



# Acacia Pharma Group plc

Non-Confidential Corporate Presentation  
January 2021

Our Vision:  
Delivering innovative products to  
enhance surgical patients' recovery

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# Acacia Pharma Group – in Summary

## Acacia Pharma Group plc: commercial stage integrated specialty pharma company

- IPO 2018 on Euronext Brussels (ticker: ACPH)
- Key focus: surgeries, procedures, cancer therapy
- Products to increase procedural throughput in even greater demand due to COVID-19

## BARHEMSYS® – now FDA approved

- Broad label for prevention and treatment of Post-Operative Nausea and Vomiting (PONV)
- Key target: estimated 16 million patients a year in US with PONV after failure of generic antiemetics<sup>1</sup>
- Estimated \$2.7 billion annual total addressable market<sup>2</sup>

## BYFAVO™ – now FDA approved

- Indicated for procedural sedation in adults, supported by strong clinical data package
- Key target: 40 million procedures a year in US, including 25 million GI procedures<sup>3</sup>
- Estimated >\$1.5 billion annual total addressable market<sup>4</sup>

## Commercialization began in 2H 2020

- Key sales, marketing, medical affairs, commercial operations leadership in place
- Sales team in place and deployed against ~900 initial targeted accounts since mid-October
- Drug shortages and surgery backlog creating pent-up demand

1 Calculations based on available procedural data, applied Compound Annual Growth Rate and quantitative market research responses as follows: National Hospital Discharge Survey, 2006; National Survey of Ambulatory Surgery, 2006 (as revised in 2009); Source Healthcare; NCHS 2005; Life Science Strategy Group, LLC. Market Research; Apfel et al., 2004. 2 Based on the calculations in (1) multiplied by the number of doses per patient at a WAC price of \$85 per 10mg dose. 3 iData Research, US Market Report Procedure Numbers for Gastrointestinal Endoscopic Devices February 2019; American Society of Anesthesiologists, Practice Guidelines for Moderate Procedural Sedation and Analgesia 2018; and Quantitative Market Research prepared by The Link Group for Cosmo Technologies (March 2019). 4 Based on the calculation in (4) multiplied by the number of doses per patient at a WAC price of \$39 per dose.

## Leadership Team with Experience to Deliver the Vision

Mike Bolinder  
CEO



- Joined 2015, became CEO 1 August 2019
- 18 years in pharma sales & marketing
- Relevant commercial experience with OFIRMEV® at Cadence/Mallinckrodt



Gary Gemignani  
CFO



- Joined as CFO January 2020
- 30+ years finance experience in healthcare
- Relevant CFO experience in early commercial stage pharma



Dr Gabriel Fox  
CMO



- Joined as CMO 2008
- 24 years in pharmaceutical medicine
- Relevant development and medical-marketing experience in repurposed drugs



# Late Stage Commercial Product Pipeline

Product	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Filing	Approval
<b>BARHEMSYS®</b>	Postoperative Nausea & Vomiting (PONV)	Approved					
<b>BYFAVO™</b>	Procedural Sedation	Approved					
<b>APD403</b>	Chemotherapy Induced Nausea & Vomiting						

# Patent Terms and Commercial Rights

## BARHEMSYS



- Orange Book listed, current patent term to 2031, expected ability to extend<sup>1</sup>
- IP protection in all major pharmaceutical markets:
  - Intend to directly commercialize in the US
  - Exploring partnership opportunities OUS
- Approved for PONV, developing for CINV

## BYFAVO



- Orange Book listing expected soon, current patent term to 2031, expected ability to extend<sup>1</sup>
- In-licensed commercial rights for US (largest pharmaceutical market)
- Approved for procedural sedation, can develop for ICU sedation and general anesthesia

<sup>1</sup> Patent extension currently under review by US Patent and Trademark Office for BARHEMSYS and request is expected to be made for BYFAVO. Management believes the patent terms will be extended to 2034 for both BARHEMSYS and BYFAVO.



# COVID-19 Situation and Impact

“The OR accounts for up to 65% of hospital profit margin, so this missing volume is cutting deeply into cash flow and net income.”

—Becker's Hospital Review<sup>1</sup>

## COVID-19 impact on hospitals and surgical centers

- Non-essential surgeries cancelled creating a significant backlog
- Physical access to hospital decision-makers even more restricted

## Hospital profits have suffered and need to be restored quickly

- Surgeries and procedures are major contributors to hospital profits
- Providers need to dramatically increase throughput to regain lost profits

## We believe our products and team are ideally positioned to help

- BARHEMSYS and BYFAVO can help improve patient throughput – both now even more relevant and of greater interest to customers
- Our strong relationships are helping us gain access to key decision-makers

<sup>1</sup> How to rebuild surgical revenue after COVID-19, **Becker's Hospital Review**, accessed via <https://www.beckershospitalreview.com/strategy/how-to-rebuild-surgical-revenue-after-covid-19-even-if-you-just-lost-60-of-your-or-volume.html>



# **BARHEMSYS<sup>®</sup>**

(amisulpride for injection)

**The first and only FDA-approved  
product for PONV rescue treatment<sup>1</sup>**

<sup>1</sup> FDA labels for other recommended treatments do not include treatment after failed prophylaxis. Treatment agents recommended by Society for Ambulatory Anesthesiology Consensus Guidelines (2014). Habib et al (2019): no agent has previously been shown in a prospective trial to be more effective than a placebo for treating PONV for patients who have failed prophylaxis.

  
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# BARHEMSYS® and the US Opportunity in PONV

## BARHEMSYS Addresses the major unmet need in PONV

- BARHEMSYS is the **only FDA-approved drug for PONV rescue** after failed prophylaxis<sup>1</sup>
- Dopamine D<sub>2</sub>/D<sub>3</sub> antagonist with **broad, differentiated label**
- Offers significant **economic savings** to hospital vs current standard of care

## Large US market opportunity in PONV<sup>2</sup>

- Estimated ~65m eligible surgeries annually, ~49m patients receive preventative antiemetics<sup>4</sup>
- Estimated **~16m patients still develop PONV and need rescue treatment**<sup>3</sup>
- **Total addressable PONV rescue market estimated at ~\$2.7 billion/year**<sup>4</sup>

## Concentrated market, addressable by small direct sales force

- Estimated 80% of surgeries carried out in ~1,200 hospitals<sup>5</sup>
- 30 sales territories address accounts with greatest immediate opportunity
- **Sales team began customer engagement in mid-October**

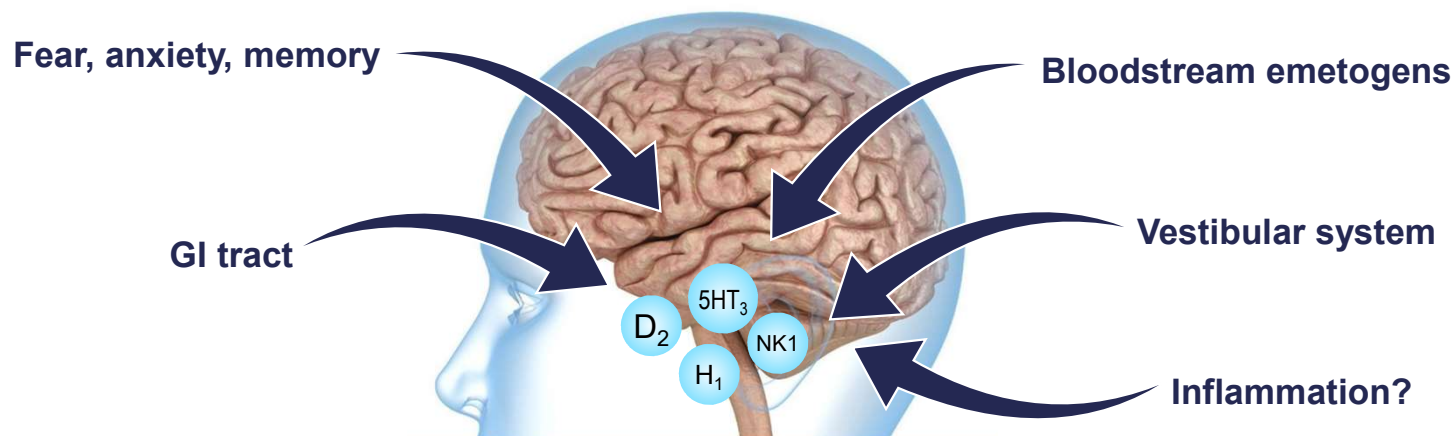
## High gross profit and secure supply chain

- **Cost of goods ~10% of sale price**
- Five-year room temperature shelf-life
- Substantial product inventory to minimize supply risk

1 FDA labels for other recommended treatments do not include treatment after failed prophylaxis, 2 This is the belief of the Company. 3 Company market size estimates based upon: 2006 National Hospital Discharge Survey; National Survey of Ambulatory Surgery, 2006 (as revised in 2009); LSSG Quantitative Research November 2014; Apfel, NEJM 2004. Calculations based on available procedural data, applied Compound Annual Growth Rate and quantitative market research responses. 4 Based upon WAC price of \$85 per 10mg rescue dose with, on average, 2 rescue doses per patient, and the above estimates. 5 Symphony Health, Source Non Retail, August 2017 - July 2018.

# Nausea and Vomiting is a Complex Process

Managed by combinations of antiemetics targeting multiple mechanisms



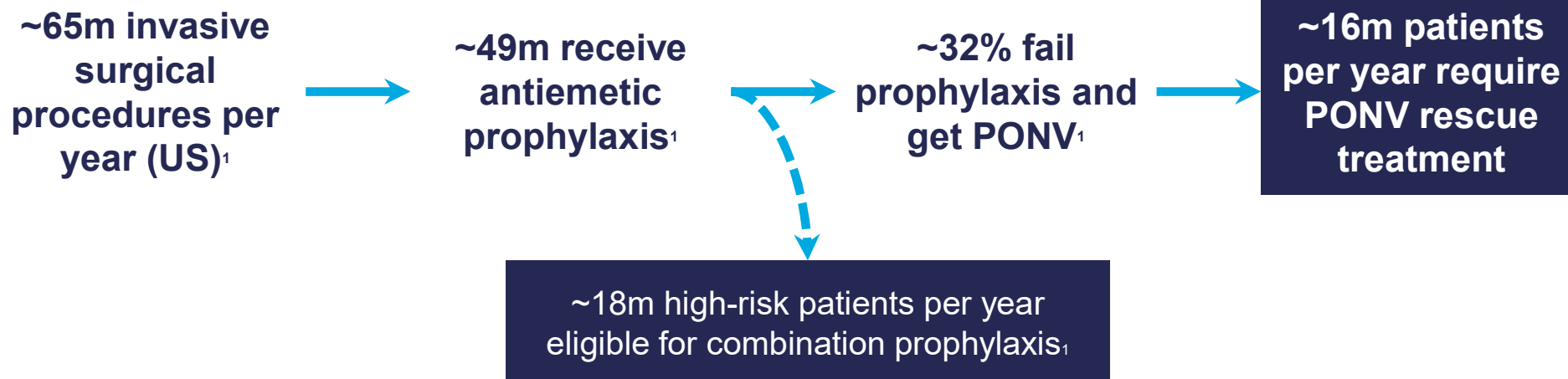
Multiple pathways, including:

- Serotonin ( $5-HT_3$ )
- **Dopamine ( $D_2$ )**
- Histamine
- $NK1$

Current standard of care for PONV prophylaxis<sup>1</sup>:  
5- $HT_3$  antagonist  
(e.g. ondansetron)  
± corticosteroid

**Despite this >30% of surgical patients still get PONV<sup>2</sup>**

## Targeting PONV Rescue Market



**Total estimated addressable market in PONV rescue ≈ \$2.7B per year**

Secondary market in combination prophylaxis in highest-risk patients, estimated to be worth \$765M per year<sup>2</sup>

<sup>1</sup> Company market size estimates based upon: 2006 National Hospital Discharge Survey; National Survey of Ambulatory Surgery, 2006 (as revised in 2009); LSSG Quantitative Research November 2014; Apfel et al, 2004. Calculations based on available procedural data, applied Compound Annual Growth Rate and quantitative market research responses. <sup>2</sup> Based on WAC price of \$85 per 10 mg rescue dose and average 2 rescue doses per patient; \$42.50 per 5 mg prophylaxis dose.

## Generic Options for Rescue Treatment are Problematic

“ When PONV prophylaxis has failed, patients should receive antiemetic treatment from a different pharmacological class to the PONV prophylaxis”

– Consensus Guidelines<sup>1</sup>

Antiemetic	Can't redose	Efficacy issues	Safety issues	Current share of rescue patients <sup>4</sup>
Ondansetron	X <sub>1</sub>			69%
Dexamethasone	X <sub>1</sub>	X <sub>2</sub>		19%
Metoclopramide		X <sub>1</sub>	X <sub>1</sub>	19%
Promethazine			X <sub>1</sub>	11%
<b>BARHEMSYS</b>	✓ <sub>3</sub>	✓ <sub>3</sub>	✓ <sub>3</sub>	<b>INTENT TO PRESCRIBE<sup>4</sup></b> <b>61%</b>

# BARHEMSYS® – Compelling Clinical and Commercial Proposition

## Only FDA-approved product for PONV rescue<sup>1</sup>

- Only drug proven in randomized clinical trial to work in PONV rescue<sup>2</sup>
- Excellent safety profile demonstrated in clinical studies
- Also demonstrated to be effective for prevention

## Throughput and health economic benefits

- 35-minute reduction in PACU stay
- 6-hour reduction in hospital stay
- Offers significant economic savings to hospital vs current standard of care

## Convenient, easy to use, high margin product

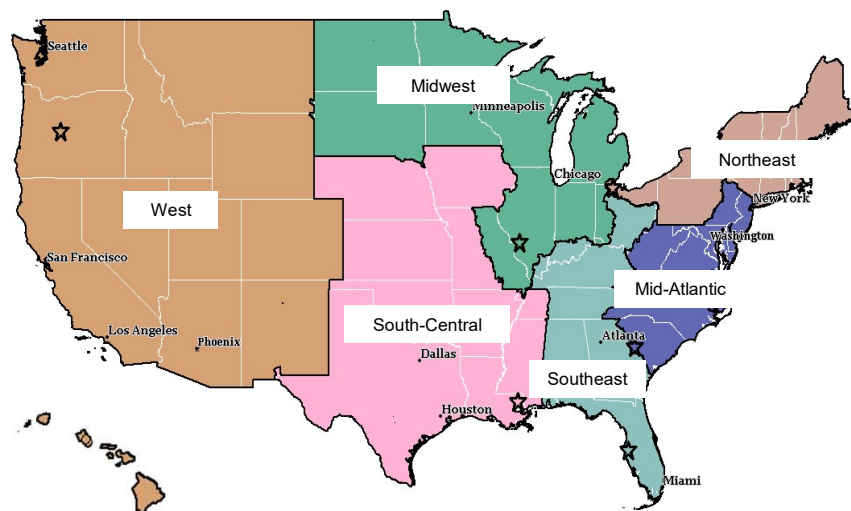
- 5-year room temperature shelf-life
- Fits in auto-dispensing (Pyxis™) machines
- Cost of goods ~10% of sale price

## Helps post-COVID pressure to get through surgical backlog

- Shorter time in PACU allows increased surgical throughput
- Better efficacy and safety means better recovery and patient experience



# Highly Experienced Commercial Team in Hospital Space



Team has direct experience successfully launching **OFIRMEV** into same market to same key customers

## Field Force Design

- 1 VP of Sales
- 1 National Accounts Group Leader
- 1 National MSL Group Leader
- 6 Sales Regions each with:
  - 1 RBD
  - 1 MSL
  - 1 National Account Director
  - 5 Hospital Territory Managers

### Commercial Leadership Team

**28+**  
Years avg  
industry

**60+**  
Launches

### Sales Leadership Team

**22**  
Years avg  
industry

**18+**  
Years  
hospital

### National Accounts Team

**24**  
Years avg  
industry

**21+**  
Years  
hospital

### Medical Science Liaison Team

**22**  
Years avg  
industry

**10+**  
Years as  
MSL



# Commercial Roll-out Underway

## Manufacturing and distribution networks in place

- Substantial API and finished product manufactured to de-risk supply chain<sup>1</sup>
- Service agreements in place with 3<sup>rd</sup> party logistics provider and key wholesalers
- Contracting discussions underway with top Group Purchasing Organizations and Integrated Delivery Networks

## PONV and BARHEMSYS education campaigns ongoing

- Presence at major congresses
- Print and online advertising
- F2F and virtual meetings in key centers

## Strong KOL and advocate support

- Leading PONV experts involved in BARHEMSYS clinical development trials
- Additional anesthesia, surgery and pharmacy KOLs being educated

## Early adopting sites and formulary champions identified

- Extensive institution profiling already undertaken
- Key clinical champions identified in hundreds of hospitals



# Formulary Reviews Began 2H 2020

## Post-COVID pressures improve our access to key decision-makers

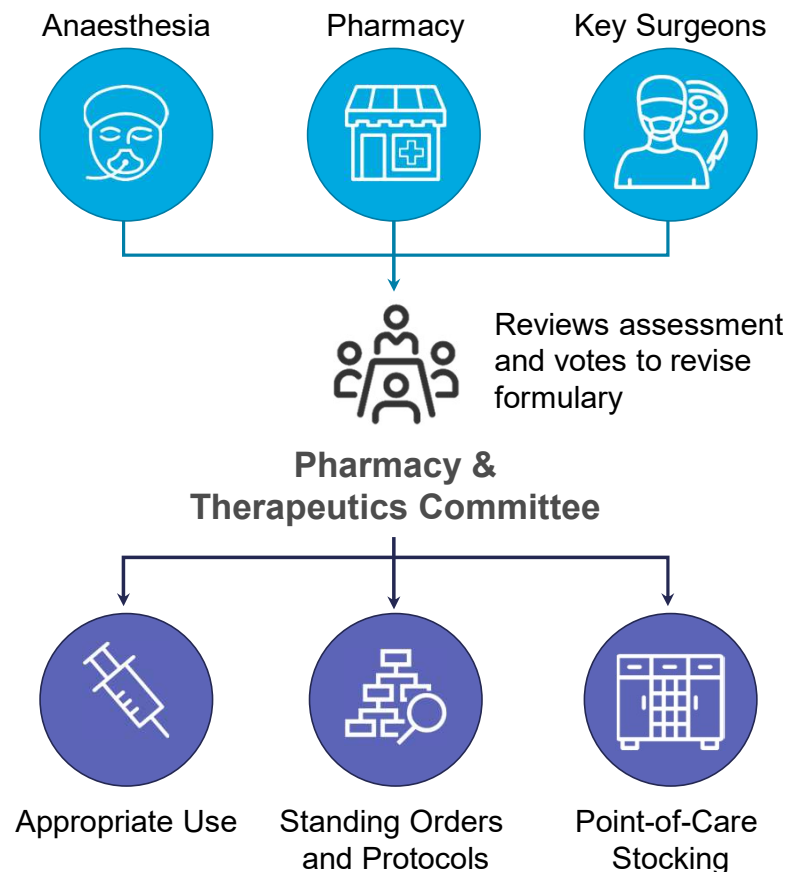
- Surgery backlogs are major issues for US hospitals
- **Value of BARHEMSYS in improving throughput facilitates our access to key decision-makers**

## Demonstrate unmet need, appropriate use & health economic benefit

- Existing products unsuitable for rescue
- **BARHEMSYS is only FDA-approved product for rescue**
- Offers significant economic savings to hospital vs current standard of care

## Formulary adoption and pull-through

- P&T Committee approval typically takes 9-12 months on average<sup>2</sup>
- Protocols, standing orders and point-of-care supplies drive sales pull-through



# Major Follow-on Opportunity in Chemotherapy Induced Nausea & Vomiting (CINV) for APD403

CINV market opportunity is similar to PONV

- ~4 million cycles of highly emetogenic chemotherapy (HEC) every year in US<sup>1</sup>
- **Preventive anti-emetics recommended for 4 days per cycle<sup>2</sup>**

Significant unmet need remains in delayed phase CINV

- Despite use of three-antiemetic cocktail, **50% of patients still suffer with delayed CINV<sup>3</sup>**
- Oncologists target zero tolerance of CINV<sup>2</sup>

One further pivotal trial required to support new indication

- Positive data in one randomized trial: **significant reduction in incidence of delayed CINV<sup>3</sup>**
- Further trial to be conducted by 2022

>90%



patients get CINV when receiving HEC<sup>4</sup>

Two phases of CINV<sup>4</sup>:



**Acute**  
(Day 1)

**Delayed**  
(Day 2-5)

Delayed



CINV

is the **unmet medical need**

Potential NDA submission:



**2023**

32%



**relative risk reduction** of delayed CINV<sup>3</sup>

1 Morgan Stanley analyst note on Tesaro, 2012, Deutsche Bank analyst note on Tesaro, 2013, Edison analyst note on Tesaro, 2014, NCCN Guidelines for antiemesis, 2017.

2 NCCN Guidelines 2017. 3 Calculated from DN10016 study report. 4 Roila et al (2010), Hesketh (2011).



**BYFAVO™**

(remimazolam) for injection

Rapid onset/offset procedural  
sedative with favorable safety profile

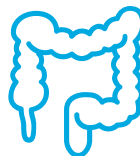
  
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# Procedural Sedation Market Opportunity



**~40 million<sup>1</sup>**

procedures each year  
requiring sedation



**~25 million**

GI procedures performed  
each year<sup>2</sup>



**>80%**

GI procedures have sedation administered  
by an anesthesia provider<sup>3</sup>



**>6 million**

Interventional  
Radiology<sup>4</sup>



**~4 million**

Ophthalmic  
Procedures<sup>5</sup>



**~1 million**

Bronchoscopy<sup>6</sup>



**~1.5 million**

Cosmetic/  
Plastic Surgery<sup>7</sup>

**Total addressable market in procedural sedation >\$1.5B/year<sup>8</sup>**

1 Calculations based on available procedural data, applied Compound Annual Growth Rate and quantitative market research responses. 40 million includes other opportunities: CC (MHA National) EP (cardiology), Dental (areadentist), Plastic Surgery (American Society of Plastic Surgeons), ECT (MHA National). 2 iData Research, US Market Report Procedure Numbers for Gastrointestinal Endoscopies Nov 2016; CDC website. 3 Quantitative Market Research prepared by The Link Group for Cosmo Technologies (March 2019). 4 Report on interventional Radiology November/December 2007. 5 American Medical Association 2011. 6 iData Bronchoscopy 2019 report. 7 American Society of Plastic Surgeons 2018. 8 Based on the calculation in iData Research, US Market Report Procedure Numbers for Gastrointestinal Endoscopic Devices February 2019; American Society of Anesthesiologists, Practice Guidelines for Moderate Procedural Sedation and Analgesia 2018; and Quantitative Market Research prepared by The Link Group for Cosmo Technologies (March 2019) multiplied by the number of doses per patient at a WAC price of \$39 per dose.



# BYFAVO Addresses Unmet Need in Procedural Sedation

## Propofol

*fast acting but  
significant safety issues<sup>1,2</sup>*

- Rapid onset and offset anesthetic with narrow therapeutic index<sup>1</sup>
- **Dose-related cardiorespiratory depression**, pain at injection site<sup>1</sup>
- Non-linear dosing effects due to individual variability<sup>4</sup>
- **Needs continuous monitoring by anesthesiologist, no reversal agent<sup>2</sup>**
- Lipid formulation susceptible to bacterial contamination<sup>4</sup>

## Midazolam

*better safety profile but  
longer onset and recovery<sup>1,2</sup>*

- Benzodiazepine sedative, reversible by flumazenil<sup>1</sup>
- **Slower onset and offset<sup>2,3</sup>**
- Metabolized by cytochrome system; individual variability affects sedation<sup>1</sup>
- Active metabolite can accumulate and cause prolonged sedation<sup>2</sup>
- **Risk of respiratory depression<sup>1</sup>**

## BYFAVO

*fast acting AND favorable  
safety profile<sup>1,2</sup>*

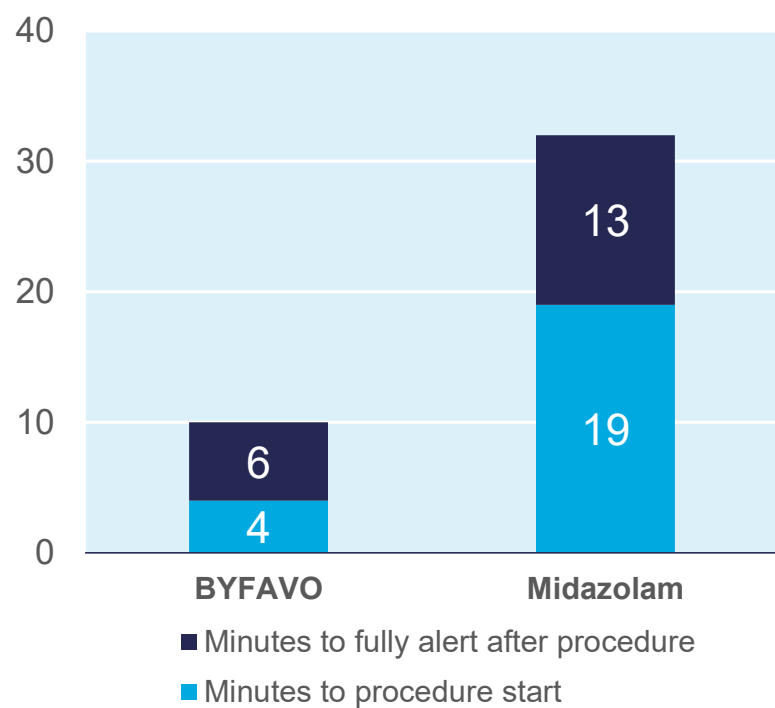
- **Rapid onset/offset<sup>1,2,3</sup>** benzodiazepine
- Rapid biotransformation into inactive metabolites via non-specific tissue esterases – not dependent on liver enzymes<sup>1</sup>
- **Predictable behavior, no pharmacokinetic drug interactions<sup>5</sup>**
- **Reliable sedation, reliable safety profile<sup>1</sup>**
- Reversible by flumazenil<sup>1</sup>

1 Colao J, et al. *J Anesth Clin Res*. 2016; 7:690. 2 Whizar-Lugo V, et al. *J Anesth Crit Care*. 2016; 4(6): 00166. 3 Rex DK et al. *Gastrointest Endosc*. 2018 Sep;88(3):427-437.  
4 Prescribing label for Propofol. 5 Prescribing label for BYFAVO.



## Rapid Onset/Offset with a Favorable Safety Profile<sup>1</sup>

**Average Procedure Timings<sup>1</sup>**



**Key Adverse Events<sup>1</sup>**

	BYFAVO	Midazolam
Any adverse event	74%	91%
Vascular disorders	62%	81%
Cardiac disorders	18%	26%
Respiratory disorders	4%	6%

# BYFAVO™ – Compelling Clinical Proposition

## Approved with a broad label

- Indicated for **procedural sedation in adults** in procedures lasting 30 mins or less
- Substantial clinical data package shows **compelling efficacy and safety** in colonoscopies and bronchoscopies, including least fit patients

## Throughput and health economic benefits

- **Rapid onset/offset enables shorter procedure times and greater patient throughput for hospitals and surgical centers compared to other recommended treatments**

## Commercial synergy with BARHEMSYS

- Target prescribers: **anesthesiologists and proceduralists in hospitals and ambulatory surgery centers**

## Helps post-COVID pressure to alleviate procedural backlog

- **Shorter procedure times allow increased procedural volumes**
- Both midazolam and propofol currently on FDA drug shortages list



# Acacia Pharma Group – Financial Summary

## Listed on Euronext Brussels exchange

- IPO in March 2018
- ~87.5m shares outstanding
- ~80% free float

## Cash position

- Cash balance at June 30, 2020 was ~\$24.6m
- Raised \$30m August 2020

## Debt

- Hercules ~\$8.6m outstanding as of June 30, 2020
- Cosmo ~\$27m outstanding loan

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