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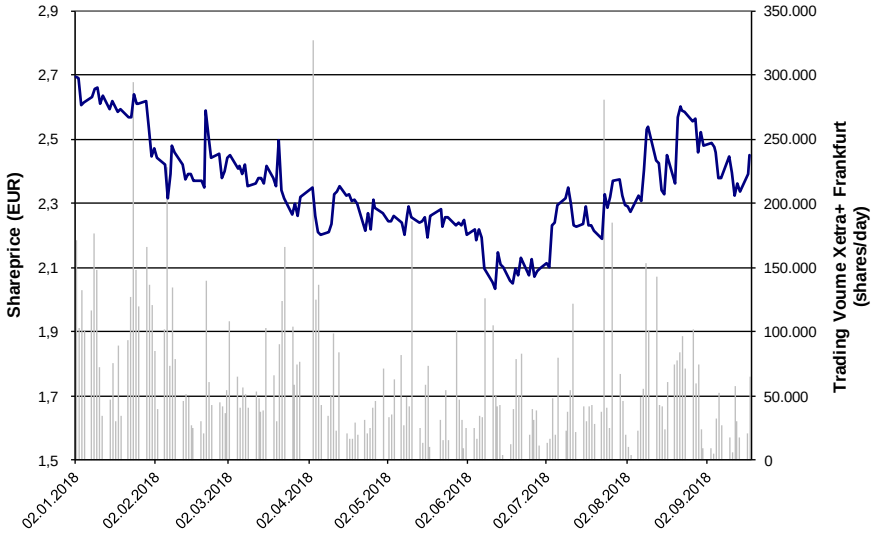
PAION AG is listed on Frankfurt Stock Exchange with a current market capitalization of ~ €150m (€2.25 per share)

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

Market capitalization:
EUR ~ 150 m

Liquidity
(3-month period Xetra):
3.2 million shares traded

Stock Performance 2018
(price and volume in EUR)



Market Data
(EUR in million except per share data)

Capitalization (as of 06 November 2018)	
Current Share Price	€ 2.25
FD Shares Outstanding	63.8
Market Cap	~ € 150
Mean target price of 3 analyst reports (Edison, Oddo BHF, First Berlin)	€ 4.12

Remimazolam status and potential in three indications

Indication	Status of Development: PC	Ph I	Ph II	Ph III	Estimated peak sales potential (worldwide p.a.)	Partners
General Anesthesia	Japan (NDA filing in preparation)				500m US$	Mundipharma (Japan) Cosmo (U.S.) Yichang Humanwell (China) (T)R-Pharm (Russia+CIS, Turkey, MENA) Pendopharm (Canada) Hana Pharm (South Korea)
General Anesthesia	EU (Phase III ongoing)					
Procedural Sedation	U.S. (NDA filing in preparation)				500m US$	
ICU Sedation	Japan				500m US$	

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Events 2018

Scientific Advice EMA

Hana Pharm starts remimazolam Phase III trial in South Korea

Publication of remimazolam Phase III colonoscopy data

PAION AG raises EUR 5.2 million in private placement

Hana Pharm successfully completes patient recruitment of a remimazolam Phase III trial in South Korea

Jan | Feb | March | Apr | May | June | July | August | September | October | November

Kick-off Meeting Mundipharma, Tokyo

Invest 2018, Stuttgart

R-Pharm successfully completes patient recruitment of a remimazolam Phase III trial in Russia

Start of EU Phase III trial in GA

R-Pharm successfully completes Phase III trial in Russia

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Remimazolam – Multiple potential opportunities in sedation/anesthesia

Definition of general anesthesia and levels of sedation/analgesia (American Society of Anesthesiologists, 1999 – modified)

	Minimal sedation "anxiolysis"	**Moderate sedation / analgesia** "conscious sedation"	**Deep sedation / analgesia**	**General anesthesia**
Responsiveness	Normal response to verbal communication	Purposeful response to verbal or tactile stimulation	Purposeful response following repeated or painful stimulation	Unarousable even with painful stimulus
Airway	Unaffected	No intervention required	Intervention may be required	Intervention often required
Spontaneous Ventilation	Unaffected	Adequate	May be inadequate	Frequently inadequate
Cardiovascular function	Unaffected	Usually maintained	Usually maintained	May be impaired

Midazolam — **Potential use for remimazolam** — **Propofol**

- Colonoscopy
- Upper GI endoscopy
- Bronchoscopy
- Trauma e.g. limb-resetting, wound dressing
- Biopsies
- Major surgery
- Minor procedures
- ICU sedation
- MRI / Scanning procedures

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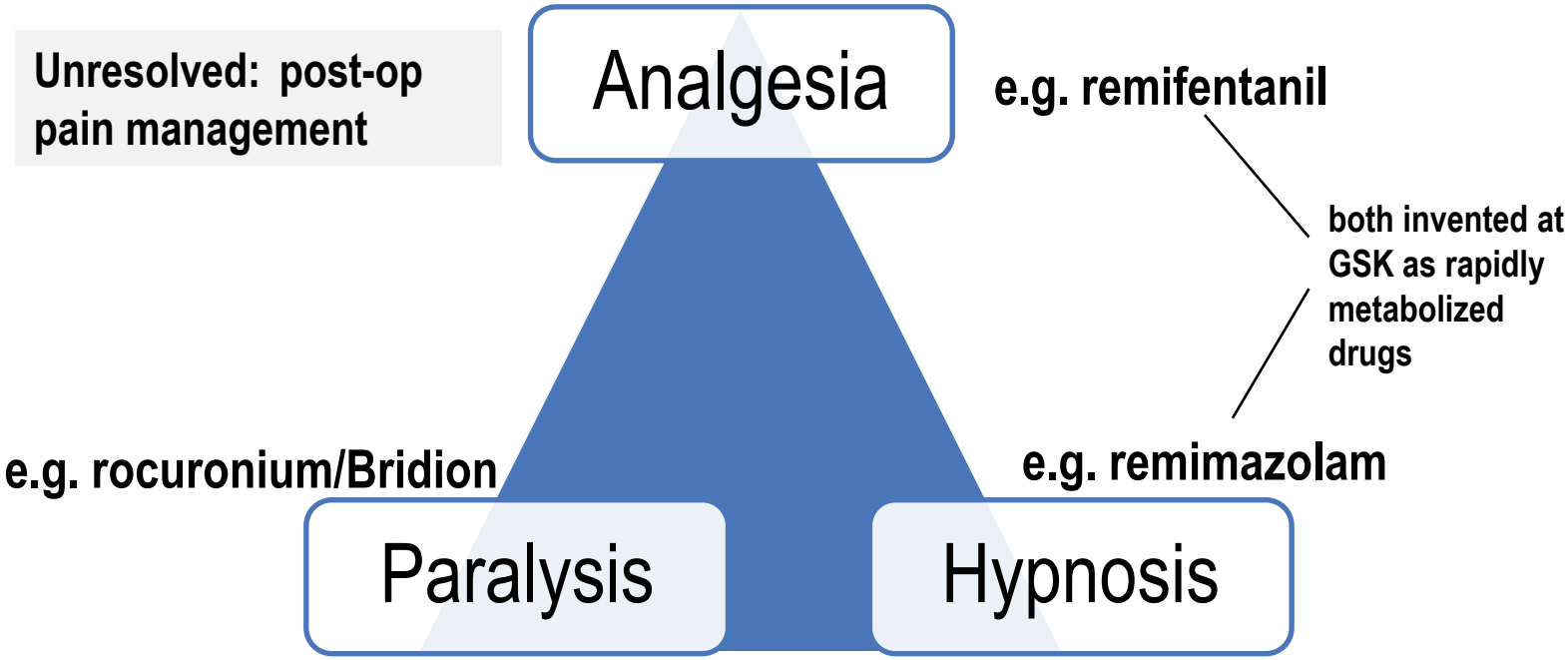
Triad of anesthesia



- **The anesthesiologist is responsible for peri-operative pain and sedation management**
- **Remifentanil and remimazolam are an excellent combination in General Anesthesia**

From American Society for Anesthesiology Guidelines for Patient Care in Anesthesiology: Perianesthetic care means being responsible for … Selection and administration of anesthetic agents to render the patient insensible to pain, while providing a level of comfort and relaxation commensurate with the invasiveness and physiologic stress of the planned procedure.

The ideal drug would combine „the best of both worlds“…

said Physicians at the first ever Market Research in 2008

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

→ **Remimazolam offers the opportunity to substitute both midazolam and propofol in a growing market setting**

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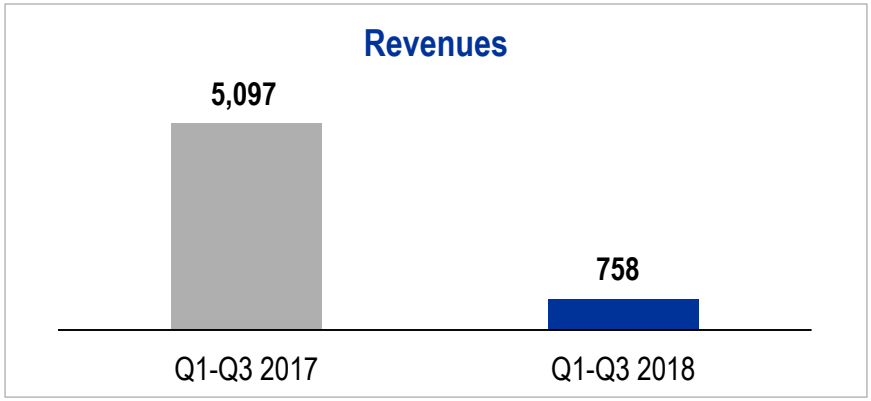
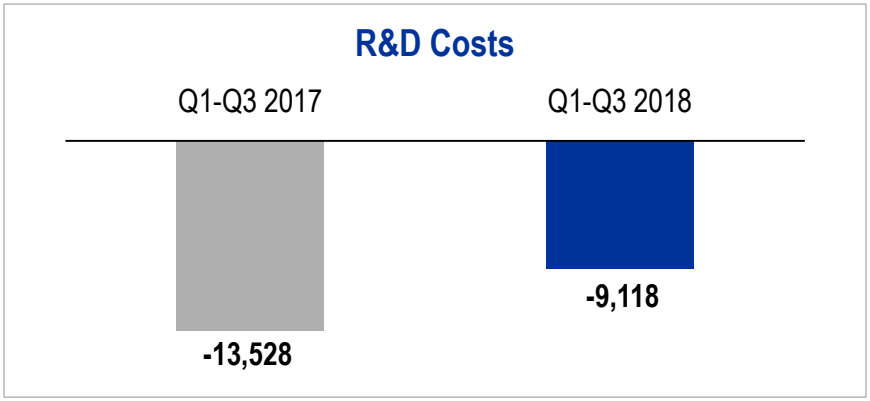
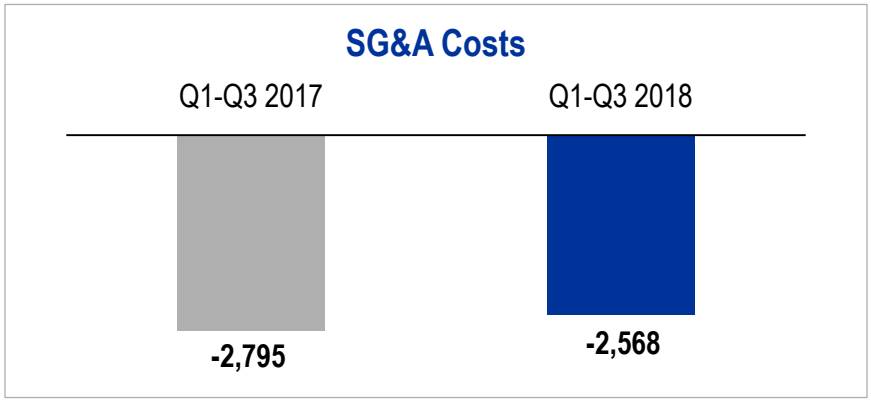
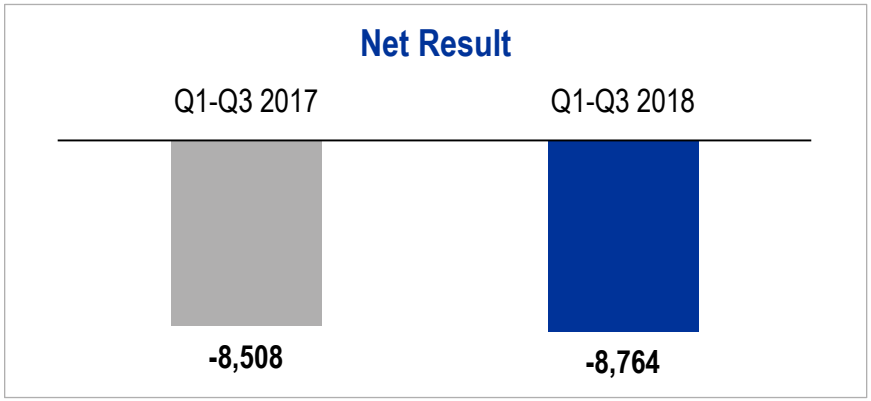
Consolidated statement of comprehensive income

In accordance with IFRS (all figures in EUR k)









- Revenues mainly relate to upfront payment from Mundipharma received in January 2018
- R&D costs mainly relate to EU Phase III study, validation of commercial scale production and preparatory activities for filing for market approval for remimazolam

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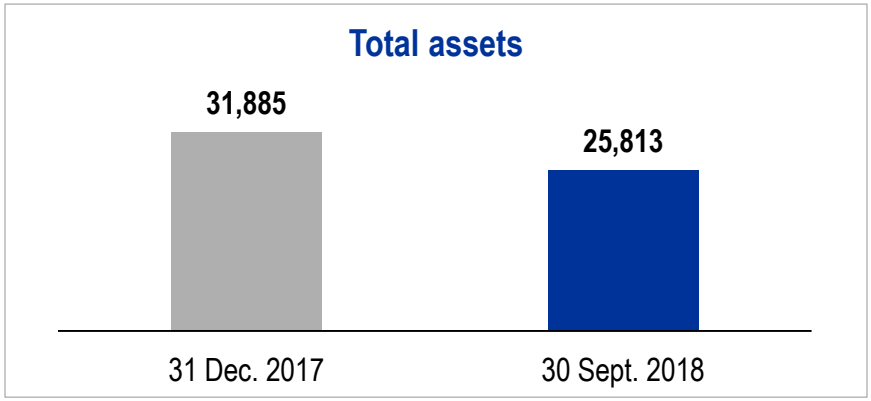
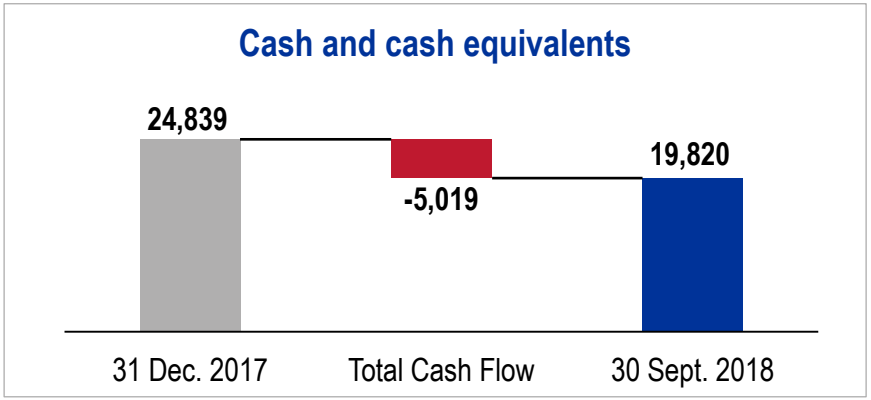
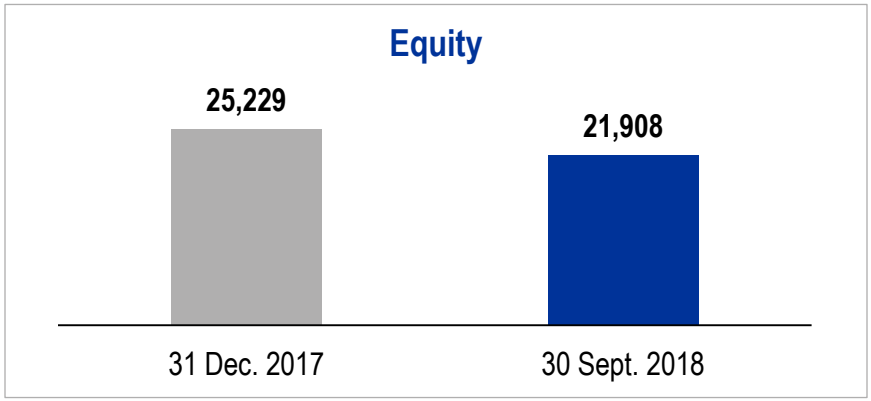
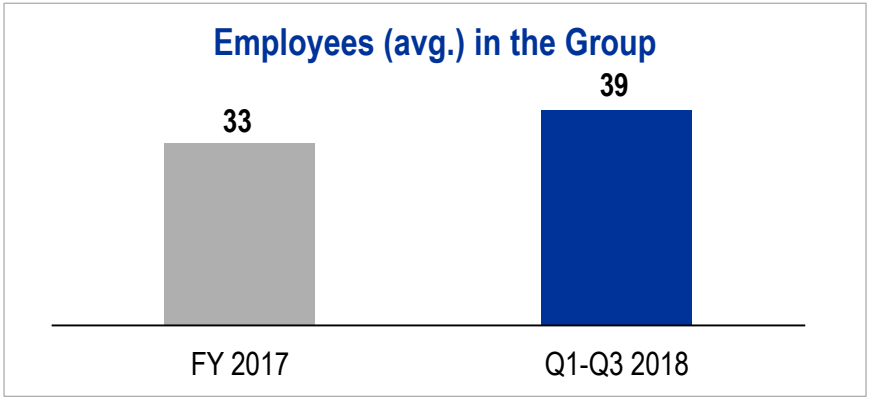
Balance sheet and employees

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









→ Equity ratio as of 30 September 2018 was 84.9%

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Financial Outlook 2018

		Actual FY 2017 EUR million	Plan FY 2018 EUR million	Comments
Revenues		€ 5.8 m	**~ € 3 m**	Revenues in connection with regulatory filing in Japan and Japanese license agreement
Costs	R&D	€ 17.9 m	**~ € 12 m – 14 m**	Significant R&D expenses due to continuation of development program of remimazolam including EU Phase III study, but lower than in 2017
	SG&A	€ 3.8 m	**~ € 3.5 m – 4 m**	SG&A costs will be comparable to prior year
Tax credits		€ 3.8 m	**~ € 2.5 m**	Tax credits on portion of R&D expenses from UK tax authorities
Net result		€ -12.1 m	**~ € -10 m – -12.5 m**	Net loss will be comparable to 2017

Liquidity

→ Funds of approximately € 10 m required until filing for market approval in general anesthesia in the EU

→ Cash reach until beginning of 2020 based on current planning

- Including expected UK tax credits on parts of research and development expenses
- Including expected incoming milestone payments in connection with filings in the U.S. and Japan

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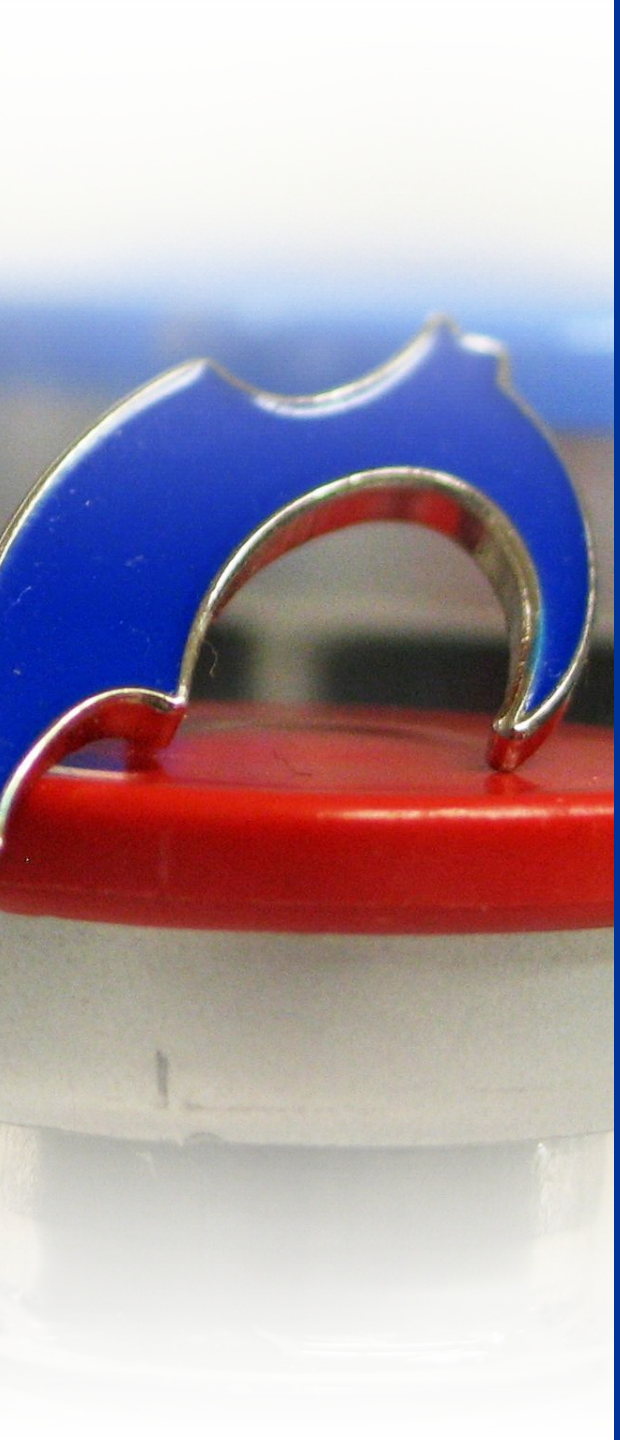

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Remimazolam – Potential to address important issues

Need for improvement in the sedation/anesthesia space

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

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Remimazolam – NDA filing preparation in GA and PS

Class	• First-in-class ultra-short-acting intravenous benzodiazepine sedative/anesthetic
IP	• Besylate salt – Protection until at least 2031 in the U.S. • Formulation Patent – Protection until at least 2033 in the EU • Dosing Patent – Protection until at least 2033 in Japan • Growing IP portfolio to secure attractive period of market exclusivity in major markets
Safety	• Extensive safety and efficacy database → ~ 2,000 volunteers/patients to date
Lead indications	• Procedural sedation in the U.S. • General anesthesia in EU, Japan, Russia and South Korea • Further attractive potential in ICU sedation → Estimated market opportunity >$500 m globally for each indication alone
Results to date indicate	• Solid efficacy and safety in studied populations • Rapid onset and offset of action • Appropriate depth of sedation • Favorable hemodynamic stability

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Remimazolam – Procedural Sedation

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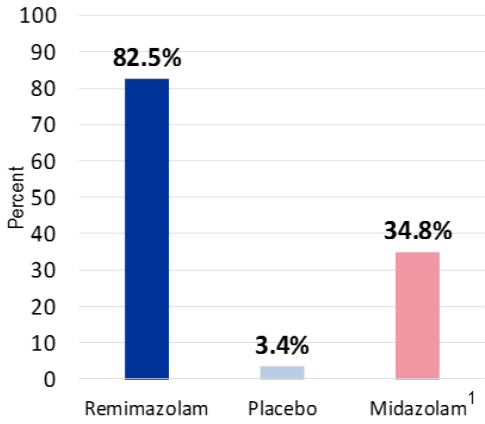
Remimazolam: Clinical development program successfully completed in Procedural Sedation

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)

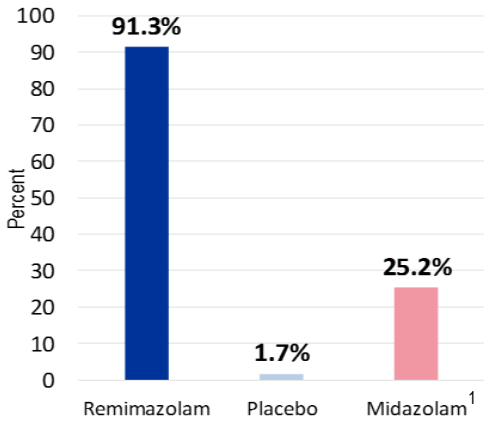
Success of procedure



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

Phase III colonoscopy (mostly ASA I–III)

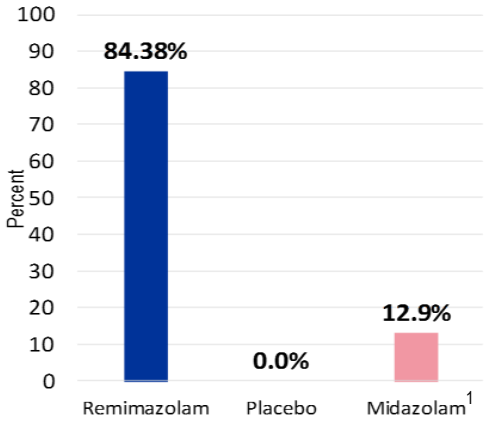
Success of procedure



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

ASA III/IV patients

Success of procedure



1. Open label

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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	**4.1**
Midazolam – 1.75/1.0 mg (1.0/0.5 mg in the elderly and debilitated)	15.9

Time to end of procedure to fully alert	minutes
Remimazolam – 5.0/2.5 mg	**7.2**
Midazolam – 1.75/1.0 mg	15.7

→ **With an average reduction of 20 min/procedure and an average number of procedures of 10/day/doctor with midazolam, centers could increase throughput significantly**

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Remimazolam – Next Steps in the U.S.

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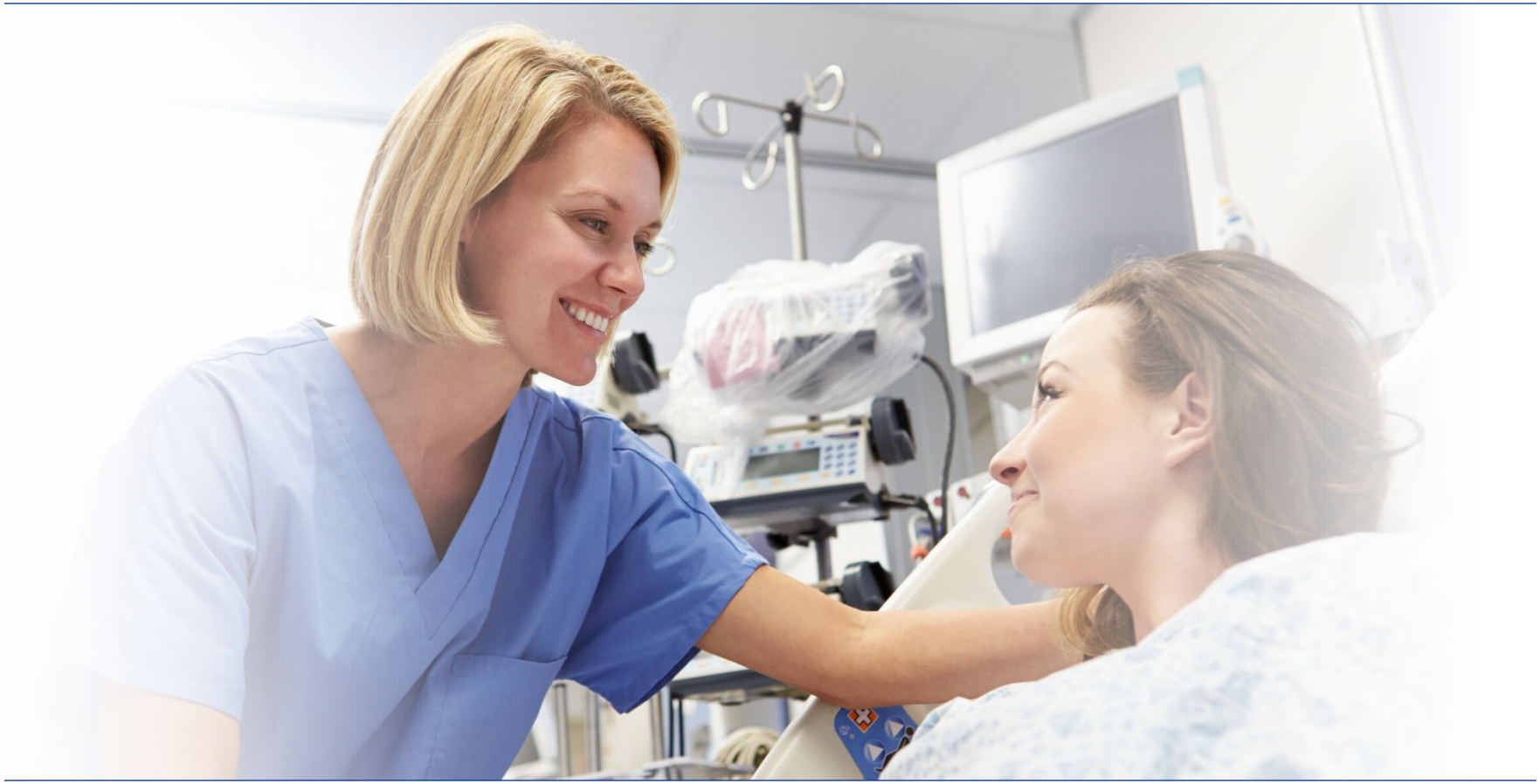
Remimazolam – General Anesthesia



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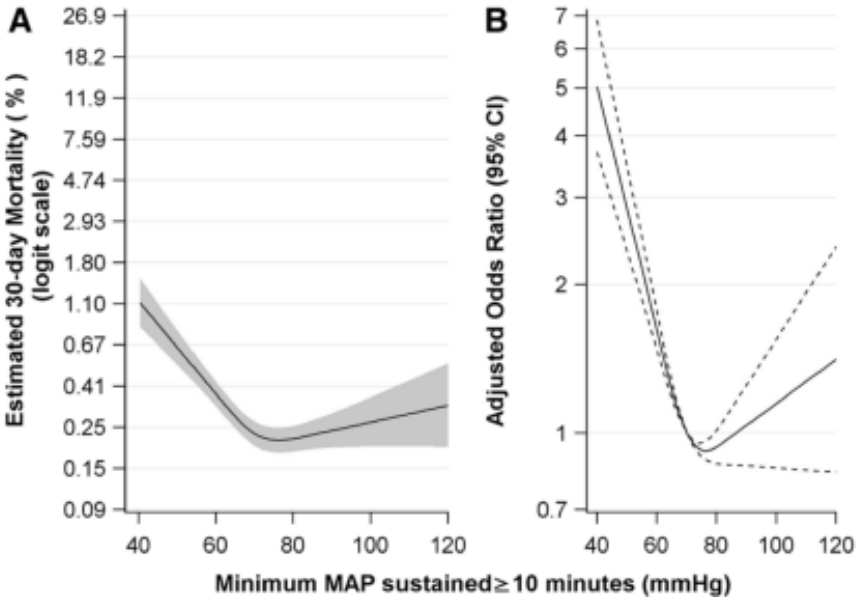
Hemodynamic stability - the unmet need in General Anesthesia

Intraoperative Mean Arterial Pressure Variability and 30-day Mortality in Patients Having Noncardiac Surgery

Edward J. Mascha, Ph.D., Dongsheng Yang, M.S., Stephanie Weiss, M.D., Daniel I. Sessler, M.D.

ANESTHESIOLOGY 2015; 123:79-91

- Baseline and intraoperative variables plus 30-day mortality were obtained for 104,401 adults having noncardiac surgery lasting 60 min or longer
- Decreasing the minimum value of MAP that was sustained for more than 10 min was associated with higher odds of mortality when that minimum was less than 70 mmHg



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General Anesthesia – Room for improvement

- Little innovation in anesthetic drug development in recent years
- Ageing 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

→ With remimazolam, there is a significantly lower incidence of hypotension in surgical patients undergoing General Anesthesia compared to propofol[5]
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. ONO study report _Data on file

EU Lead indication: General Anesthesia

- EU Phase III study (~ N=500) started in July 2018
  - Multicenter, randomized and active-controlled European (EU) Phase III trial in approximately 500 patients undergoing elective surgery
  - Countries: Germany, France, Italy, Switzerland, The Netherlands, UK, Belgium

~ N=363 remimazolam

~ N=137 propofol

- Evaluation of efficacy and safety incl. hemodynamic stability
- Comparison between remimazolam and propofol

Primary objective: Efficacy (non-inferiority of remimazolam compared to propofol)

Key secondary objective: Improved hemodynamic stability compared to propofol

Next steps

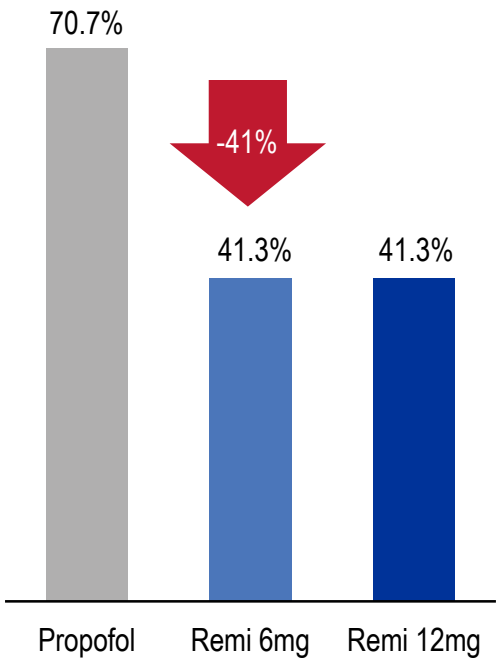
- Completion of patient recruitment expected in 2019
- Positive Phase III trial in combination with previously completed clinical studies in Europe and Japan should be sufficient for filing in the EU based on EMA scientific advice
- Plan to commercialize remimazolam in the EU alone but also open to potential value-generating partnerships

Remimazolam clinical data (General Anesthesia): Phase IIb/III pivotal trial: post hoc analyses

In Hypotension

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

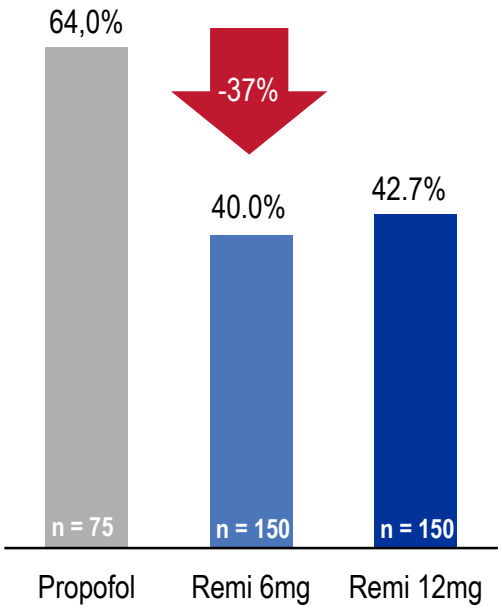
NNT = 3.4



Need for Vasopressors

Share of patients with any vasopressor entire study

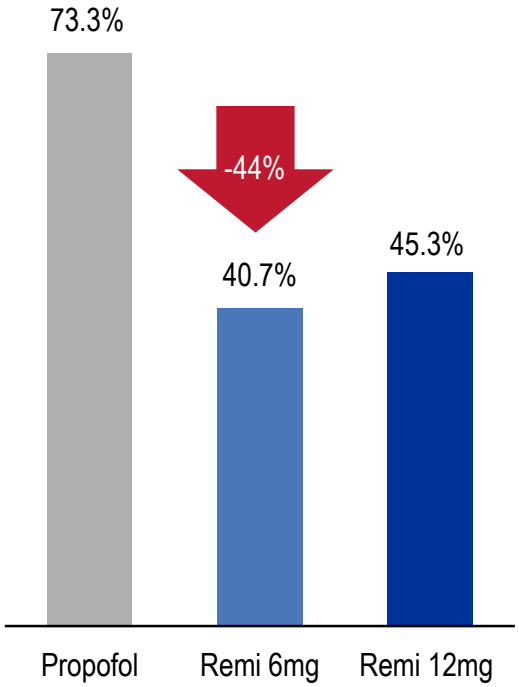
NNT = 4.2



Too deep sedation

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

NNT = 3.1



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Europe – Launch indication targets hospital surgical General Anesthesia, representing 28.6 million patients/year

Hospital

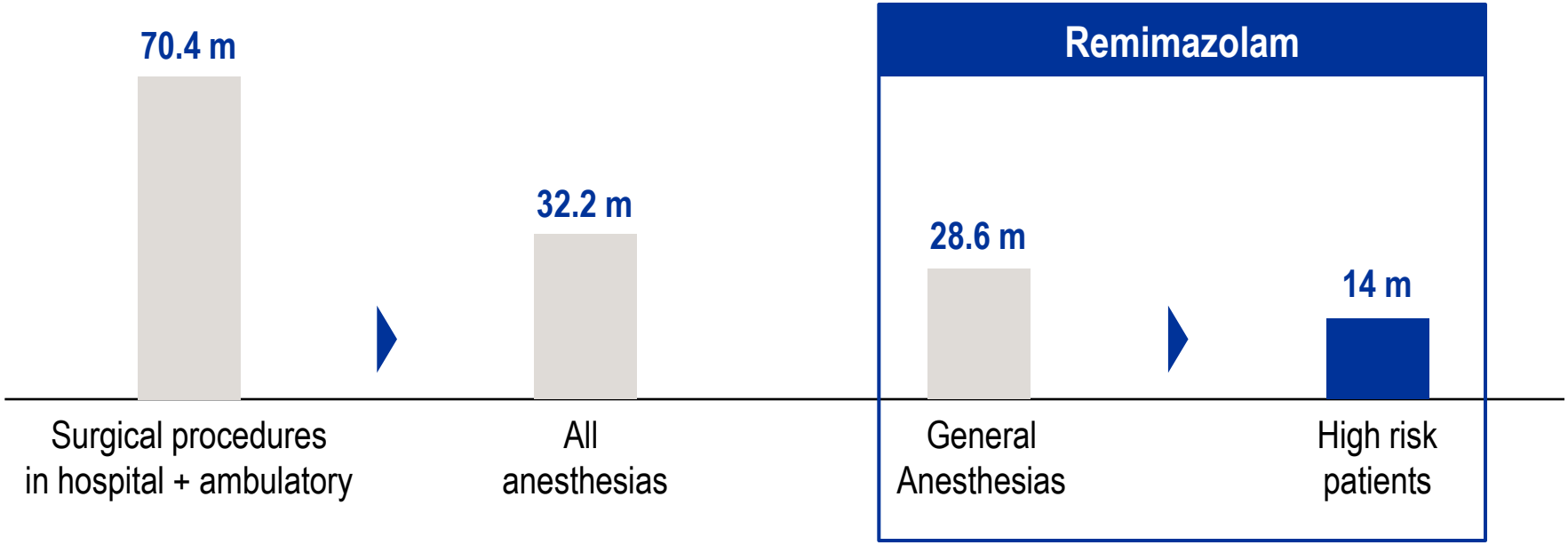
Out-Patient

Remimazolam

ICU Sedation	Surgical General Anesthesia	Procedural Sedation (e.g. day cases)	Procedural Sedation

- General Anesthesia has been short on pharmaceutical development during the last decades and there remains room for innovation
- Sedative and anesthetic safety is continuously reviewed as part of quality assessments and includes: efficacy, unintended intra-operational awareness, respiratory depression, hemodynamic stability, post-operative/procedure emergence and recovery, long term effects of anesthesia and patient morbidity and mortality

Europe: 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

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Remimazolam – ICU Sedation

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ICU sedation is an attractive business opportunity

Hospital

Out-Patient

Remimazolam

- ICU Sedation
- Surgical General Anesthesia
- Procedural Sedation (e.g. day cases)

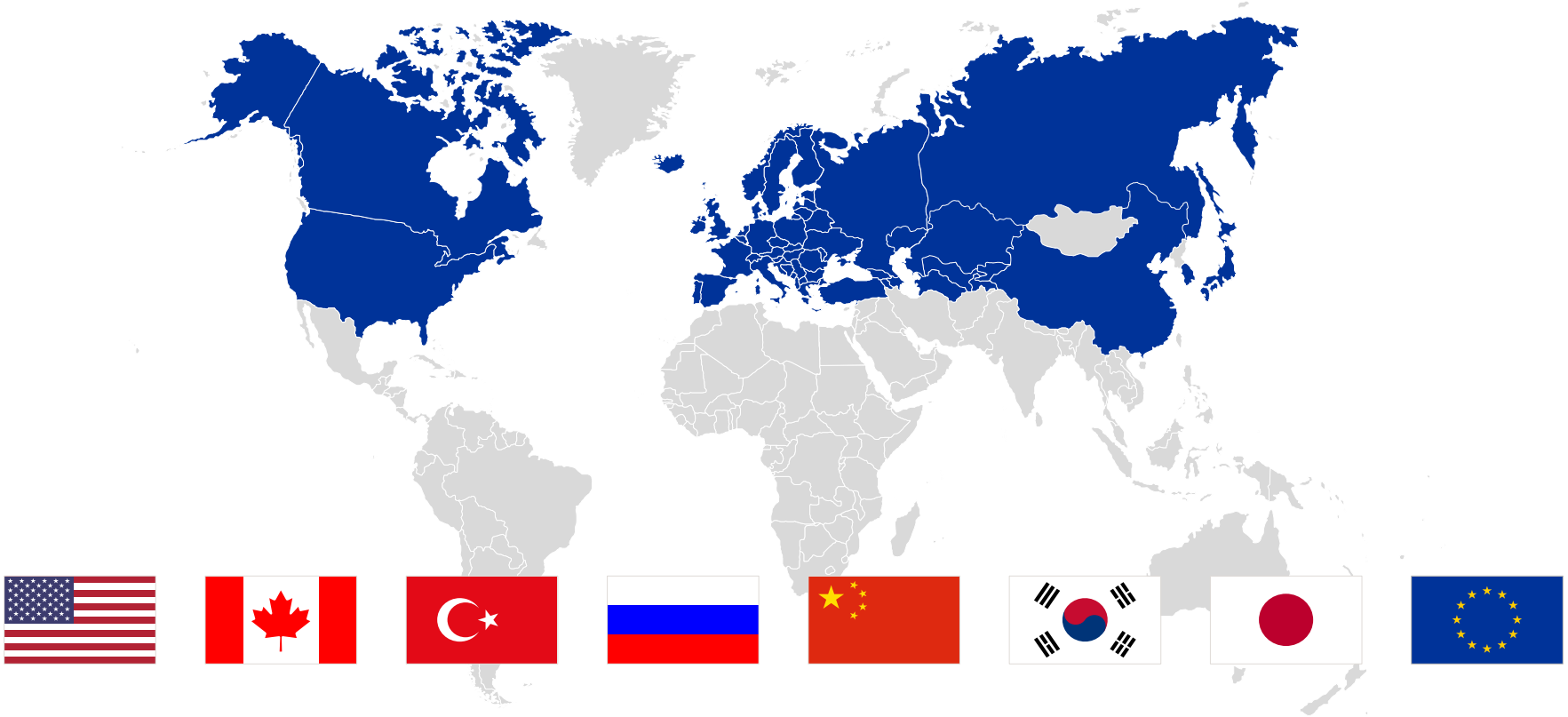
- Procedural Sedation

PAION

Approximately 14 million ICU patient days requiring ICU sedation in the U.S. and EU combined per year

- PAION estimates that there are approximately 14 million ICU patient days requiring ICU sedation in the U.S. and EU combined per year
- Demand for safer agents such as remimazolam, given the fact that elderly patients are much more likely to suffer from systemic health problems
- Medical need to improve hemodynamic stability
- 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
  - Therefore initially development in general anesthesia has priority for PAION
  - Development for ICU sedation requires additional funds
  - Potential for co-development with PAION's partners

Driving remimazolam forward – PAION and partner activities



All regions with development and regulatory activities:

Partners continue development and preparatory filing activities (Yichang Humanwell, Hana Pharm, R-Pharm, TR-Pharm, Pharmascience, Cosmo, Mundipharma)

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Remimazolam – Beyond the U.S. and EU opportunity

Japan – Mundipharma

- **Lead indication: General Anesthesia**
- Completed development program
- Partnered to Mundipharma in December 2017
- Mundipharma plans to file towards the end of 2018

South Korea – Hana Pharm

- **Lead indication: General Anesthesia**
- Hana Pharm successfully completed patient recruitment of a Phase III trial in general anesthesia in October 2018
- Hana Pharm plans to file for market approval based on the Japanese dossier
- Before filing for market approval, the production process needs to be established in South Korea
- Hana Pharm plans to file for market approval in 2020

Remimazolam – Beyond the U.S. and EU opportunity

Russia – R-Pharm

- **Lead indication: General Anesthesia**
- R-Pharm successfully completed a Phase III trial in General Anesthesia in November 2018
- R-Pharm plans to file for market approval in Q1 2019

Turkey – TR-Pharm

- **General Anesthesia + Procedural Sedation**
- Plans to file for market approval based on the U.S. dossier or the Japanese dossier (whichever comes first)

Remimazolam – Beyond the U.S. and EU opportunity

Canada – Pharmascience

- **Lead indication: Procedural Sedation**
- Pharmascience plans to file for market approval in Canada based on the U.S. dossier

China – Yichang Humanwell

- **General Anesthesia + Procedural Sedation**

“String of pearls”

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[1]	~ EUR 3.8 m	Tiered (starting at 15%)
Cosmo, U.S. (2016)	EUR 20 m[2]	EUR 42.5 m	20%–25%[3]
Mundipharma, Japan (2017)	EUR 1 m	EUR 25 m	Up to over 20%[4]
Total	**EUR 34.8 m**	**~ EUR 88.8 m**	

1. This amount relates to the premium received in the course of the private placement in the amount of EUR 4 million in July 2014 which was disclosed as revenue in 2014
2. Includes EUR 10 million received via a private placement in June 2016 and via a capital increase with subscription rights conducted in February 2017 as well as an upfront payment of EUR 10 million
3. Subject to adjustments under specific circumstances, but not below 15% of net sales
4. Royalties range from low double-digits to over 20%.

AGENDA

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Upcoming milestones

- Completion of EU Phase III trial in the EU
- Potential filings in other regions
- Potential filing in Procedural Sedation in the U.S.
- Potential filing in General Anesthesia in Japan

2018

PAION

Three building blocks will ensure PAION's global leadership in acute and critical care

1

Accelerated Life Cycle Management of remimazolam
Launch in multiple indications across different regions

2

Forward Integration
Integrate forward in selected regions with creative deal making for others

3

Portfolio Enrichment
Be focused and open-minded for acute and critical care

PAION

Forward integration is a natural and necessary step to become a sustainable and profitable pharma company

Building Blocks

- Exploit remimazolam
- **Forward integrate**
- Enrich portfolio

- PAION does not have a technology platform to constantly create and deliver new products
- To become a leader in its field, forward integration is essential for PAION, especially in the EU in the near term
- Forward integration creates higher value for shareholders

PAION

Q&A

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