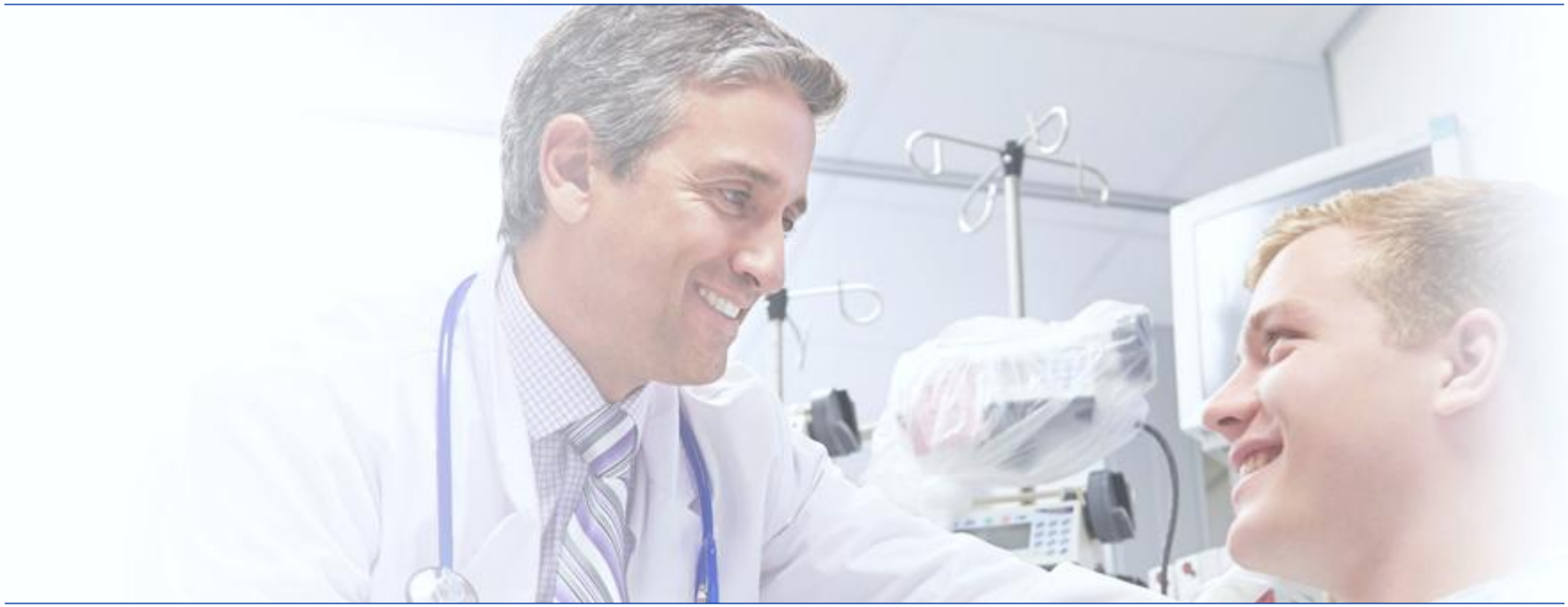
PAION Earnings Call

Financial Results 2017



Dr. Wolfgang Söhngen, CEO | Abdelghani Omari, CFO

Conference Call | 22 March 2018

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Remimazolam – A success story

2017
- Completion of U.S. Phase III program (ASA III/IV + bronchoscopy trial)
- Mundipharma becomes partner for remimazolam in Japan

2016
- Cosmo becomes partner for remimazolam in the U.S.
- Completion of U.S. Phase III colonoscopy trial

2015
- Start of the remimazolam Phase III programs in procedural sedation in the U.S. and general anesthesia in the EU

2014
- Capital measures of EUR 61 million secured for remimazolam Phase III programs

2013
- Japanese Phase III program with remimazolam successfully completed
- Several license agreements with national champions in the anesthesia space (“String of pearls” strategy)

2012
- Sale of all Desmoteplase rights to Lundbeck (EUR 20 million) allows PAION to accelerate the development of remimazolam

2010
- PAION completes Phase II program in procedural sedation in the U.S.

2008
- PAION acquires CeNeS Pharmaceuticals plc with remimazolam

2007
- First Desmoteplase Phase III trial (DIAS 2) fails to meet primary endpoint, PAION identifies suitable patient population and successfully expands partnership with Lundbeck

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Agenda

1. **Corporate Overview and Highlights 2017**
2. Financials
3. Remimazolam Update
4. Outlook and Vision

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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 34, HQ in Aachen, Germany: PAION AG with a subsidiary in Cambridge (UK): PAION UK Ltd

~ EUR 24.8 million cash and cash equivalents (end of 2017)

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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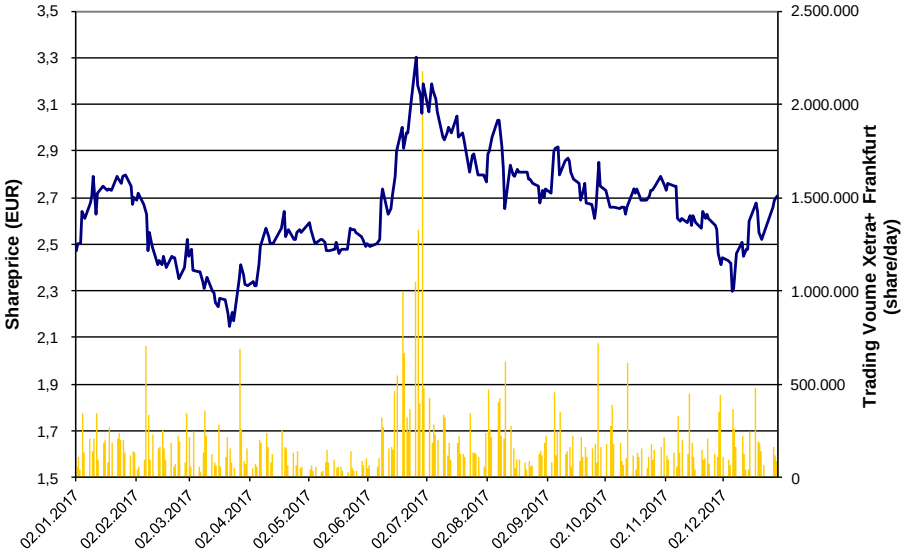
PAION AG is listed on Frankfurt Stock Exchange with a current market capitalization of ~ €150m (€2.45 per share)

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

Market capitalization:
EUR ~ 150 m

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

Stock Performance 2017 (price and volume in EUR)



Market Data (EUR in million except per share data)

Capitalization	
Current Share Price	€ 2.38
FD Shares Outstanding	61.1
Market Cap	€ 150
Mean target price of 3 analyst reports (Edison, Oddo BHF, First Berlin)	€ 4.12

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Highlights 2017 1/3

Important achievements driving our business forward

Clinical Trials (U.S.)

Positive results from two clinical trials with remimazolam

- U.S. Phase III trial in procedural sedation during bronchoscopy
  - Primary efficacy endpoint successfully achieved
  - Excellent safety profile of remimazolam confirmed
- U.S. clinical safety trial in high-risk patients undergoing colonoscopy
  - Remimazolam administration appeared safe
  - Efficacy and efficiency gains comparable to confirmatory U.S. Phase III pivotal trials

Clinical Trials (Other)

Remimazolam license partner R-Pharm has started a Phase III trial in general anesthesia

- Multicentre, single-blind randomized comparative clinical trial of efficacy and safety of remimazolam and propofol in 150 surgery patients undergoing general anesthesia

Clinical development progress with remimazolam by Hana Pharm in South Korea

- Hana Pharm plans to start a Phase III trial in general anesthesia and filing in 2018

Highlights 2017 2/3

Important achievements driving our business forward

Regulatory

Remimazolam partner Pharmascience had pre-NDS (New Drug Submission) meeting with Health Canada

- Non-clinical and clinical data package, including the human abuse liability data available at the time, were regarded as adequate for filing

Expertise

Supervisory Board changes reflect advancing development of company

- Dr. Dr. Irina Antonijevic – 16 years of drug development experience in various pharma organizations
- Dr. Chris Tanner – Cosmo Pharmaceuticals Board member, previously CFO

Patents

European Patent Office grants formulation patent for remimazolam in the EU

- Patent strengthens the overall exclusivity of remimazolam in the EU until 2033

Japan Patent Office grants dosing patent for remimazolam in Japan

- Patent strengthens the overall exclusivity of remimazolam in Japan until 2033

Highlights 2017 3/3

Important achievements driving our business forward

String of pearls

PAION grants exclusive license to Mundipharma for development and commercialization of remimazolam in Japan

- EUR 1 m upfront payment to PAION
- Additional regulatory and commercial milestone payments of up to EUR 25 m
- Royalties ranging from low double-digits to over 20%

FDA

FDA considers current human abuse liability program with Remimazolam in the U.S. as sufficient

- No second abuse liability study with intranasal application required

Finances

Two financings successfully completed

- Total of ~ EUR 13 million raised
- Financial position further improved

Agenda

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Two successful capital increases completed in 2017

EUR 5 million raised through capital increase with subscription rights

U.S. institutional investor agreed to backstop offering by purchasing all new shares that were not subscribed

Subscription rate was 96.31%

EUR 8 million raised through private placement

U.S. institutional investor invested EUR 5.2 million; potential further subscription of up to 2.8 million new shares until 30 April 2018

Second largest shareholder TIAA-Cref invested EUR 2.8 million

Total gross proceeds from financings: ~EUR 13 million

Strong financial position

Total share capital of EUR 61.12 million as of 31 December 2017

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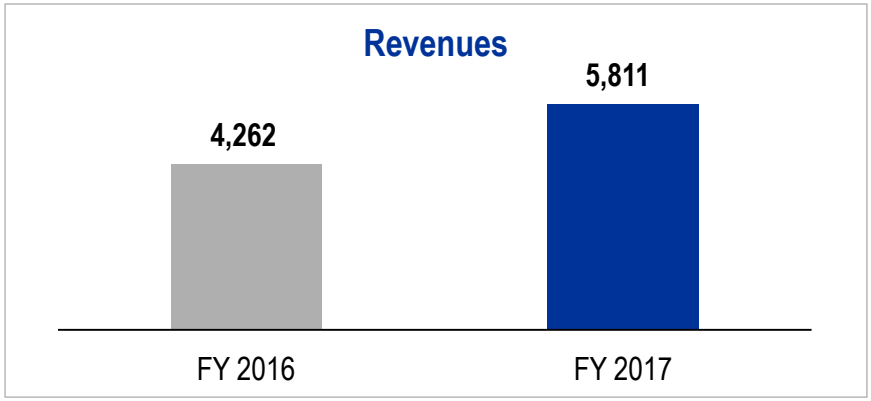
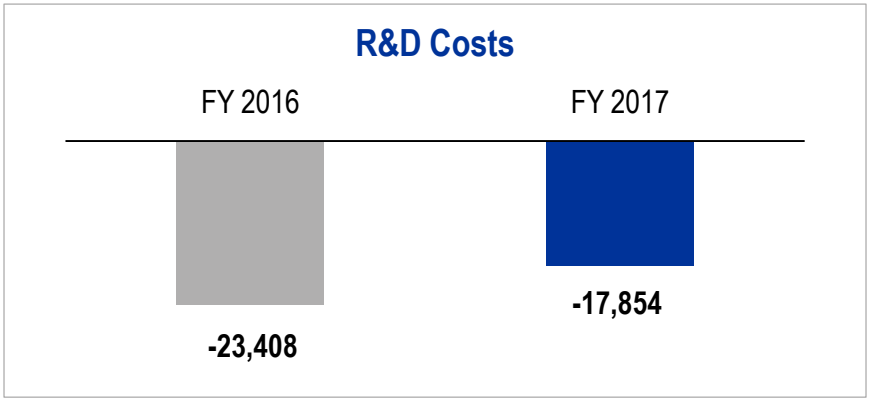
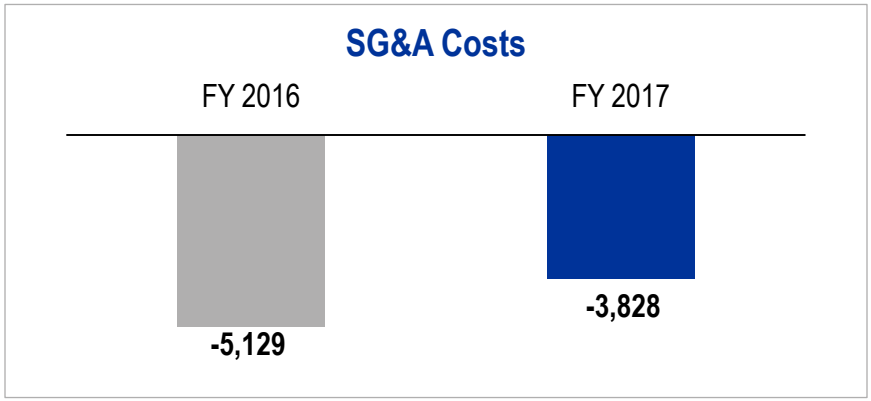
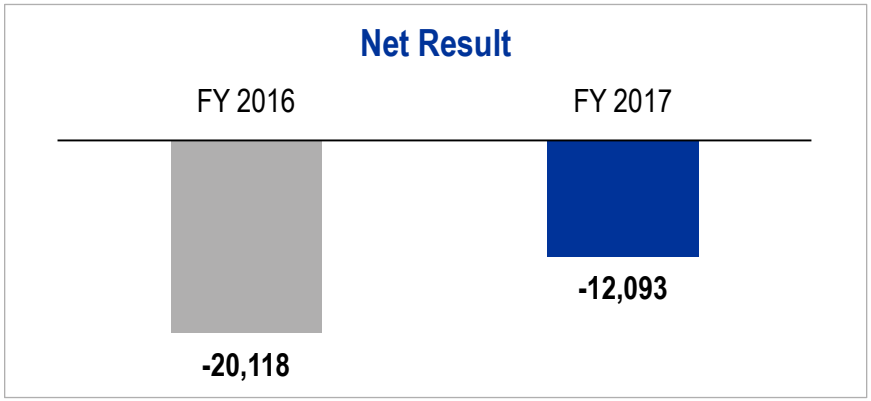
Consolidated statement of comprehensive income

In accordance with IFRS (all figures in EUR k)









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- Revenues mainly relate to upfront payment from Cosmo received in 2016
- R&D costs mainly relate to U.S. clinical development program; decrease primarily due to lower expenses for Phase III studies partly compensated by higher expenses for Phase I studies

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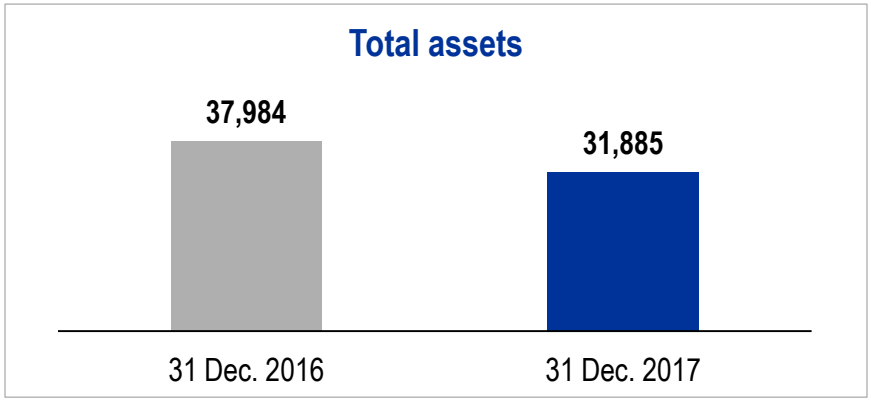
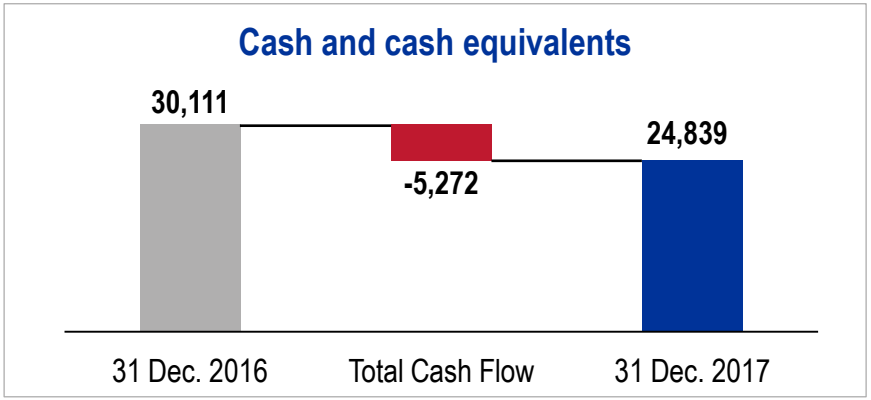
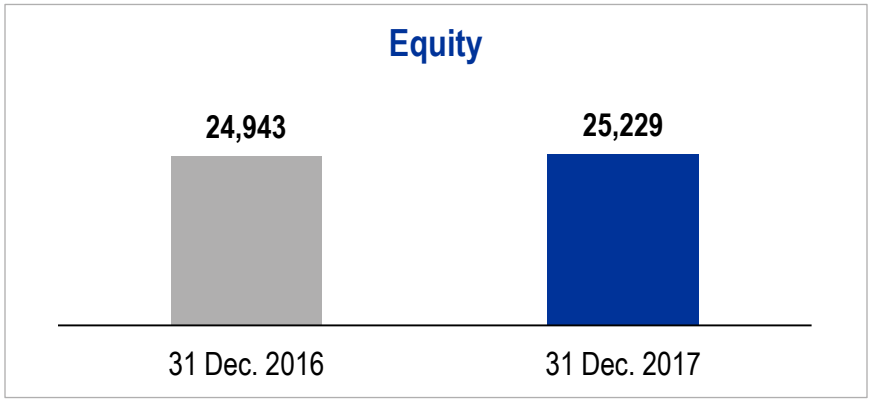
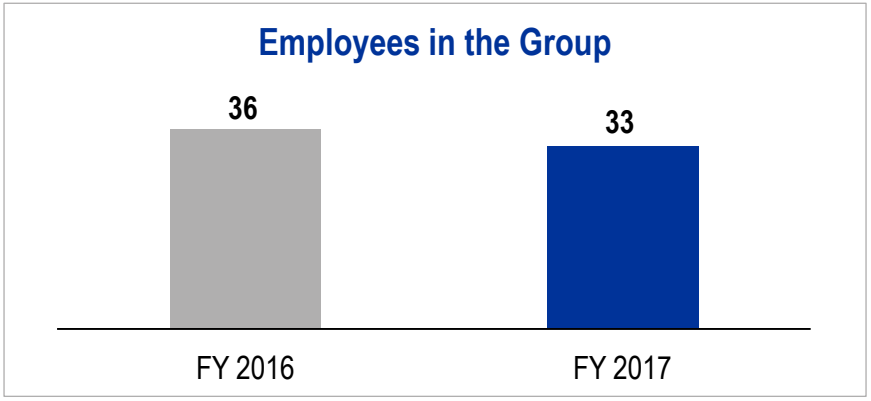
Balance sheet and employees

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









→ Equity ratio as of 31 December 2017 was 79.1%

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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	**~ € 15 m – 17 m**	Significant R&D expenses due to continuation of development program of remimazolam including EU Phase III study
	SG&A	€ 3.8 m	**~ € 3.5 m – 4 m**	SG&A costs will be comparable to prior year
Tax credits		€ 3.8 m	**~ € 3 m**	Tax credits on portion of R&D expenses from UK tax authorities
Net result		€ -12.1 m	**~ € -12.5 m – -15 m**	Net loss will slightly increase

Liquidity

→ Sufficient cash to complete all remaining activities in procedural sedation in the U.S. under current planning

→ No further funds required for EU Phase III trial; but funds of approximately € 15 m required until filing for market approval in general anesthesia in the EU

→ Cash reach into second half of 2019
- 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
- Including conduct of the planned EU Phase III study

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4. Outlook and Vision

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Considered to be „the best of both worlds“ by experts

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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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

Efficency

- Predictability of overall procedure time
- Improved patient throughput

Patient experience

- Amnesia for 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 – Ready to file in two indications in 2018

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 → over 1,700 volunteers/patients to date
Lead indications	• Procedural sedation in the U.S. • GA in EU and Japan • 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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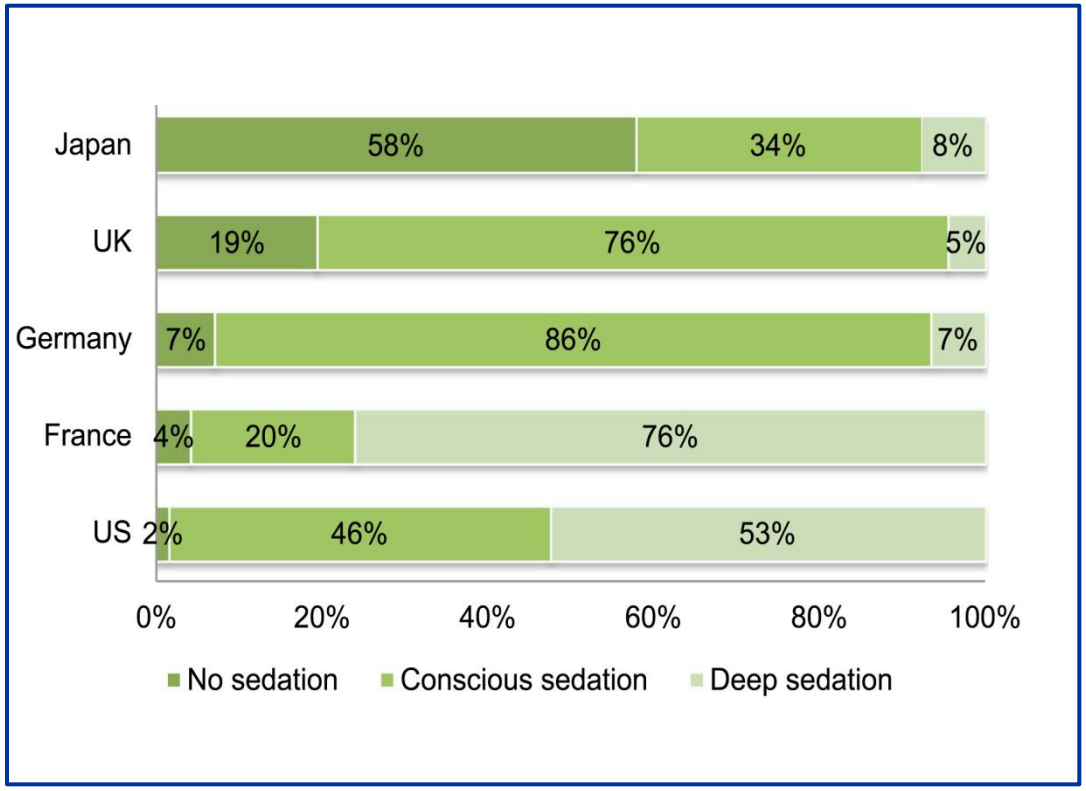
Level of sedation varies across regions and represents different clinical practice and pain tolerance



- Conscious sedation represents mostly midazolam use
- Deep sedation mostly represents propofol use
- High level of no sedation in Japan reflects cultural difference to most other markets
  - Growing market potential

Audibert et al. Contemporary Clinical Trials 2017; 116-21

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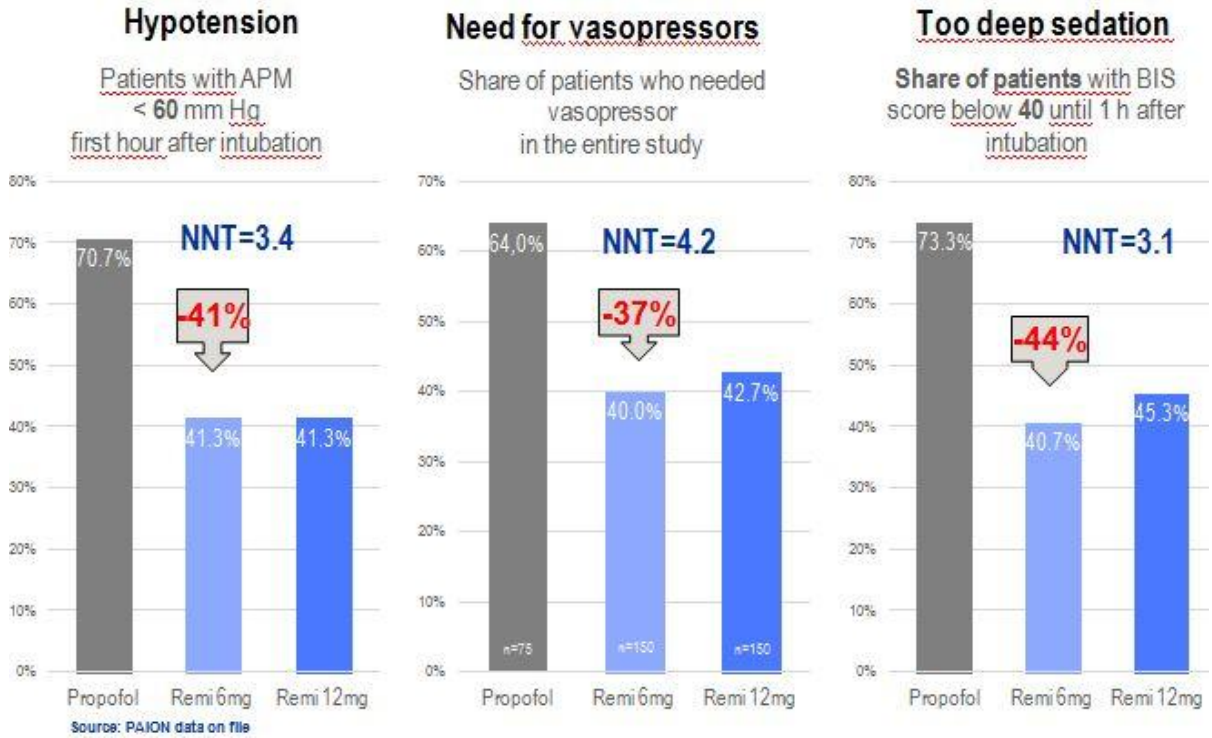
What is the unmet need? – Hemodynamic stability

- Anesthesiologists try to avoid hypotension during surgery in the elderly or seriously ill
- The association between poorer patient outcomes and hypotension is increasingly understood to occur with short time blood pressure drops
- Mean arterial pressures below absolute thresholds of 65 mm Hg or relative thresholds of 20% are progressively related to both myocardial and kidney injury
- At any given threshold, prolonged exposure was associated with increased odds
- **Remimazolam has shown to have significantly less hypotensive potential than propofol and the EU Phase III trial is designed to confirm this**



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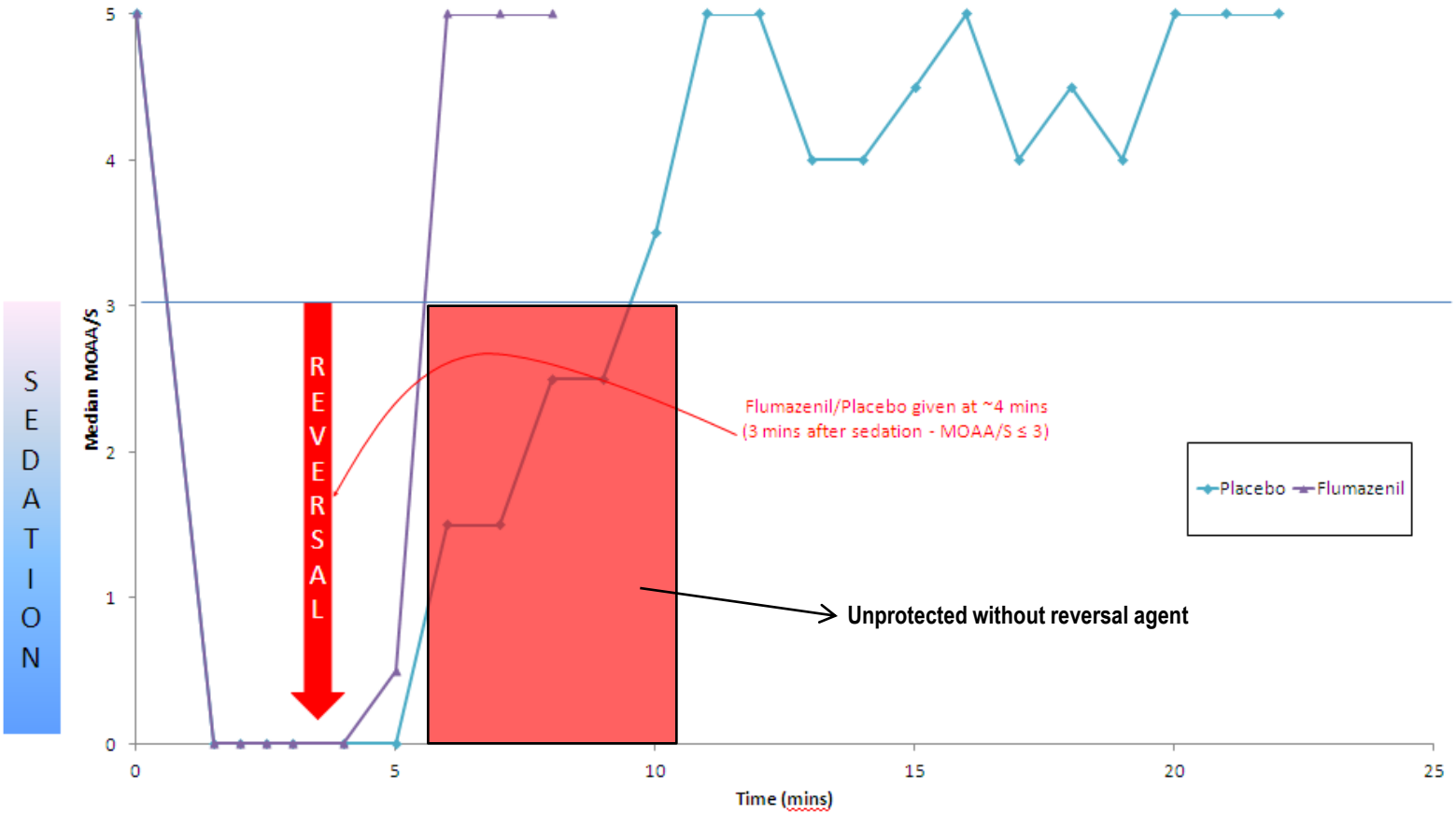
Reversability with Flumazenil is a key safety feature



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Structure of U.S. Phase III program trials in procedural sedation

(Total N all trials: 1,533 & Total N on remimazolam: 1,075)

Success of procedure as measured by:

- Completion of the procedure
- No requirement for a rescue sedative medication
- No more than 5 doses of study medication within any 15-minute window for placebo and remimazolam
- No more than 3 doses of study medication within any 12-minute window for midazolam

all patients: fentanyl
25–75 mcg initial
25 mcg top-up (to 200 mcg)

double-blind remimazolam	double-blind placebo	open label midazolam
2.5 mg - 5 mg initial 1.25 mg - 2.5 mg top-up	(midazolam "rescue")	1 mg - 1.75 mg initial 0.5 mg - 1 mg top-up (per FDA insert)

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Demographics of Phase III program covers requested age and sickness levels

	Remimazolam Phase III bronchoscopy	Remimazolam Phase III colonoscopy	Remimazolam ASA III/IV colonoscopy
Mean age [years]	**62.3**	**54.9**	**62.5**
Age group >= 65 years [%]	**48.5**	**13.8**	**40.3**
Gender male vs. female [%]	45.9 vs. 54.1	47.6 vs. 52.4	55.8 vs. 44.2
Mean height [cm]	168.6	169.6	170.2
Mean weight [kg]	80.8	83.1	90.4
Mean BMI [kg / m^2]	28.3	29.0	30.8
ASA III [%]	**37.6**	**6.6**	**51.9**

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Phase III bronchoscopy study overview procedural results

- Remimazolam outperformed the placebo arm and the open-label midazolam arm in the primary and all important secondary endpoints

	Remimazolam	Placebo	Midazolam (Open Label)
Procedural Success	82.5%	3.4%	34.8%
Use of Rescue Sedation	16.2%	96.6%	56.6%
Time from First Dose to Start of Procedure	5.0 min	17.0 min	16.0 min
End of Procedure to Fully Alert	6.0 min	14.0 min	12.0 min
Time to “back to normal”	404.0 min	935.0 min	478.5 min

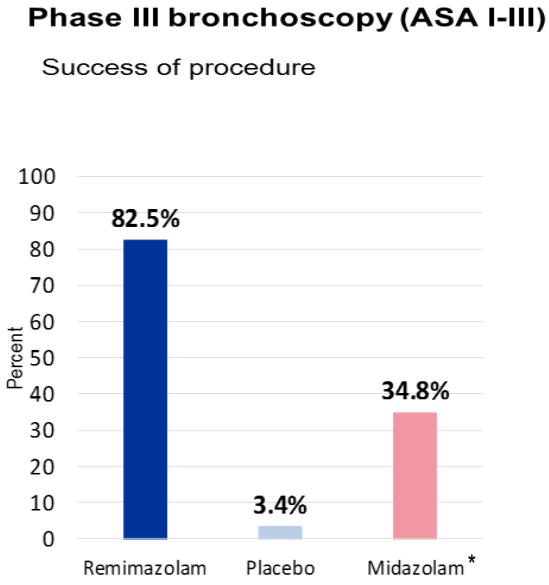
Remimazolam: Comparable results in different populations

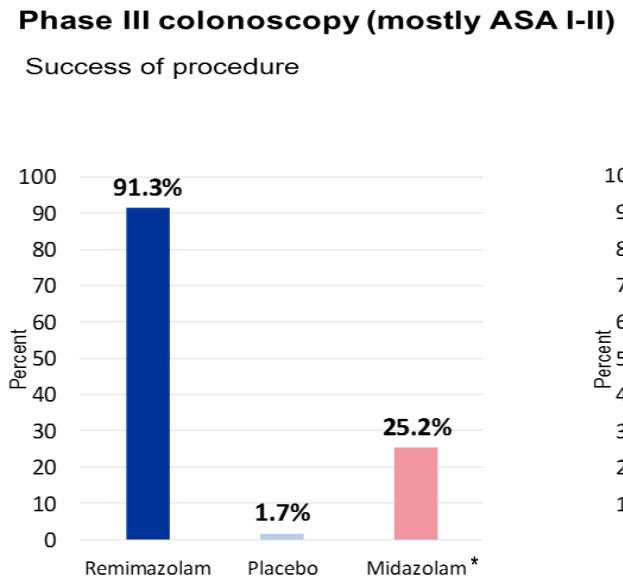
Three U.S. trials with positive results

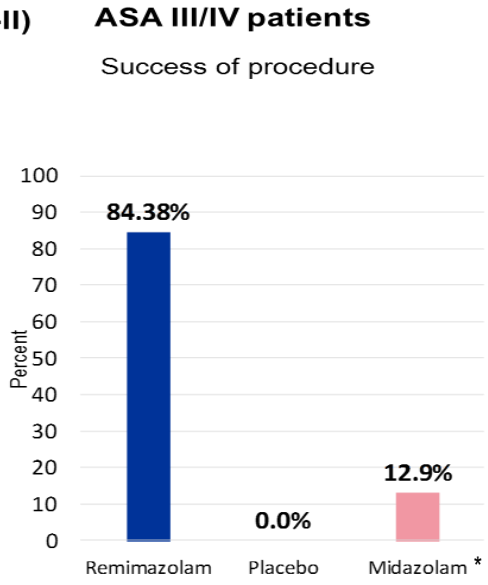
Phase III trial in procedural sedation in patients undergoing bronchoscopy (n=446)

Phase III trial in procedural sedation in patients undergoing colonoscopy (n=461)

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







* 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

Clinical Need and Challenges

Advantages and disadvantages of currently used procedural sedatives

Midazolam	Propofol
Advantages	**Advantages**
Sedation: 19 min	Sedation: 3-5 minutes
Reversal agent (Flumazenil)	Short-acting sedative
Favorable cardiorespiratory profile	Quick onset and offset
Disadvantages	**Disadvantages**
'Shortest-acting' BDZ (but not as short as propofol)	Cardiorespiratory depression
Variable/prolonged sedation	Pain on injection
Slow onset of adequate sedation when used per label	No reversal agent
Re-sedation potential with flumazenil	

Propofol is not approved for procedural sedation in Japan although it is popular in other countries
Clinical need for a short-acting agent like propofol with the safety profile of midazolam

David Bernstein, Tokyo, JSCA 2017

Remimazolam – Next Steps in the U.S.

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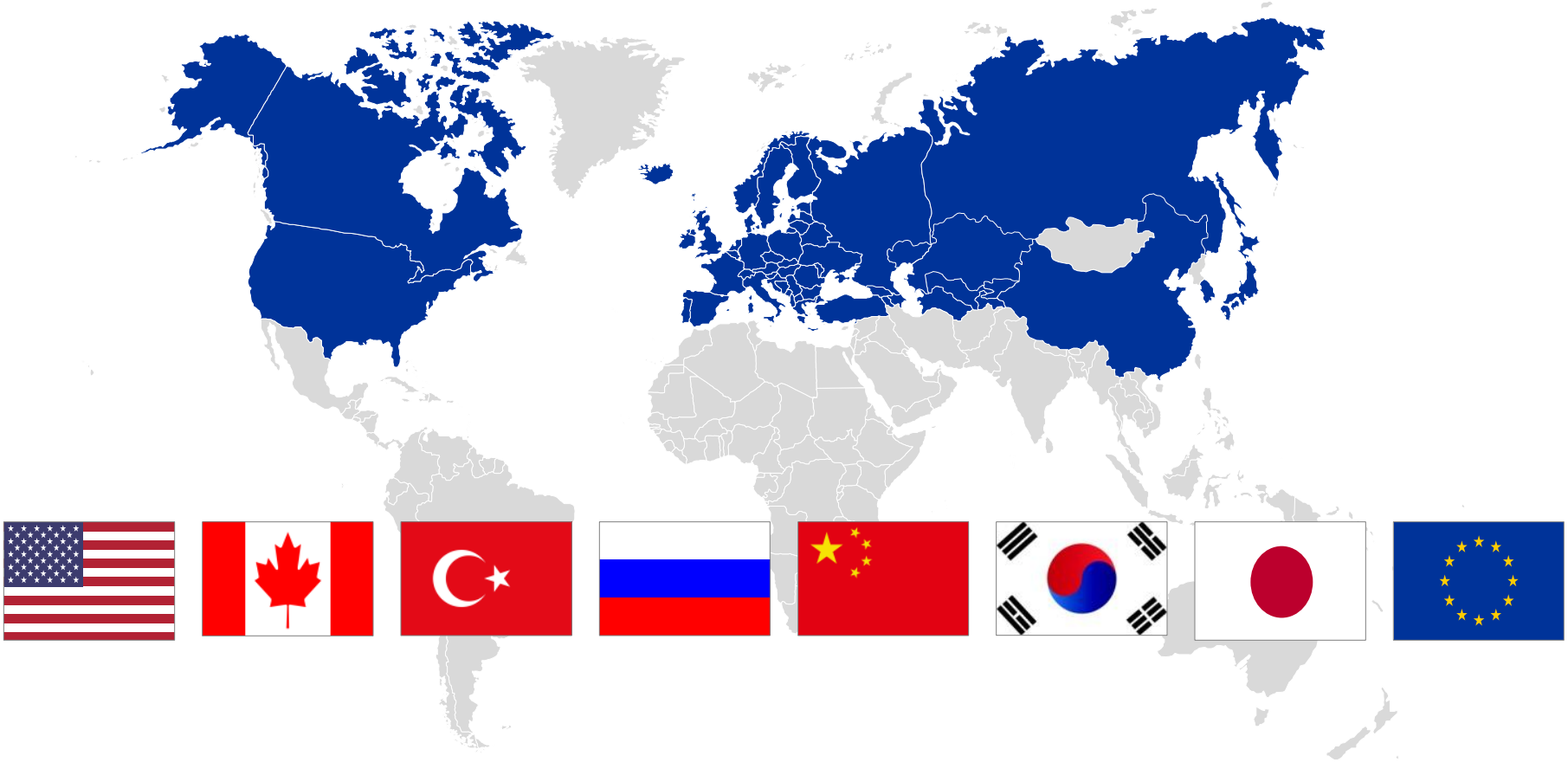
Driving remimazolam forward – PAION and partner activities



All regions with development and regulatory activities:
Partners continue development and preparatory filing activities
(Yichang Humanwell, Hana Pharm, R-Pharm, TR-Pharm, Pendopharm, Cosmo, Mundipharma)

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Remimazolam – Beyond the U.S. opportunity

EU

- **Lead indication**: General anesthesia
- Phase I study to support sample size calculation for an EU Phase III study in general anesthesia conducted
- Guidance from European Medicines Agency (EMA) determined components of new European development program
  - Approx N 450 - 500 for Phase III
- Plan to commercialize remimazolam alone in the EU but also open to potential value-generating partnerships

Japan

- **Lead indication**: General anesthesia
- Completed development program
- Partnered to Mundipharma in Dec 2017
  - EUR 1 m upfront payment
  - Additional regulatory and commercial milestone payments of up to EUR 25 m
  - Royalties ranging from low double-digits to over 20%
- Mundipharma plans to file in 2018

Remimazolam – Beyond the U.S. opportunity

Russia – R-Pharm

- **Lead indication**: General anesthesia
- R-Pharm announced the start of a Phase III study with remimazolam in general anesthesia in Russia in August 2017
- Completion of the study is expected still in the first half of 2018
- Subsequently, R-Pharm plans filing for market approval which is currently planned end of 2018

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. 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
- Yichang Humanwell is going to conduct two clinical studies with remimazolam in China; one Phase III study in procedural sedation and one Phase II study in general anesthesia

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Remimazolam – Beyond the U.S. opportunity

South Korea

- **Lead indication**: General anesthesia
- Hana Pharm is going to conduct a Phase III study with remimazolam in general anesthesia in South Korea
- Completion of the study is expected in 2018
- Hana Pharm plans to file for market approval based on the Japanese dossier

“String of pearls”

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

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

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

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

****) Received after the balance sheet date.

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

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4. **Outlook and Vision**

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Upcoming milestones

2018

- Potential filing in other regions
- Potential filing in PS in the U.S.
- Potential filing in GA in Japan
- Start Phase III in GA

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

Time

1

Accelerated Life Cycle Management of Remimazolam
Launch in multiple indications across different regions before exclusivity window closes

2

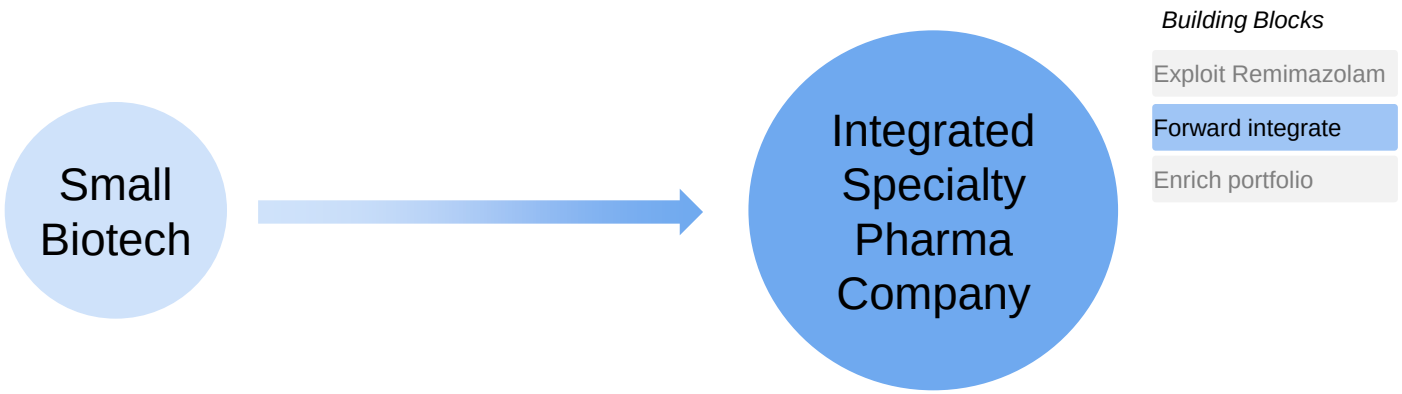
Forward Integration and Creative Partnering
Integrate forward in selected regions with creative deal-making for others

3

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

PAION

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



- PAION does not have a technology platform to constantly create and deliver new products
- Single product development companies risk getting stuck or being acquired

- To become a leader in its field, forward integration is essential for PAION, especially in the EU in the near term
- Forward integration removes the risk of not finding partners (there are few credible and knowledgeable players) and avoids the vulnerability of any chosen partners underperforming

In the long term, partnering may partially be replaced by own-commercialization and distributor deals

Building Blocks

- Exploit Remimazolam
- Forward integrate
- Enrich portfolio

	Immediate Opportunities	Future Opportunities
EU	• PS launch in UK and France • Followed by a broader European launch	• GA for pan-European, ICU and IN/ped
US	• PS for colonoscopists through partner • PS for other specialties through partner GA through partner	• First and subsequent non-remimazolam product/solution through partner
RoW	• GA and PS through partners	• Distributors for remaining indications

In the near future, PAION plans to forward integrate in the EU, expand the win-win partnerships in the U.S. and in RoW

PAION

Anesthesia alone is also not sufficient to move beyond being a “one product company”: acute and critical care is the future

Building Blocks

- Exploit Remimazolam
- Forward integrate
- Enrich portfolio

Anesthesia falls within a broader area of acute and critical care

Acute and Critical Care

Locations

- Hospitals
- Intervention Centres
- Clinics

Specialists

- Anesthetist
- Interventionalist
- Critical Care Physician

PAION’s understanding of the “24/7” nature of acute care and connections to both anesthetists and interventionalists positions it well to expand beyond remimazolam

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For portfolio enrichment PAION is open-minded across indications and products to secure its need for growth

Indications and products relevant to the acute/critical care physician community (anesthetists, interventionalists, critical care physicians)

Building Blocks

- Exploit Remimazolam
- Forward integrate
- Enrich portfolio

Indications

- Anesthesia
  - Conscious sedation
  - Induction and maintenance
  - ICU sedation
- Pain Management
- Other Critical Care

  (avoiding chronic care, e.g. sepsis, lung injury)
  - Blood pressure and fluid management
  - Infections
  - Acute intoxication
  - Bleeding
  - Medical Devices

Products

- Prescription (Rx)
  - (e.g. remimazolam)
- Novel drug delivery / reformulation for existing acute care drugs
- Generic (Gx)
  - (e.g. remifentanil)
- Devices/Solutions
  - (e.g. fluid management devices)

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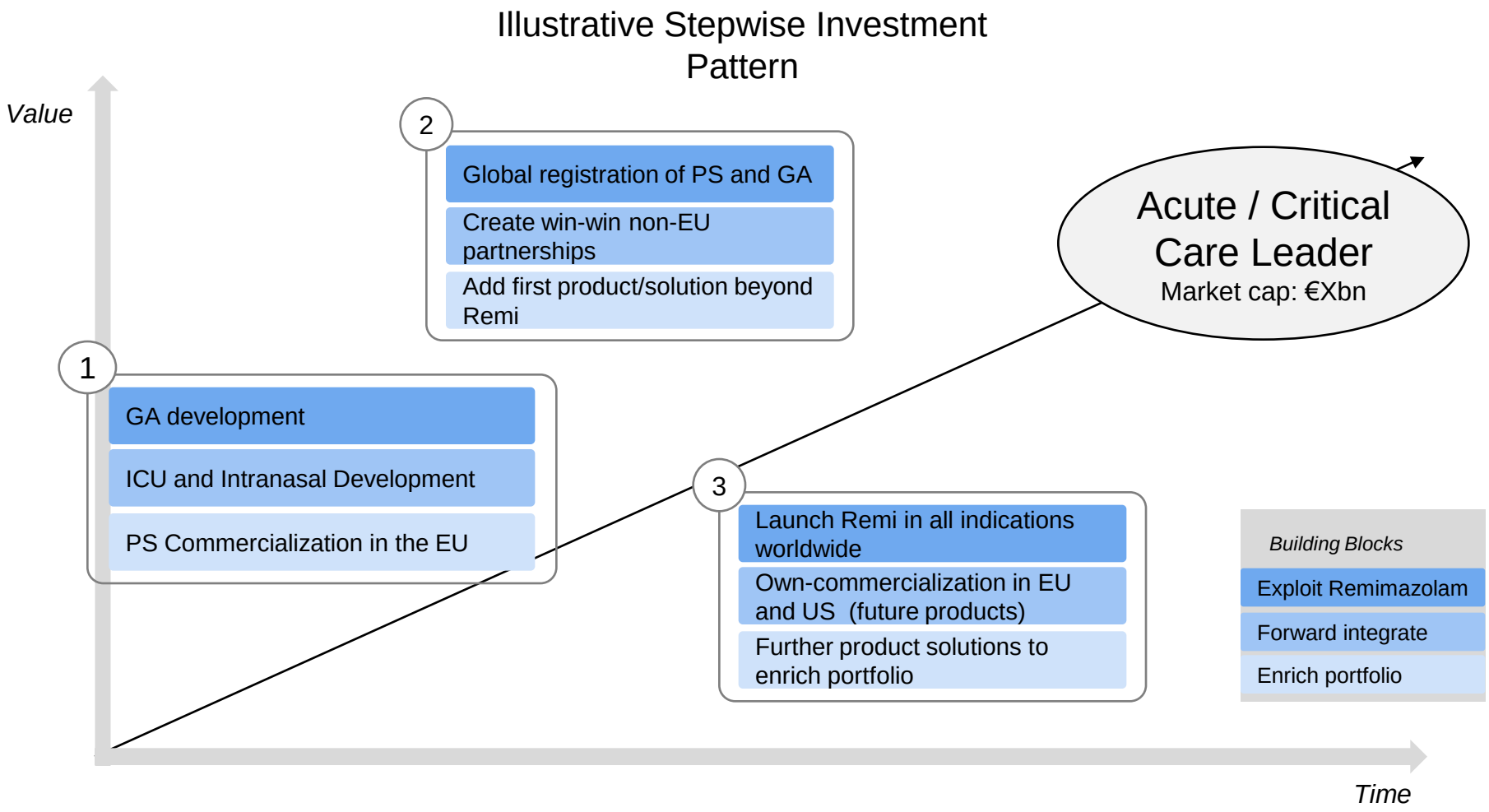
To achieve its ambition, PAION needs to accelerate its strategic evolution across the three building blocks in parallel



Further upside is available by adding the intranasal indication and securing pipeline/product deals and partnerships

1	**Intranasal/Pediatric** Initial investments are modest and an intranasal formulation generates strong IP and has many indications	Investment required
2	**Enrich portfolio** Depends on having deal opportunities and must be funded in addition	Could be achieved using shares as currency
3	**Enhance and modify partnerships** *Case by case for each region, balancing upfronts and future cash flows, e.g. Japan where GA filing is in progress*	Could require investment if take on development

PAION

Q&A

Contact:
PAION AG
Martinstrasse 10–12
52062 Aachen – Germany

Phone +49 241 44 53-0
info@paion.com
www.paion.com