

# Update on ABP-700



## Forward looking statements

Statements contained in these slides about The Medicines Company (the “Company”), the Company’s products and product candidates, clinical trial results, regulatory submissions, product or indication launches, the Company’s future financial and operating results, and future opportunities for the Company, that are not purely historical, and all other statements that are not purely historical, may be deemed to be forward-looking statements for purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995. Without limiting the foregoing, the words “believes,” “anticipates,” “plans,” “expects,” “intends,” “potential,” “estimates,” “outlook” and similar expressions are intended to identify forward-looking statements. There are a number of important factors that could cause actual results or events to differ materially from those indicated by such

forward looking statements, including: the extent of the commercial success of our products; the Company’s ability to develop its global operations and penetrate foreign markets; whether the Company’s patent and other litigation is resolved in a timely and satisfactory manner; whether the results of preclinical studies or early clinical trials will be indicative of the results of later clinical trials; whether the Company’s product candidates will advance in the clinical trials process on a timely basis or at all; whether the clinical trial results will warrant submission of applications for regulatory approval; whether the Company will make regulatory submissions for product candidates on a timely basis or at all; whether the Company’s product candidates will receive approvals from regulatory agencies on a timely basis or at all; whether the Company’s ongoing and planned commercial launches will be

successful; whether physicians, patients and other key decision makers will accept clinical trial results, whether we can successfully enter into strategic partnerships and such other factors as are set forth in the risk factors detailed from time to time in the Company’s periodic reports filed with the Securities and Exchange Commission (“SEC”) including, without limitation, the risk factors detailed in the Company’s Form 10-Q filed with the SEC on August 7, 2015, which are incorporated herein by reference. The Company specifically disclaims any obligation to update these forward-looking statements. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this presentation. All forward-looking statements are qualified in their entirety by this cautionary statement.

# ABP-700

## Panel Members

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Dr. Talmage Egan	Chairman, Department of Anesthesiology, University of Utah Health Care
Dr. Doug Raines	Professor of Anesthesia, Massachusetts General Hospital and Harvard Medical School, and inventor of ABP-700
Dr. Michel Struys	Professor and Chairman, Department of Anesthesiology, University Medical Center Groningen, Netherlands
Dr. Robert Sneyd	Dean and Professor of Anesthesia, Plymouth University Peninsula Schools of Medicine and Dentistry, Plymouth, UK

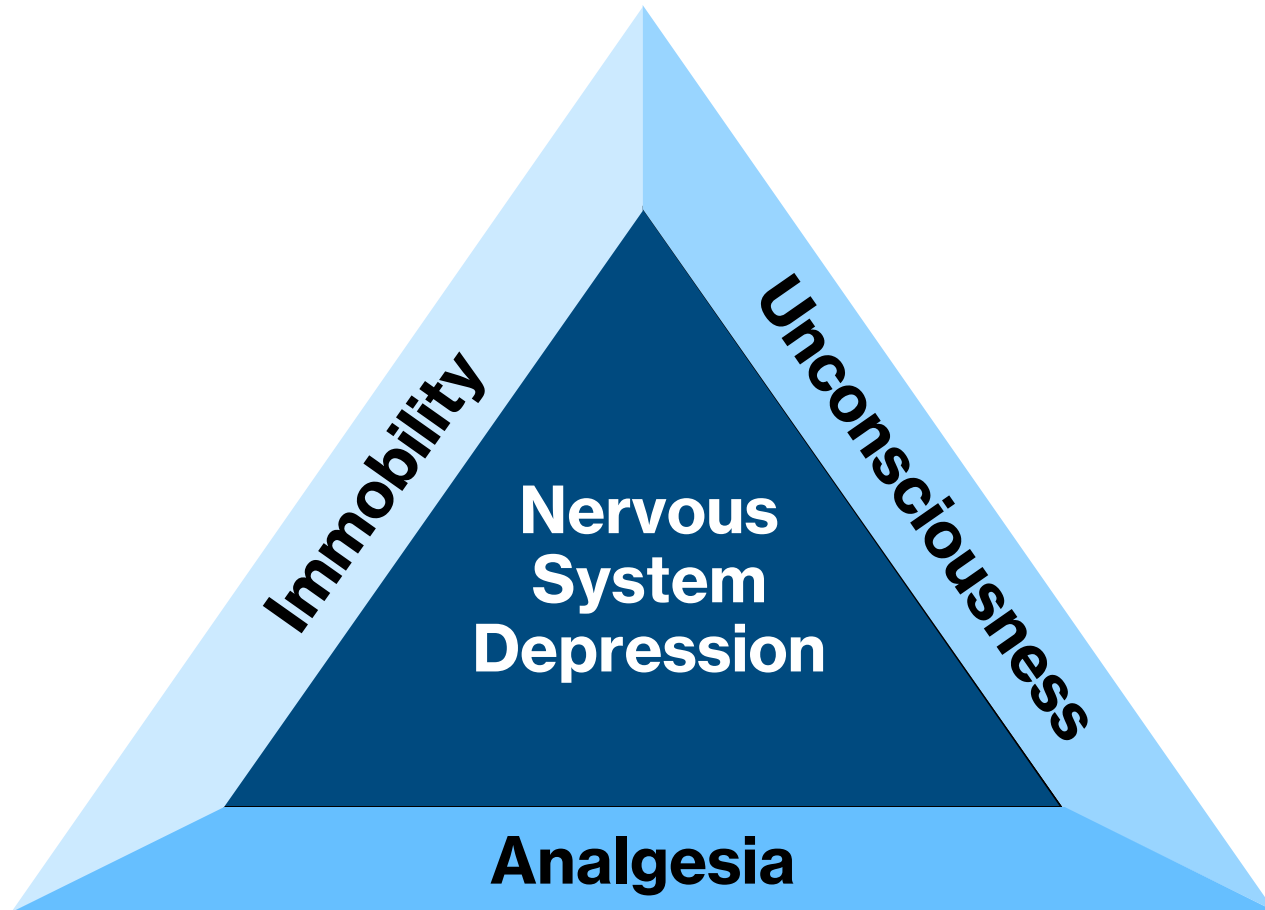
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DISCLAIMER: The physicians on the panel – Drs. Egan, Raines, Struys, and Sneyd – are advisors to The Medicines Company and have received compensation for services rendered. They are not employees of The Medicines Company.

# Anesthesia

## Modern construct

**Anesthesia is a reversible coma**



# Anesthesia

## Spectrum of clinical states

**Lower doses produce sedation, bigger doses produce anesthesia**



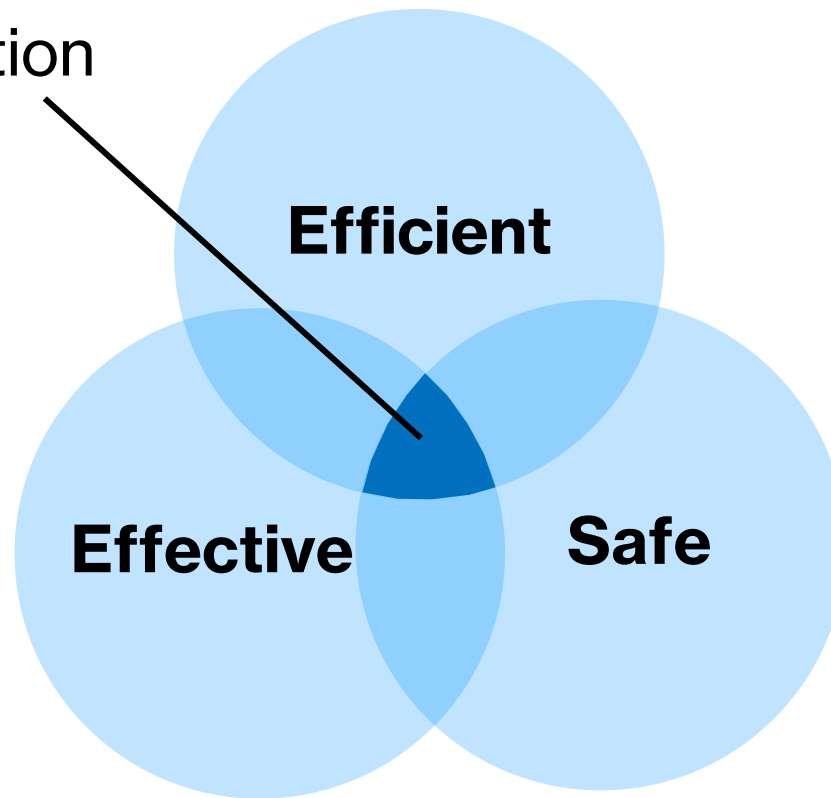
Increasing Drug Dosage 

 Recovery

# Anesthesia

## Unique challenge

Anesthesia  
pharmacology is  
at this intersection



Drugs and Dosages

# Anesthesia

## Properties of an ideal IV agent

- Water soluble
- Rapidly metabolized
- Rapid equilibrium between plasma and brain
- Nominal CV changes
- Minimal ventilatory depression
- Low incidence of nausea and vomiting
- No pain on injection

# Anesthesia

## ABP-700

### Massachusetts General Hospital, Department of Anesthesia

Designed to improve safety & efficiency

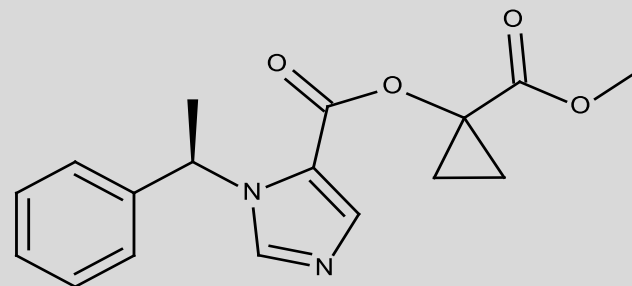
Soft-drug analogue of etomidate

Extensive intellectual property

Attractive profile in animal studies

Designed to be a potentially better tool  
to care for patients

**ABP-700**



**ABP-700 is an investigational agent not approved for commercial use in any market.  
Results included herein are based on preliminary Phase I data.**



# ABP-700

## Phase 1 Program

Study	Dose	Parameters	Subjects
01	Bolus to maximum tolerated dose (MTD)	Safety, Pharma, efficacy	60
02	Infusion to MTD; concomitant medications	Safety, PK, efficacy	60
03	Bolus; concomitant medications	Safety, PK, efficacy	60
04	Infusion; concomitant medications	Dose optimization for light moderate sedation	60
05	Infusion; concomitant medications	Dose optimization for deep sedation and anesthesia	60

MTD: Maximum tolerated dose; PK: Pharmacokinetics

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# ABP-700

## Phase 1 results (AVN01)

- Pharmacokinetics linear, dose proportional
- Dose dependent effect
- Rapid reversing of anesthetic effect
- Normal adrenal responsiveness to stimulation
- No blood pressure reduction vs. placebo
- Preserves respiratory status at clinically relevant doses
- Promising safety and tolerability profile

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# ABP-700

## Treatment Emergent Adverse Event Summary (prevalence $\geq$ 2 subjects)

	PBO N=10	0.10 mg/kg N=5	0.175 mg/kg N=5	0.25 mg/kg N=5	0.35 mg/kg N=5	0.50 mg/kg N=5	0.75 mg/kg N=5	1.00 mg/kg N=5
<b>MedDRA Preferred Term</b>								
Hyperventilation	-	-	-	-	-	5	5	-
Apnea	-	-	-	-	-	1	3	5
Muscle Twitching	-	-	-	5	3	-	-	[1]
Sinus Tachycardia	-	-	2	-	1	-	1	3 [1]
Catheter Site Related Reaction	1	-	1	1	-	-	1	1
Eye Disorder*	1	-	3	-	1	-	-	-
Increased Blood Pressure	-	-	1	-	-	-	-	3 [1]
Restlessness	-	-	-	-	-	-	-	3
Hiccups	-	-	-	-	-	-	-	3
Abnormal Respiration	-	-	-	-	-	-	-	3
Anaesthetic Complication Neurological <sup>†</sup>	-	-	-	-	1	1	[1]	-
Involuntary Muscle Movements <sup>‡</sup>	-	-	-	-	-	1	[1]	[1]
Oxygen Saturation Decreased	-	-	-	-	-	-	-	[2]
Fatigue	-	-	-	-	2	-	-	-

Verbatim terms: rhythmic movement of eyes, eye lid fluttering and eye lid twitching

<sup>†</sup> Verbatim term: emergence delirium

<sup>‡</sup> Preferred terms: myoclonus, dyskinesia

n = Total # of subjects experiencing a mild AE

[ ] = Total # of subjects experiencing a moderate AE. AEs were self-limiting.

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# ABP-700

## Phase 1 results (AVN02-AVN04)

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AVN02	Propofol active comparator Infusions for moderate sedation (less than MTD) Minimal impact on respiratory function
AVN03	Minimization of IMM Unchanged PD and safety profile with concomitant medications
AVN04	30 minute infusions Light/Moderate sedation No adverse hemodynamic or respiratory effects No clinically relevant IMM or myoclonus

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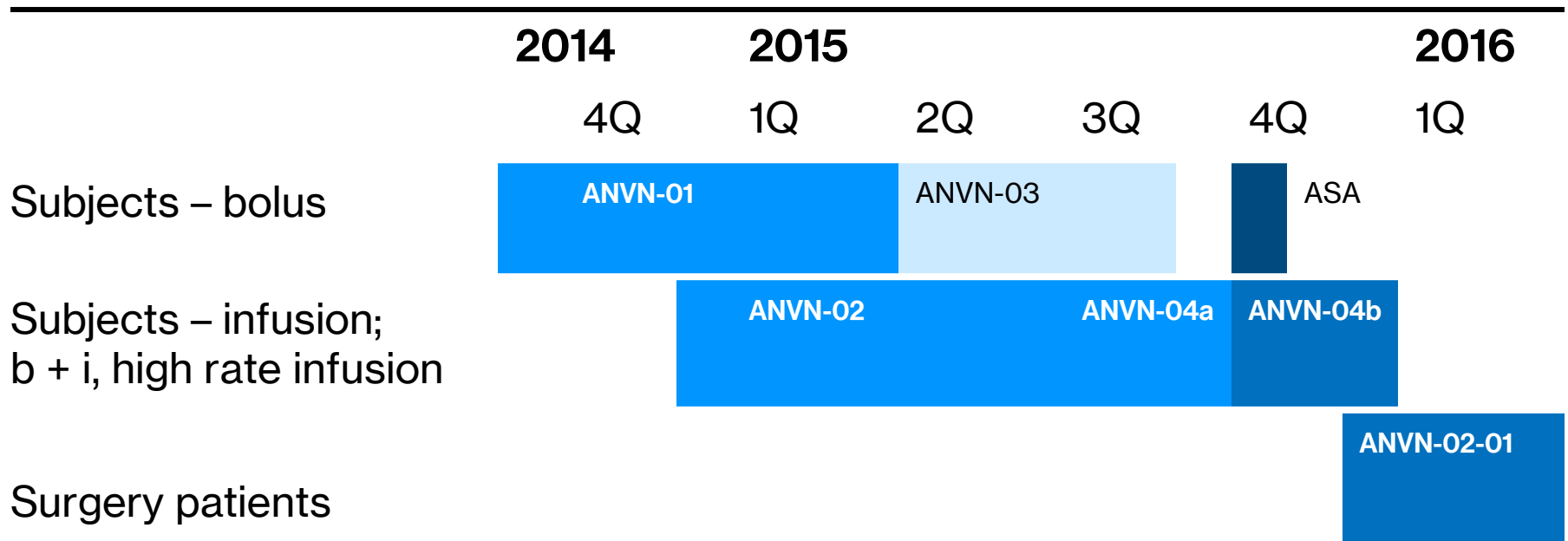
MTD: Maximum tolerated dose; IMM: Involuntary muscle movements

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# ABP-700

## Next steps

### Complete high dose infusion program; start phase II

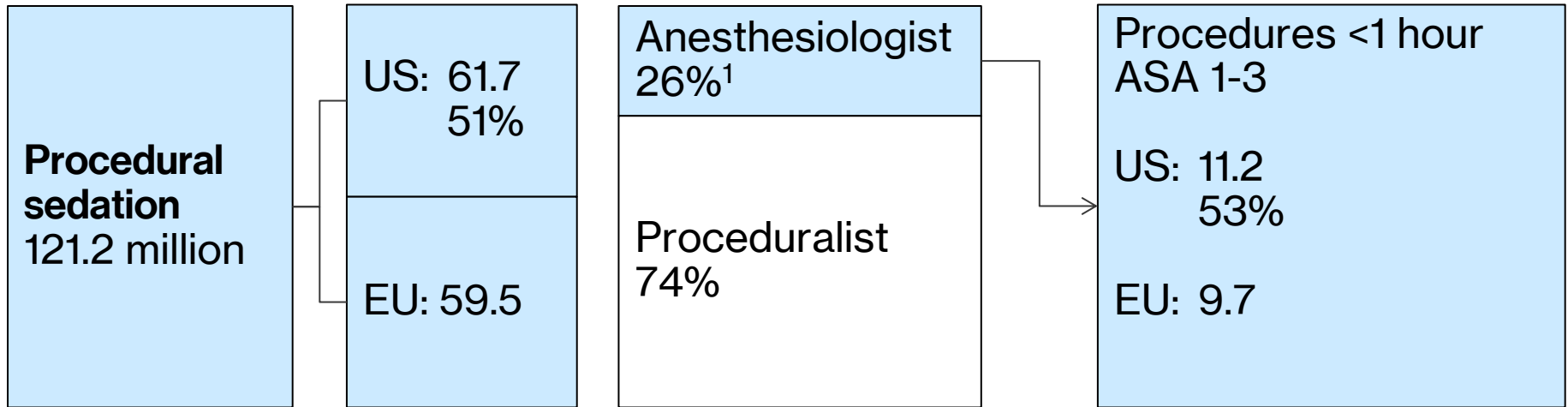


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# Spotlight on anesthesia

## Anesthesia and conscious sedation opportunity

**US and EU procedures total ~184 million**



MDCO data

1. Estimate based on US data; EU higher

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# ABP-700

## Development plan

**Efficient, stepwise, global clinical program anticipated<sup>1</sup>**

	<b>Subjects (2014-15)</b>	<b>Patients (2015- )</b>	
<b>Population (active drug)</b>	Normal (n >100)	Induction general anesthesia Procedural sedation (n ~500)	Safety (n ~ 1500)
<b>Dosage</b>	Bolus Infusion	Bolus, infusion, bolus+infusion	
<b>Comparator(s)</b>	Placebo Propofol	Propofol, etomidate, inhaled anesthetics	
<b>Concomitant medication</b>	Fentanyl Sufentanyl Remifentanyl Midazolam	Wide range of opiates, benzodiazepines, muscle relaxants, anti-emetics	
<b>Special studies</b>		e.g. Pediatrics, at risk elderly, ICU, QTC	

1: Subject to discussion with regulatory agencies

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# Summary





# Q&A

