AMYLYX®

AVEXITIDE WEBCAST AND IN-PERSON KEY OPINION LEADER EVENT

New Analyses of Avexitide in Post-Bariatric Hypoglycemia Presented at ENDO 2025, including Population Pharmacokinetic and Pharmacodynamic Data and Composite Data from the Phase 2b Trial

July 13, 2025

Maggie, living with Post-Bariatric Hypoglycemia (PBH)

Opening Remarks

Lindsey Allen

Vice President, Investor Relations
& Communications at Amylyx

DISCLAIMER

Statements contained in this presentation regarding matters that are not historical facts are “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Such statements include, but are not limited to, the potential of avexitide as a treatment for PBH; and expectations regarding the timing for recruitment completion and topline data readout of the Phase 3 LUCIDITY trial of avexitide in PBH. Any forward-looking statements in this presentation are based on management’s current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. Risks that contribute to the uncertain nature of the forward-looking statements include: the success, cost, and timing of Amylyx’ program development activities, including ongoing and planned clinical trials, Amylyx’ ability to execute on its development and regulatory strategy, regulatory developments, Amylyx’ cash runway and ability to fund operations, as well as the risks and uncertainties set forth in Amylyx’ United States Securities and Exchange Commission (SEC) filings, including Amylyx’ Annual Report on Form 10-K for the year ended December 31, 2024, and subsequent filings with the SEC. All forward-looking statements contained in this presentation speak only as of the date on which they were made. Amylyx undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

Agenda

Opening Remarks & PBH Community Video	**Lindsey Allen**, Vice President, Investor Relations & Communications at Amylyx
Understanding PBH & the Unmet Need	**Helen Lawler, MD**, Investigator on the LUCIDITY Clinical Trial, Co-Lead Investigator of the Phase 2 PREVENT Clinical Trial, and Associate Professor of Medicine in Endocrinology at University of Colorado at Denver School of Medicine
Scientific Rationale for Avexitide in PBH & Overview of the Avexitide Clinical Data	**Colleen Craig, MD**, Co-lead Investigator of Proof-of-Concept and First-in-Human Studies of Avexitide in PBH, Leader of Avexitide Development Program During Phase 2 PREVENT Clinical Trial, and Scientific Advisor and Consultant for Amylyx
Clinical Perspective on PBH & Review of Composite Level 2/3 Events in Phase 2b Trial	**Marilyn Tan, MD, FACE**, Principal Investigator of the LUCIDITY Clinical Trial, Co-Lead Investigator of the Phase 2 PREVENT Clinical Trial, and Clinical Associate Professor of Medicine at Stanford University School of Medicine
Review of Avexitide PK/PD Profile and LUCIDITY Phase 3 Trial Design	**Jamie Timmons, MD**, Vice President, Medical Affairs at Amylyx
Closing Remarks	**Josh Cohen**, Co-Chief Executive Officer at Amylyx
Q&A	Moderated by **Camille Bedrosian, MD**, Chief Medical Officer of Amylyx

Speakers' Bios

Helen Lawler, MD

Investigator on the LUCIDITY Clinical Trial, Co-Lead Investigator of the Phase 2 PREVENT Clinical Trial, and Associate Professor of Medicine in Endocrinology at University of Colorado at Denver School of Medicine

Colleen Craig, MD

Co-lead Investigator of Proof-of-Concept and First-in-Human Studies of Avexitide in PBH, Leader of Avexitide Development Program During Phase 2 PREVENT Clinical Trial, and Scientific Advisor and Consultant for Amylyx

Marilyn Tan, MD, FACE

Principal Investigator of the LUCIDITY Clinical Trial, Co-Lead Investigator of the Phase 2 PREVENT Clinical Trial, and Clinical Associate Professor of Medicine at Stanford University School of Medicine

Jamie Timmons, MD

Vice President, Medical Affairs at Amylyx

PBH Community Video

Understanding PBH and the Unmet Need

Helen Lawler, MD

Investigator on the LUCIDITY Clinical Trial, Co-Lead Investigator of the Phase 2 PREVENT Clinical Trial, and Associate Professor of Medicine in Endocrinology at University of Colorado at Denver School of Medicine

Relevant Disclosures: Dr. Lawler has received research payments from Amylyx Pharmaceuticals and Vogenx in her role as a site investigator and received consulting payments from Amylyx and Vogenx.

POST-BARIATRIC HYPOGLYCEMIA (PBH)

- Hypoglycemia occurs 1-3 hours after eating (worse with higher carbohydrate foods)
- PBH typically develops around 2-3 years post surgery
- Rapid transit of glucose to small intestine triggers GLP-1 secretion which stimulates insulin release from the pancreas and subsequent hypoglycemia
- Hypoglycemia can be severe and debilitating

Autonomic Symptoms		**Neuroglycopenic Symptoms**	
Adrenergic	**Cholinergic**		
Palpitations	Diaphoresis	Confusion	Blurred vision
Tremulousness	Paresthesia	Slurred speech	Seizure
Anxiety	Hunger	Weakness	Coma
Nausea		Dizziness	

MANAGEMENT OF POST BARIATRIC HYPOGLYCEMIA

DIETARY INTERVENTION (first line)

- Only low glycemic index carbohydrates
- Mixed meals - ample protein and healthy fat, high fiber foods
- Each meal: < 4 g added sugar, < 30 g carbs/meal
- Avoid liquid with meals

CURRENT MANAGEMENT APPROACHES (None are FDA approved for PBH)	LIMITATIONS
Continuous glucose monitor (CGM)	Insurance coverage is often difficult; compression lows; inaccuracies
Glucagon	Treatment failure; Generally only used as a rescue treatment
Cornstarch	Treatment failure, bloating, gas, abdominal pain
Acarbose	Treatment failure, bloating, gas, abdominal pain
Diazoxide	Treatment failure, edema, hirsutism, hypotension
Somatostatin analogues (i.e. – octreotide)	Treatment failure, diarrhea, cost
GLP-1 receptor agonist	Treatment failure, unwanted weight loss, N/V, cost
Surgical Approaches	Invasive; life-altering; a rare last resort

POST BARIATRIC HYPOGLYCEMIA RESEARCH

FORMER DEVELOPMENT TARGETS

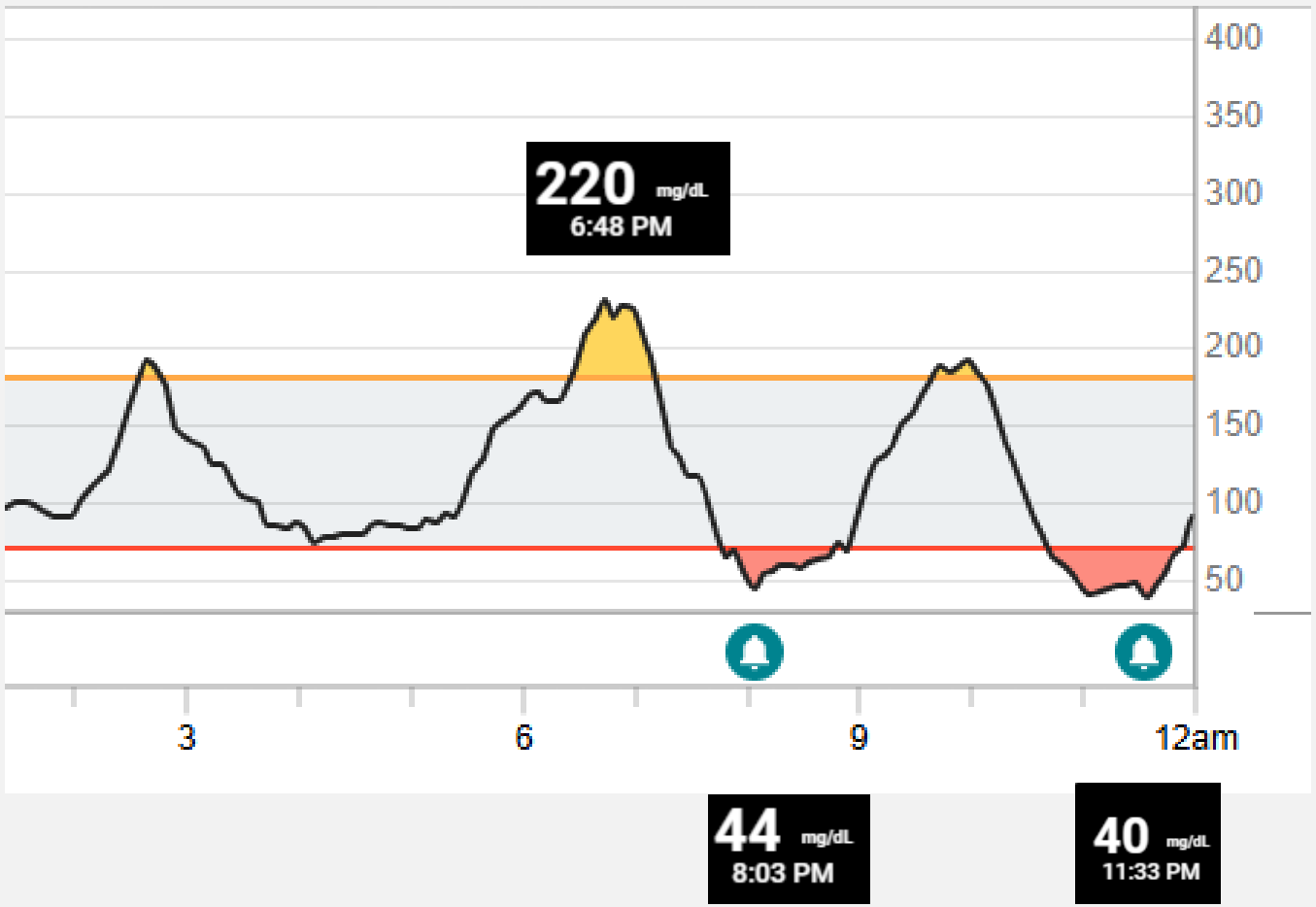
- Mini-dose RTU glucagon (300µg)
- XOMA 358
- canagliflozin
- empagliflozin

CURRENT CLINICAL TRIALS

- GLP-1 receptor antagonist (avexitide)
- pasireotide
- mizagliflozin
- MBX 1416

PATIENTS WITH PBH

- Woman in late-30s who works as a healthcare specialist and eats nothing all day in order to maintain employment
- Woman in late-40s employed as a city bus driver who can no longer work due to hypoglycemia
- Woman in early-40s and woman in late-40s who opted to have total pancreatectomies as hypoglycemia was so debilitating
- Man in early-50s who follows a ketogenic diet to try to prevent hypoglycemia yet continues to have low blood sugars and difficulty maintaining a healthy weight



PBH: GAPS IN TREATMENT AND KNOWLEDGE

- Lack of awareness of post-bariatric hypoglycemia in medical community
    - Symptoms attributed to menopause, anxiety, etc.
- Inconsistent care pathways among providers
- No FDA-approved therapies
- Many off-label medications have intolerable side effects and high failure rates
- This is a population desperate for help to ameliorate debilitating hypoglycemia
- Opportunity to change the standard of care in this serious and underserved condition

Scientific Rationale for Avexitide in PBH & Overview of Clinical Data

Colleen Craig, MD

Co-lead Investigator of Proof-of-Concept and First-in-Human Studies of Avexitide in PBH, Leader of Avexitide Development Program During Phase 2 PREVENT Clinical Trial, and Scientific Advisor and Consultant for Amylyx

Relevant Disclosures: Dr. Craig is a part-time contract consultant for Amylyx. She is also listed as a co-inventor on certain patents and patent applications related to avexitide that are owned or controlled by Amylyx, and under certain agreements has a financial interest in the commercial success of avexitide.

Modeling the U.S. Incidence and Prevalence of Post-Bariatric Hypoglycemia

PBH is significantly underdiagnosed due to inconsistent definitions, poor coding, and a lack of routine screening, especially outside of specialty care

High rates of hypoglycemia unawareness (37-61%) suggest incidence and prevalence estimates may yet underestimate the burden of disease and **reinforcing the need for proactive monitoring**

Nearly 400,000 individuals in the U.S. experience hypoglycemia after bariatric surgery, with **over 160,000 people with PBH requiring medical management**

	Roux-en-Y gastric bypass	Sleeve gastrectomy	Total
	Prevalence		
Any PBH	275,717	111,370	**387,087**
Medically-Important PBH	118,843	48,026	**166,869**

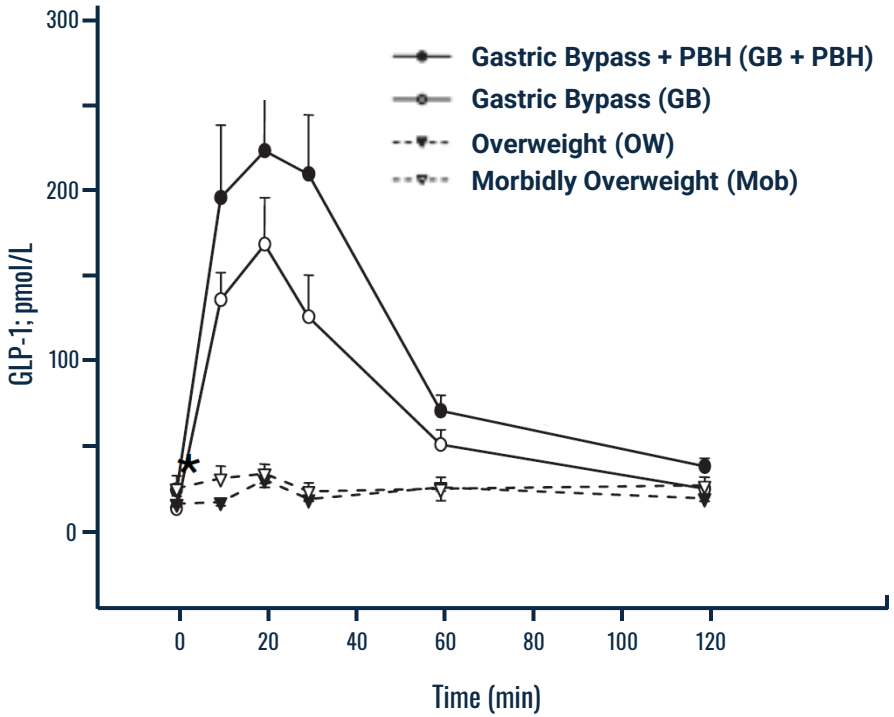
McLaughlin, T et al. (2025, July 12-15). *Prevalence of Post-bariatric Hypoglycemia in the United States,* [Poster presentation]. ENDO 2025.

Glucagon-like Peptide-1 (GLP-1) Receptor Pathway Modulates Blood Glucose Levels via Enhancement of Insulin Secretion (Incretin Effect)

GLP-1 Receptor: an Effective Target to Modulate Insulin Secretion in PBH

- GLP-1 is an incretin gut hormone; enhances secretion of insulin in response to oral meal intake.
- GLP-1 levels are up to 10-fold higher in individuals with PBH than nonsurgical controls.
- Exaggerated GLP-1 secretion in PBH results in dysregulated secretion of insulin and subsequent hypoglycemia.

GLP-1 Levels Were Up to 10-fold Higher in PBH than in Nonsurgical Controls

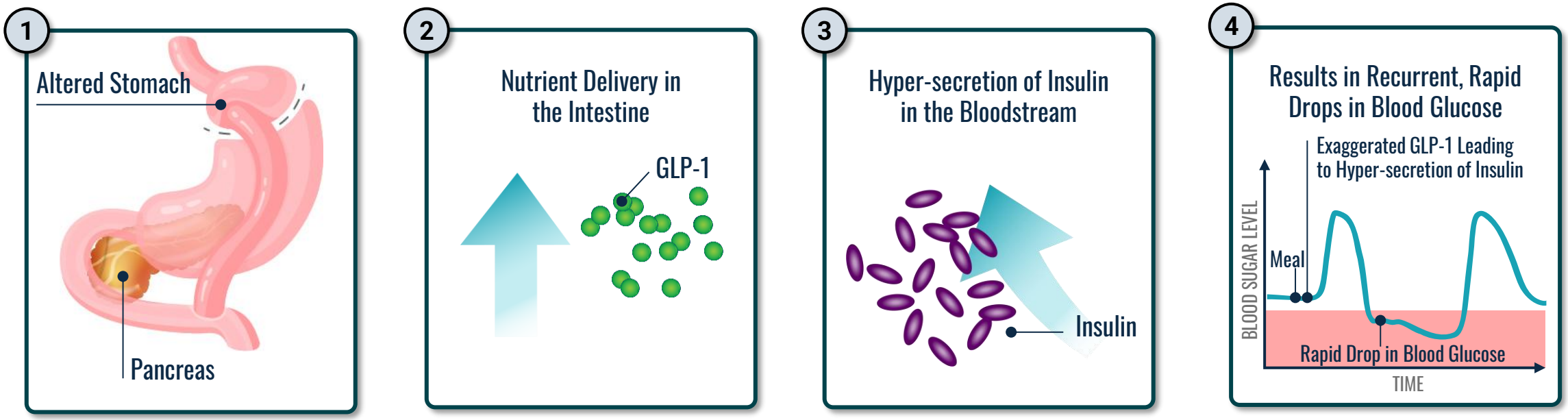


Higher GLP-1 after a mixed meal in patients with PBH after gastric bypass surgery. GLP-1 excursions are higher after a liquid mixed meal in GB PBH compared with GB (repeated-measures ANOVA, P=0.03). In addition, GLP-1 levels were 5- to 10-fold higher after GB than in nonsurgical controls (repeated- measures ANOVA, P<0.001). Fasting GLP-1 levels are shown in *inset* (*, P 0.02 vs. GB PBH, P 0.04 vs. GB).

GLP-1=Glucagon-like peptide-1; PBH=post-bariatric hypoglycemia; **1.** Salehi M, Prigeon RL, D'Alessio DA. Gastric bypass surgery enhances glucagon-like peptide 1-stimulated postprandial insulin secretion in humans. *Diabetes*. 2011 Sep;60(9):2308-14. doi: 10.2337/db11-0203. PMID: 21868791; PMCID: PMC3161307. **2.** Goldfine A. B. et al. *J Clin Endocrinol Metab. 2007;* 92(12):4678–4685. doi.org/10.1210/jc.2007-0918.

Altered Nutrient Transit after Bariatric Surgery Leads to Exaggerated GLP-1 Secretion and Hyperinsulinemic Hypoglycemia[1]

A Key Pathway in PBH Pathophysiology[2]



Altered Nutrient Transit due to anatomical changes associated with bariatric surgery (e.g., Roux-en-Y gastric bypass)

In people with PBH, GLP-1 is overproduced in the intestine after eating, **resulting in an up to 10x increase in GLP-1 levels**

This exaggerated GLP-1 secretion leads to **abnormally high insulin levels in the bloodstream**, and **subsequent hypoglycemia**

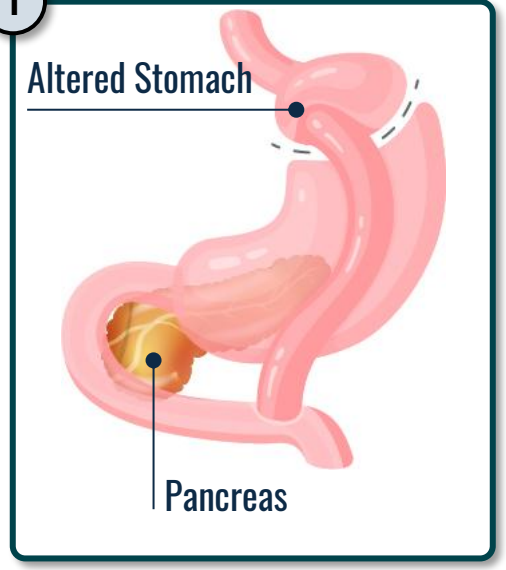
Recurrent **postprandial hypoglycemic events** can impair counterregulatory responses and deplete glycogen stores, leading to **fasting and exercise-induced events and hypoglycemia unawareness**

GLP-1=Glucagon-like peptide-1; PBH=post-bariatric hypoglycemia; **1.** Sheehan A, Patti ME. *Diabetes Metab Syndr Obes*. 2020;13:4469-4482; **2.** Craig CM, et al. *Diabetes Obes Metab*. 2017; 1-10. **3.** Thorens B,. et al. *Diabetes*.1993;42(11):1678-1682. **4.** Craig CM, et al. *Diabetes Obes Metab*. 2018;20(2):352-361. **5.** Smith NK, et al. *Neurochem Int*. 2019;128:94-105. **6.** Meloni AR, et al. *Diabetes Obes Metab*. 2013;15(1):15-27. **7.** Craig CM, et al. *Diabetologia*. 2017;60(3):531-540. **8.** Craig C, et al. *J Endocr Soc*. 2022;6(Suppl 1):A349.

Avexitide, a First-in-Class GLP-1 Receptor Antagonist, Targets a Central Pathway of PBH Pathophysiology

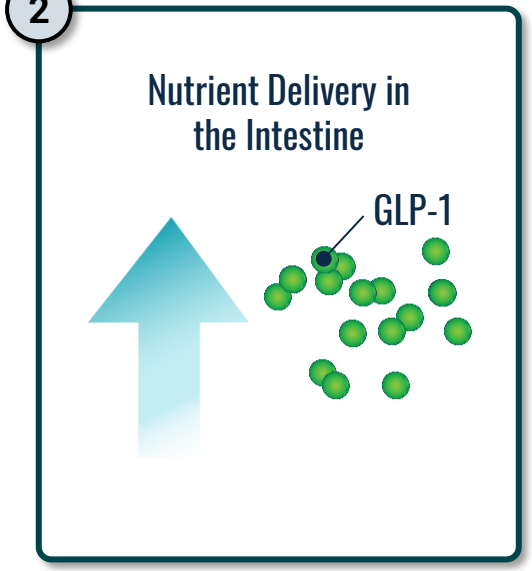
GLP-1 Receptor Antagonism

1



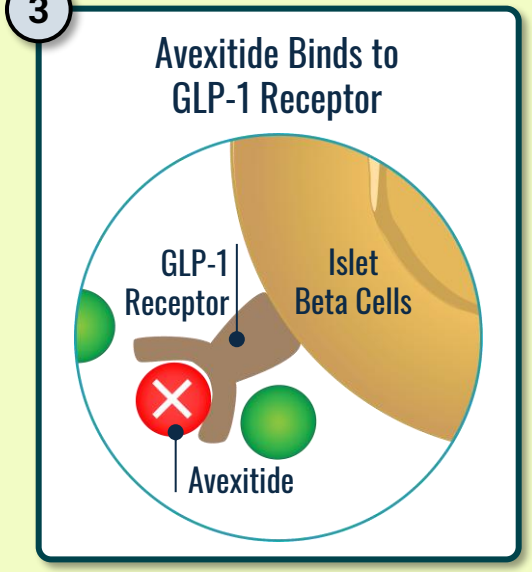
Altered Nutrient Transit due to anatomical changes associated with bariatric surgery (e.g., Roux-en-Y gastric bypass)

2



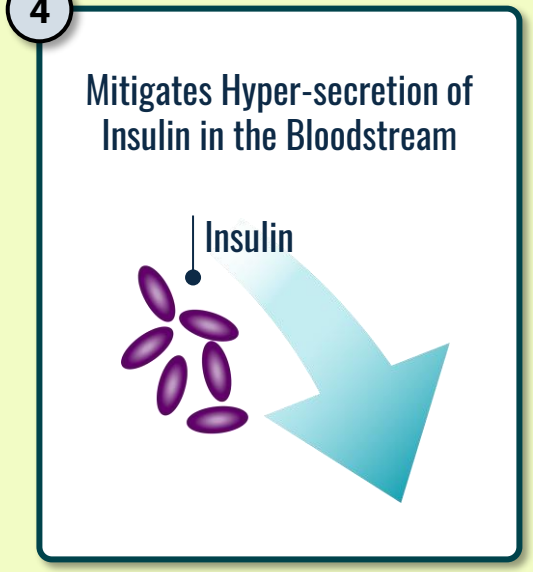
In people with PBH, GLP-1 is overproduced in the intestine after eating, **resulting in an up to 10x increase in GLP-1 levels**

3



Avexitide binds to the GLP-1 receptor on pancreatic islet beta cells to **inhibit the effect of exaggerated GLP-1**

4



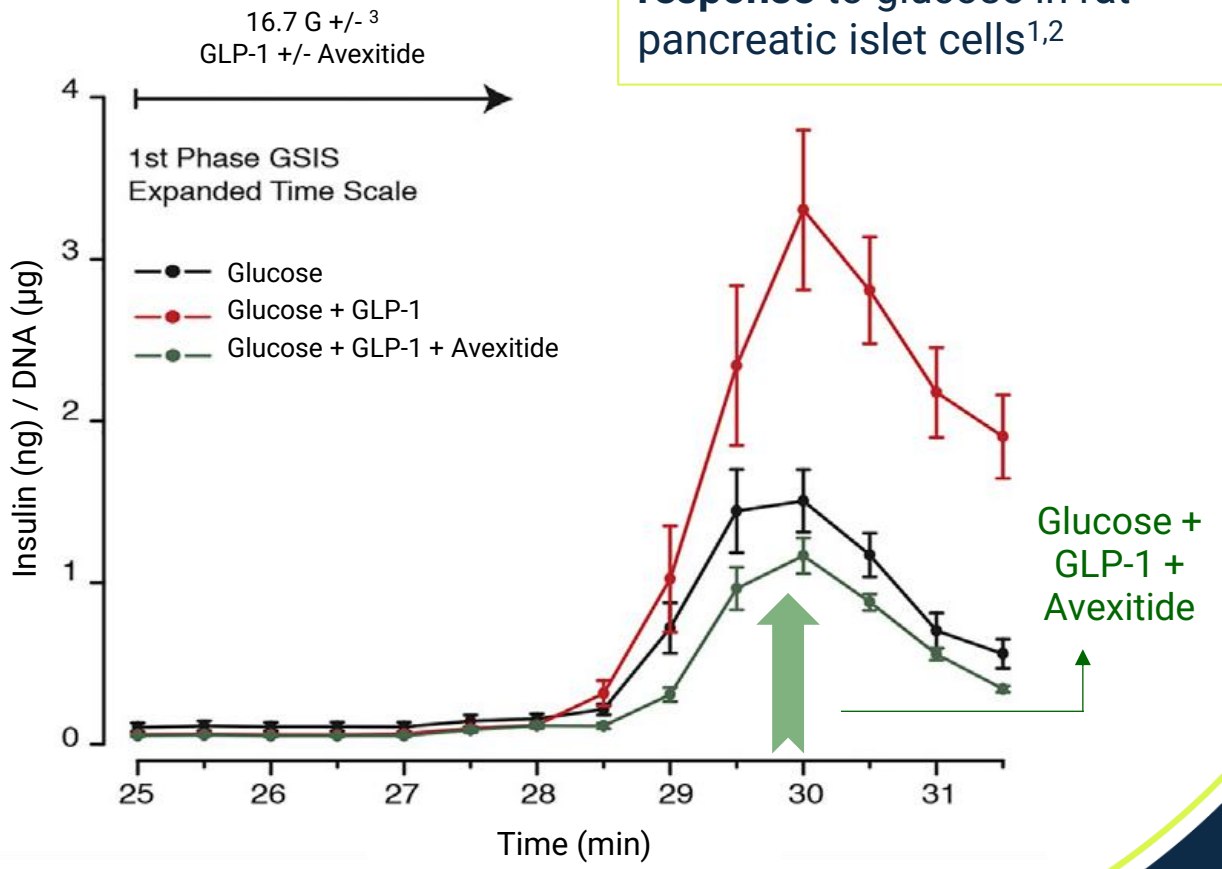
Decreased insulin secretion and stabilized glucose levels resulting from inhibition of the effect of exaggerated GLP-1

GLP-1=Glucagon-like peptide-1; PBH=post-bariatric hypoglycemia; **1.** Sheehan A, Patti ME. *Diabetes Metab Syndr Obes*. 2020;13:4469-4482; **2.** Craig CM, et al. *Diabetes Obes Metab*. 2017; 1-10. **3.** Thorens B,. et al. *Diabetes*.1993;42(11):1678-1682. **4.** Craig CM, et al. *Diabetes Obes Metab*. 2018;20(2):352-361. **5.** Smith NK, et al. *Neurochem Int*. 2019;128:94-105. **6.** Meloni AR, et al. *Diabetes Obes Metab*. 2013;15(1):15-27. **7.** Craig CM, et al. *Diabetologia*. 2017;60(3):531-540. **8.** Craig C, et al. *J Endocr Soc*. 2022;6(Suppl 1):A349.

Potentiation of Glucose-Stimulated Insulin Secretion by GLP-1 and Reversal thereof with Avexitide

- GLP-1 potentiates glucose stimulated insulin secretion (GSIS) in rat pancreatic islet cells (red line)
- Avexitide inhibits GSIS, reducing insulin concentrations (green line)
- Supporting hypothesis that GLP-1 receptor antagonism may represent a targeted therapeutic approach in PBH

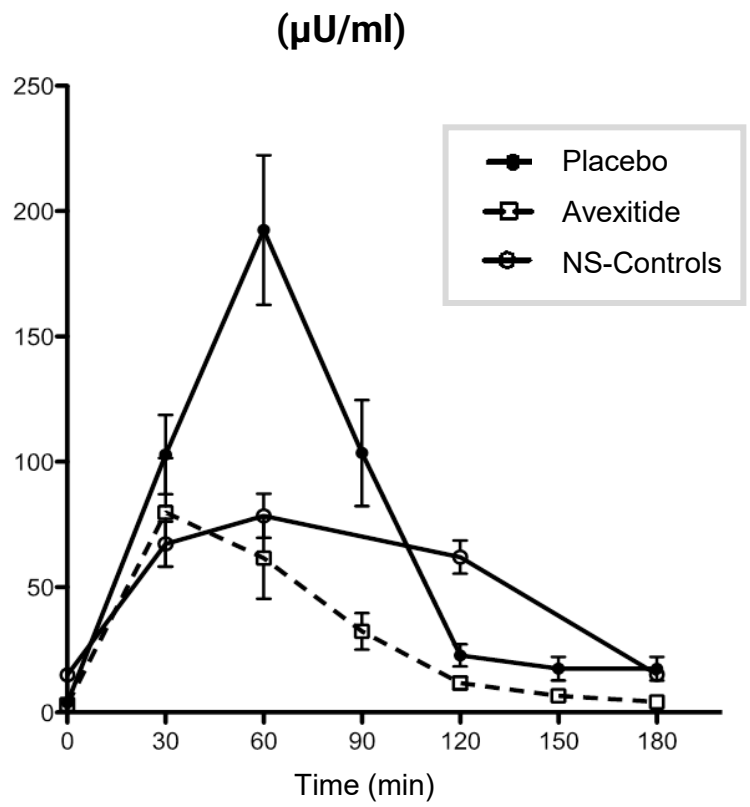
GLP-1 receptor antagonism blocks GLP-1 and **decreases insulin response** to glucose in rat pancreatic islet cells[1,2]



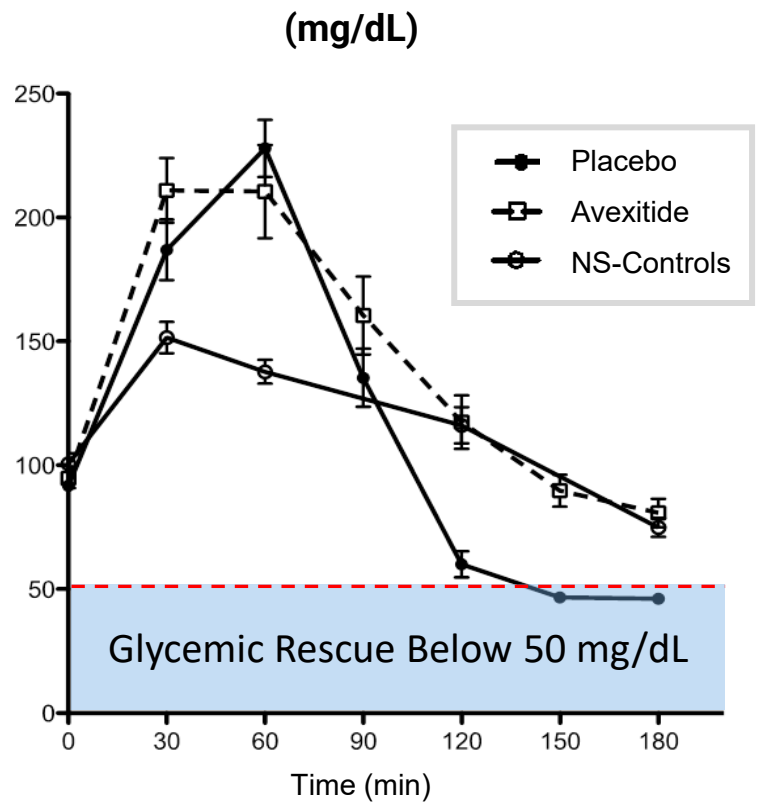
GLP-1=Glucagon-like peptide-1; PBH=post-bariatric hypoglycemia; **1.** Cabrera O. et al. *The Journal of Biological Chemistry*. 2022;298(2):101484. doi:10.1016/j.jbc.2021.101484; **2.** Averaged data from five independent experiments; **3.** Step-wise increase of glucose concentration from 2.8 to 16.7 mM (2.8G and 16.7G).

Clinical Data Underscores the Critical Role of GLP-1 in PBH and Supports the Potential of GLP-1 Receptor Antagonism as a Targeted Approach

Insulin



Glucose



Proof of Concept in Patients with PBH (N=8) Demonstrated:

- 100% prevention of hypoglycemia
- Increased the plasma glucose nadir by 70%, matching NS controls
- Ameliorated hyperinsulinemia

GLP-1=Glucagon-like peptide-1; NS-Controls=Non-surgical controls; PBH=post-bariatric hypoglycemia; Craig et al. Diabetologia 2017

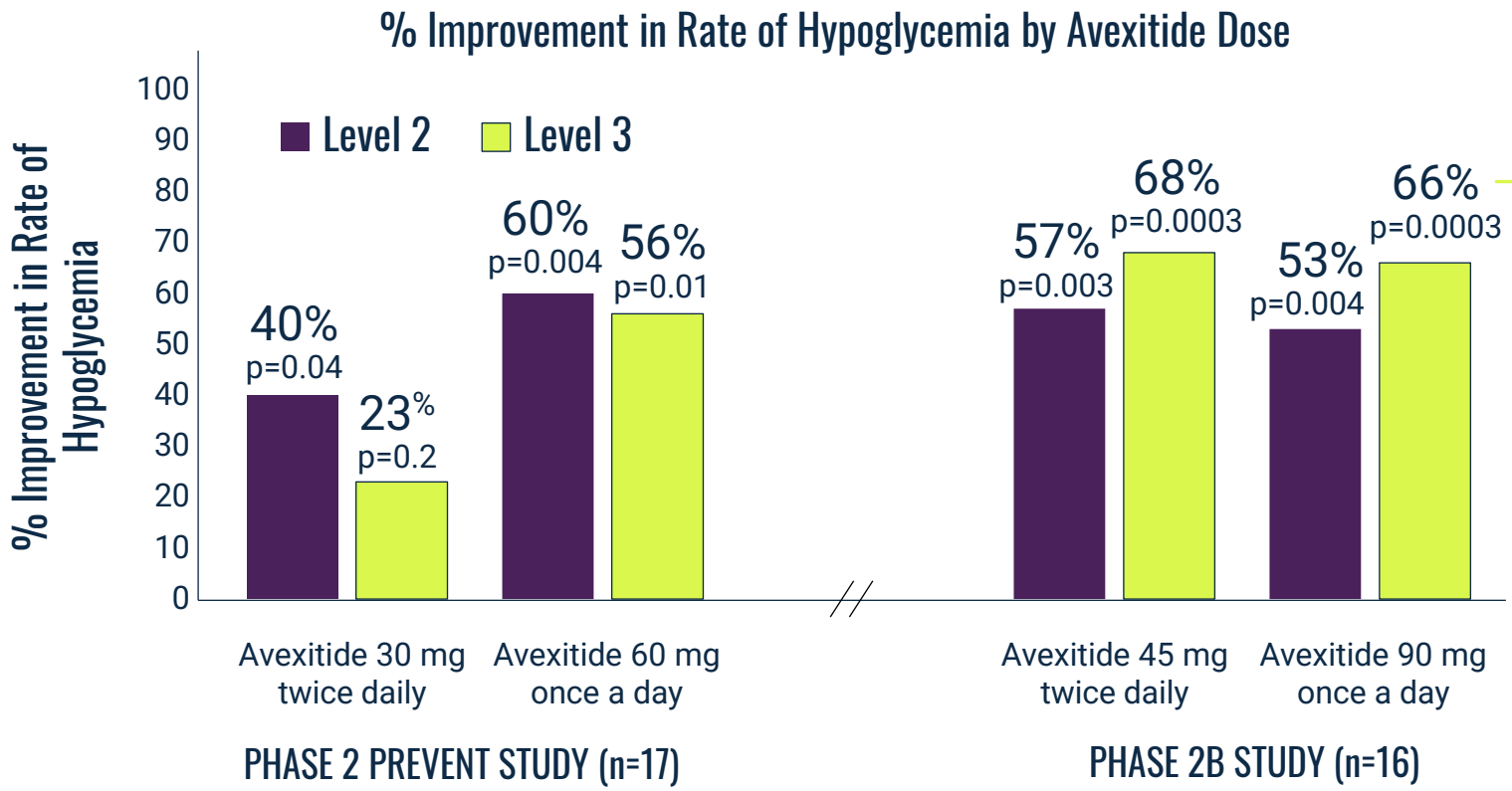
Improvement in Glucose Responses Consistently Observed with Avexitide During Standardized Meal Tests in People with PBH

	Phase 1[1]	SAD[2]	MAD[3]	Phase 2 PREVENT[4]	
	Avexitide IV infusion (n=8)	Avexitide SC injection (N=8)	Avexitide 30 mg twice daily SC injection (n=5)	Avexitide 30 mg twice daily SC injection (n=17)[5]	Avexitide 60 mg once daily SC injection (n=17)[5]
	Improvement vs. Placebo				
Postprandial Glucose Nadir	↑ **Increase** (p<0.001)	↑ **Increase** (p<0.001)	↑ **Increase** (p<0.05)	↑ **Increase** (p=0.001)	↑ **Increase** (p=0.0002)

IV=intravenous; MAD=multiple ascending dose PBH=post-bariatric hypoglycemia; SAD=single ascending dose; SC=subcutaneous; **1.** Craig, C. M. et al. *Diabetologia*. 2017;60(3):531-540. doi:10.1007/s00125-016-4179-x; **2.** Craig, C. M. et al. *Diabetes, Obesity & Metabolism*. 2018;20:352–361. doi.org/10.1111/dom.13078; **3.** Tan, M. et al. *Diabetes, Obesity & Metabolism*. 2020;22(8):1406-1416. doi:10.1111/dom.14048; **4.** Craig, C. M. et al. *The Journal of Clinical Endocrinology & Metabolism*. 2021;106(8):e3235-e3248. doi:10.1210/clinem/dgab103; **5.** 18 participants were randomized and completed the trial with 17 included in the efficacy analysis due to a major protocol deviation (glycemic rescue was not administered as indicated per protocol during the Period 1 placebo MMTT).

Avexitide Significantly Reduced Rates of Levels 2 and 3 Hypoglycemia in the 'Real-World' Setting in Two Phase 2 Clinical Trials in PBH

FDA Breakthrough Therapy Designation



Avexitide cut rates of hypoglycemic events by

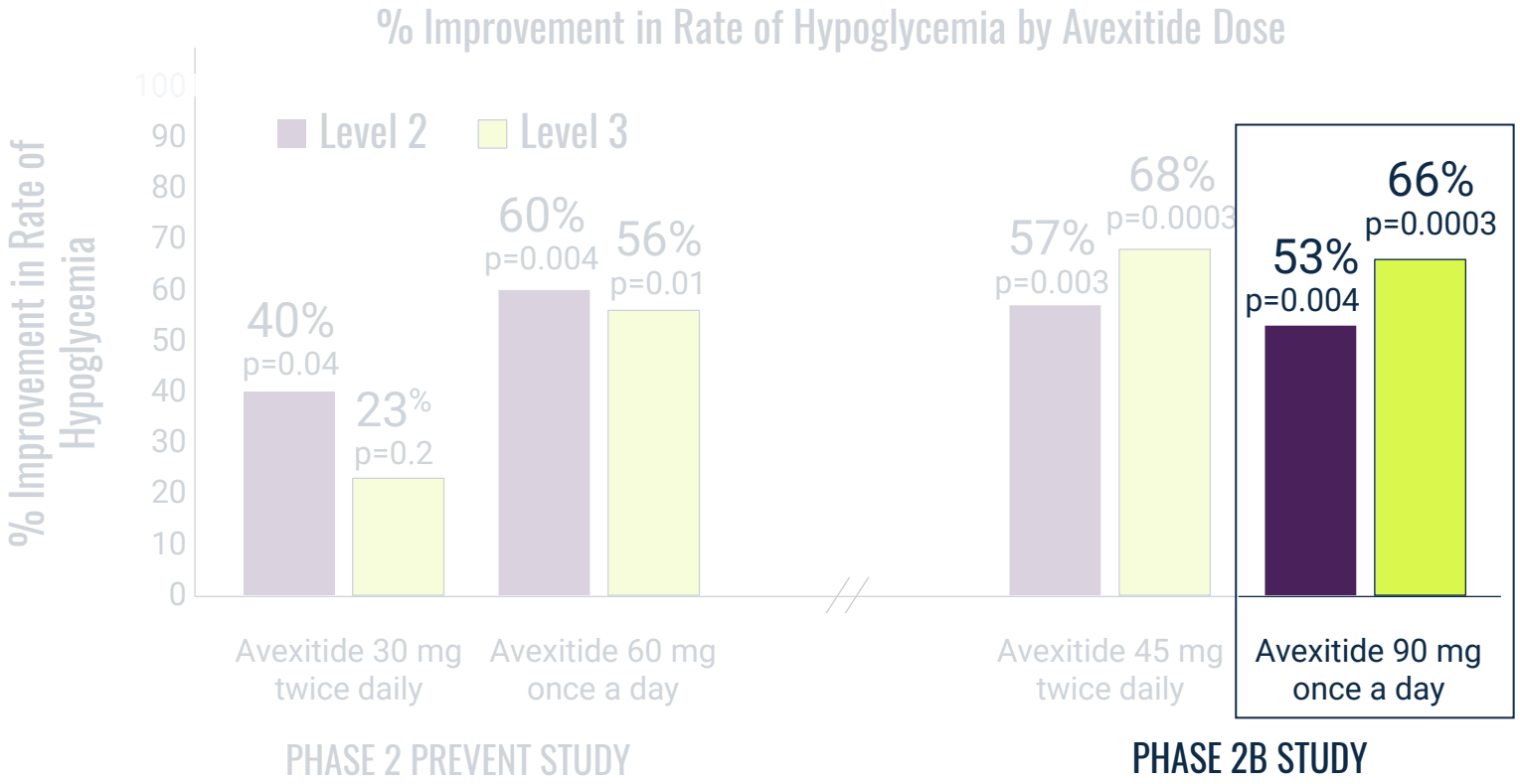
>50%

Level 2 hypoglycemia is defined as glucose <54 mg/dL (3.0 mmol/L) measured by SMBG

Level 3 hypoglycemia is defined as a severe event characterized by altered mental and/or physical functioning that requires assistance from another person for recovery

FDA=U.S. Food and Drug Administration; PBH=post-bariatric hypoglycemia; SMBG=Self-Monitoring of Blood Glucose; **1.** Craig, C. M. et al. *The Journal of Clinical Endocrinology & Metabolism.* 2021;106(8):e3235-e3248. doi.org/10.1210/jendso/bvac150.725. **2.** Tan, M. (2022). *Efficacy and Safety of Avexitide for Treatment of Hypoglycemia after Gastrointestinal Surgery: Assessment of Novel Dosing Regimens in an Expanded Indication* [Conference presentation]. ENDO Annual Symposium.

Phase 2 and Phase 2b Results Informed Dose and Endpoints in Phase 3



Phase 3 program will evaluate 90 mg once daily in people living with PBH

FDA-agreed upon primary endpoint: composite of Level 2 and Level 3 hypoglycemic events

FDA=U.S. Food and Drug Administration; PBH=post-bariatric hypoglycemia; **1.** Craig, C. M. et al. *The Journal of Clinical Endocrinology & Metabolism.* 2021;106(8):e3235-e3248. doi.org/10.1210/jendso/bvac150.725. **2.** Tan, M. (2022). *Efficacy and Safety of Avexitide for Treatment of Hypoglycemia after Gastrointestinal Surgery: Assessment of Novel Dosing Regimens in an Expanded Indication* [Conference presentation]. ENDO Annual Symposium.

Avexitide has been Well-Tolerated with Generally Mild-to-Moderate and Transient AEs and No Treatment-Related SAEs or Discontinuations

Phase 2 PREVENT Study[1]	Phase 2b Study[2]
AEs generally mild to moderate and transient	AEs generally mild to moderate and transient
No treatment-related serious AEs • 1 serious adverse event (presyncope during avexitide 60 mg once daily) occurred; reported as unrelated to study drug and self-limited	No serious AEs
Most common AEs were injection* site bruising, headache, and nausea	Most common AEs were diarrhea, headache, bloating, and injection* site reaction/bruising
No participant discontinuations	No participant discontinuations

No clinically meaningful increases in fasting or peak postprandial plasma glucose levels or appreciable increases or decreases in body weight were observed

*Injection site reactions generally mild and transient with no grade 3 events or resulting discontinuations

AE=adverse event; SAE=serious adverse event; **1.** Craig, C. M. et al. *The Journal of Clinical Endocrinology & Metabolism.* 2021;106(8):e3235-e3248. doi.org/10.1210/jendso/bvac150.725.
2. Tan, M. (2022). *Efficacy and Safety of Avexitide for Treatment of Hypoglycemia after Gastrointestinal Surgery: Assessment of Novel Dosing Regimens in an Expanded Indication* [Conference presentation]. ENDO Annual Symposium.

Clinical Perspective on Unmet Need in PBH and New Analysis from Phase 2b Avexitide Trial

Marilyn Tan, MD, FACE

Principal Investigator of the LUCIDITY Clinical Trial, Co-Lead Investigator of the Phase 2 PREVENT Clinical Trial, and Clinical Associate Professor of Medicine at Stanford University School of Medicine

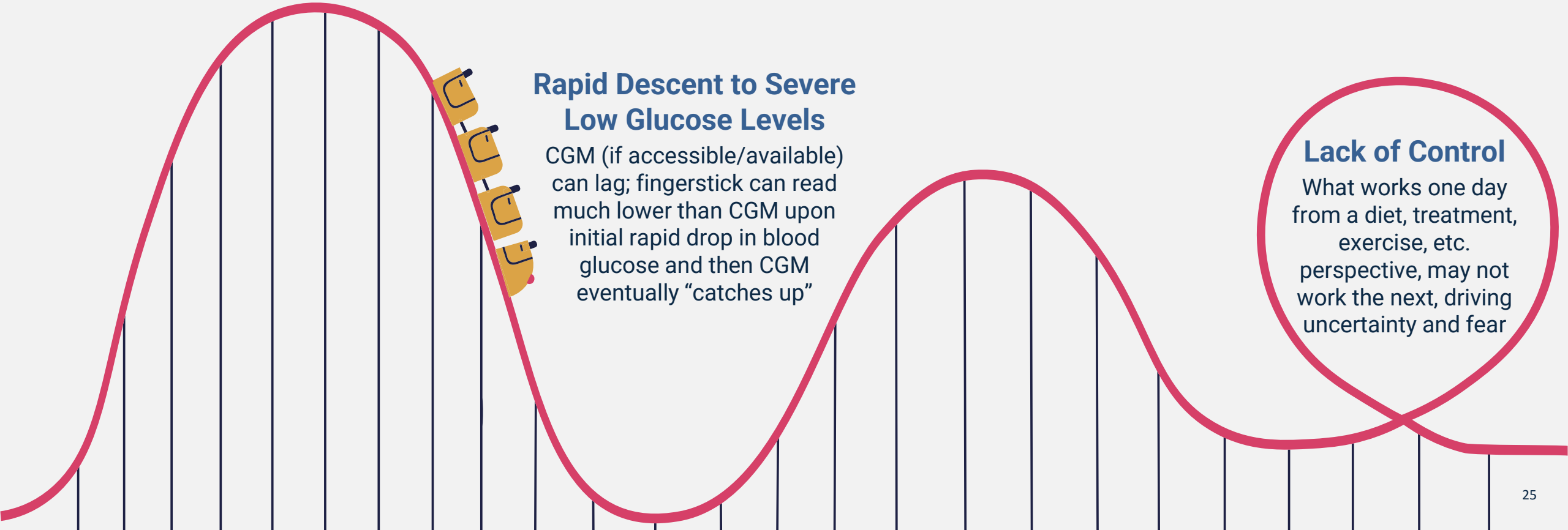
Relevant Disclosures: Dr. Tan has received research payments from Amylyx Pharmaceuticals as primary investigator and received consulting payments from Amylyx and Novo Nordisk.

Clinical Realities of Managing PBH: A “Blood Sugar Roller Coaster”

Inappropriately High Postprandial Insulin Levels in the Bloodstream

- With certain foods, the glucose rises rapidly, and patients must prepare themselves for the subsequent rapid drop in blood glucose

People living with PBH can experience multiple daily hypoglycemic events with variable frequency and severity



Rapid Descent to Severe Low Glucose Levels

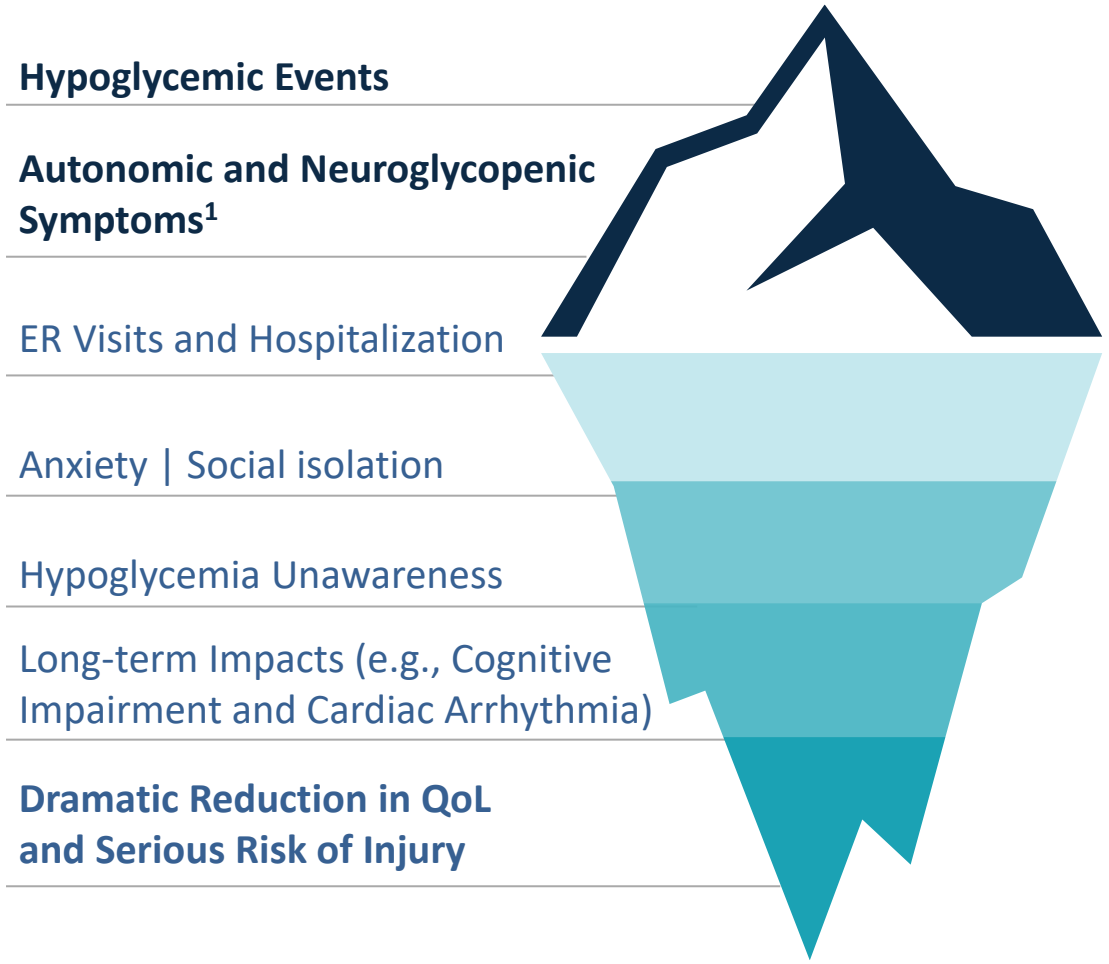
CGM (if accessible/available) can lag; fingerstick can read much lower than CGM upon initial rapid drop in blood glucose and then CGM eventually “catches up”

Lack of Control

What works one day from a diet, treatment, exercise, etc. perspective, may not work the next, driving uncertainty and fear

The Innovation Gap in PBH and Consequences of Inaction

- Diagnostic delays are common for PBH – resulting from under-recognition and the non-specific nature of symptoms that can mimic multiple other conditions
  - > Delayed diagnosis can lead to people with PBH feeling marginalized, disrespected, or feeling as if their nonspecific symptoms are “all in their head”
- People with PBH are often left to self-manage this serious metabolic condition, frequently with limited or inconsistent support from a care team
  - > Clinicians are forced to rely on restrictive dietary management, off-label medicines, and in extreme cases, surgical intervention (No FDA therapies approved for PBH)
- Cascading effects of PBH can lead to social isolation, inability to perform activities associated with independent daily living (e.g., work), serious injuries due to sudden hypoglycemic events, and increased healthcare resource utilization (e.g., ER visits)



Hypoglycemic events are just the tip of the iceberg with far-reaching impacts on the individual, their family, and the broader healthcare system

1. Autonomic symptoms may include palpitations, tremulousness, anxiety, nausea, diaphoresis, paresthesia, and hunger. Neuroglycopenic symptoms may include confusion, slurred speech, weakness, dizziness, blurred vision, seizure, and coma.

Redefining Success:
What People Living with PBH and their Care Team Need

FOR CLINICIANS

- Treatments that are effective, safe, and fit into a real-world setting
- Reduced frequency of hypoglycemic events
- Fewer emergency interventions and downstream complications
- Targeting the underlying pathophysiology

Success means shifting from managing around PBH **to truly treating it**

FOR PEOPLE LIVING WITH PBH

- More predictable symptom control that can enable independence
- Reduced fear (i.e. eating, exercise, leaving home)
- Improved flexibility in social routines (a “normal” life)
- Fewer life-threatening hypoglycemic events
- Avoiding potential malnutrition that can result from strict PBH diet

Reduction in Rate of Hypoglycemic Events with Avexitide in Post-Bariatric Hypoglycemia

Marilyn Tan, MD
Stanford University School of Medicine

Additional Authors: Colleen Craig, MD; Tracey McLaughlin, MD, MS; Zhengyu Yang, PhD; Kelly Fox, MD; Ryan Miller, MD; Helen Margaret Lawler, MD; Dawn Belt Davis, MD, PhD

Note: Avexitide is an investigational drug and has not been approved for use by any health authority (e.g., the FDA and EMA).

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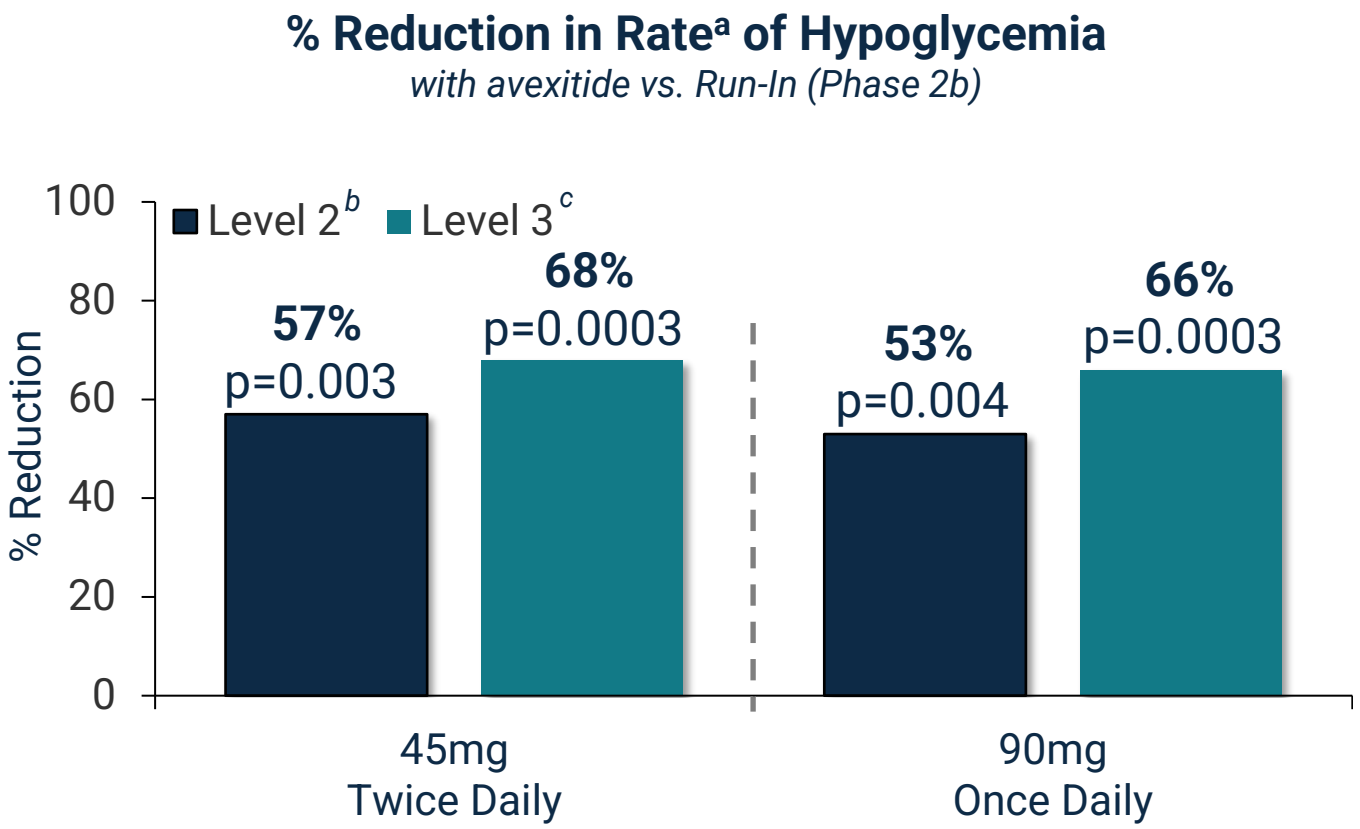
Avexitide Significantly Reduced Rates of Level 2 and 3 Hypoglycemia in the Phase 2b Clinical Trial



- The Phase 2b trial was a 28-day, open-label, investigator-initiated, crossover trial investigating **90 mg once daily and 45 mg twice daily of avexitide in PBH** following RYGB surgery and other upper gastrointestinal surgeries
- Participants receiving 90 mg once daily of avexitide, which is being evaluated in the Phase 3 LUCIDITY trial, saw a **statistically significant reduction in Level 2 and 3 hypoglycemic events**
- **Statistically significant reductions in Level 2 and 3 hypoglycemic events also were seen in the Phase 2 PREVENT trial** investigating avexitide 30 mg twice daily and 60 mg once daily
- There were **no reported serious AEs**, and AEs were mostly mild to moderate and resolved without medical treatment

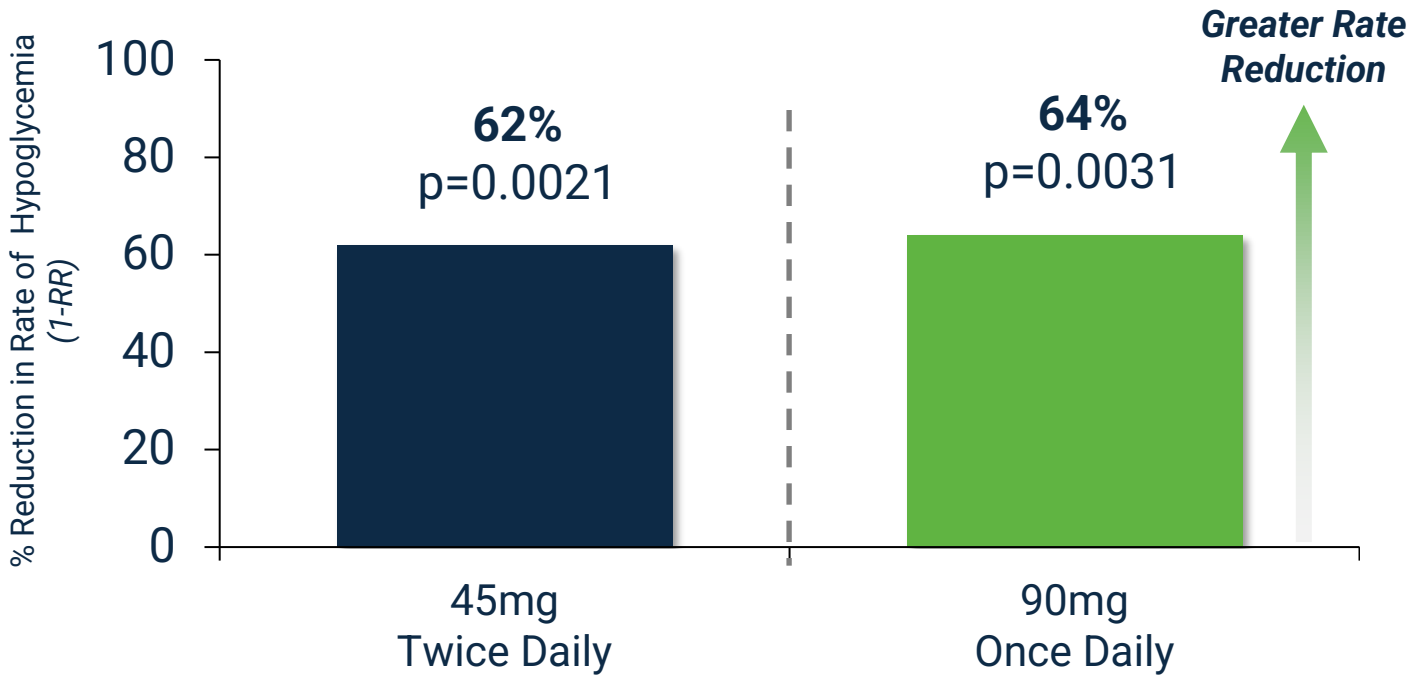
[a]Rate defined as number of episodes in each treatment period normalized to 14 days; [b]Level 2 hypoglycemia: self-monitoring of blood glucose <54 mg/dL
[c]Level 3 hypoglycemia: a severe event characterized by altered mental and/or physical functioning that requires assistance from another person for recovery whether an individual receives external assistance or not

1. Craig CM, et al. *J Clin Endocrinol Metab.* 2021;106(8):e3235-e3248. **2.** Tan M. Oral presentation at: ENDO 2022; June 11-14, 2022; Atlanta, Georgia.

Avexitide Significantly Reduced Rates of Composite Level 2 and 3 Hypoglycemia in New Exploratory Analyses from the Phase 2b Clinical Trial

% Reduction in Composite Rate[a] of Level 2[b] and 3[c] Hypoglycemia

with avexitide vs. Run-In (Phase 2b)



- **The FDA-agreed-upon primary endpoint of LUCIDITY** is reduction in the composite of Level 2 and Level 3 hypoglycemic events
- The 90 mg once daily dose, which is being evaluated in LUCIDITY, led to a **statically significant reduction in the composite rate of Level 2 and 3 events**
- With 90 mg once daily, **more than half of the participants** experienced no composite events during the treatment period
- **Consistent reductions in composite rate of Level 2 and 3 hypoglycemic events also were seen in the Phase 2 PREVENT trial** investigating avexitide 30 mg twice daily and 60 mg once daily

[a]Rate defined the weekly number of discrete events during respective treatment periods; [b]Level 2 hypoglycemia: self-monitoring of blood glucose <54 mg/dL
[c]Level 3 hypoglycemia: a severe event characterized by altered mental and/or physical functioning that requires assistance from another person for recovery whether an individual receives external assistance or not

1. Craig CM, et al. *J Clin Endocrinol Metab.* 2021;106(8):e3235-e3248. **2.** Tan M. Oral presentation at: ENDO 2022; June 11-14, 2022; Atlanta, Georgia.

Key Takeaways

- Avexitide **significantly reduced the composite rate of Level 2 and 3 hypoglycemia** in its Phase 2 and 2b trials
  - Adverse events have generally been mild to moderate and transient with no treatment-related serious adverse events and no adverse events necessitating drug discontinuation

- With the **90 mg once daily dose**, which is being further evaluated in the Phase 3 LUCIDITY trial:
  - **Statistically significant 64% reduction** in the composite rate of Level 2 and 3 events
  - More than half of the participants experienced no composite events

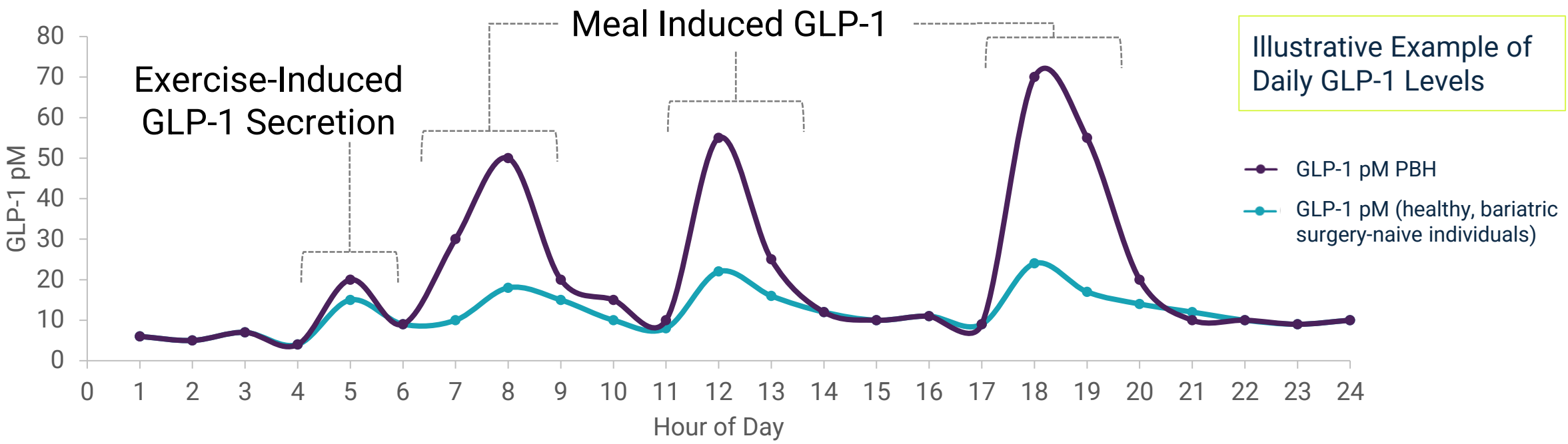
- We extend our deepest gratitude to the trial participants, their loved ones, and the trial investigators for their support of this trial

Review of Avexitide PK/PD Profile and LUCIDITY Phase 3 Clinical Trial Design

Jamie Timmons, MD

Vice President, Medical Affairs at Amylyx

Endogenous GLP-1 Levels Fluctuate Throughout the Day



- In healthy, bariatric surgery-naive individuals, fasting GLP-1 concentrations are generally low, typically <10 pM, with levels rising 2- to 3-fold after eating, peaking 20 to 30 minutes after the meal
- In PBH, an exaggerated form of these GLP-1 responses is believed to be a central pathway causing inappropriately elevated insulin levels, leading to persistent, recurrent, and debilitating hypoglycemia

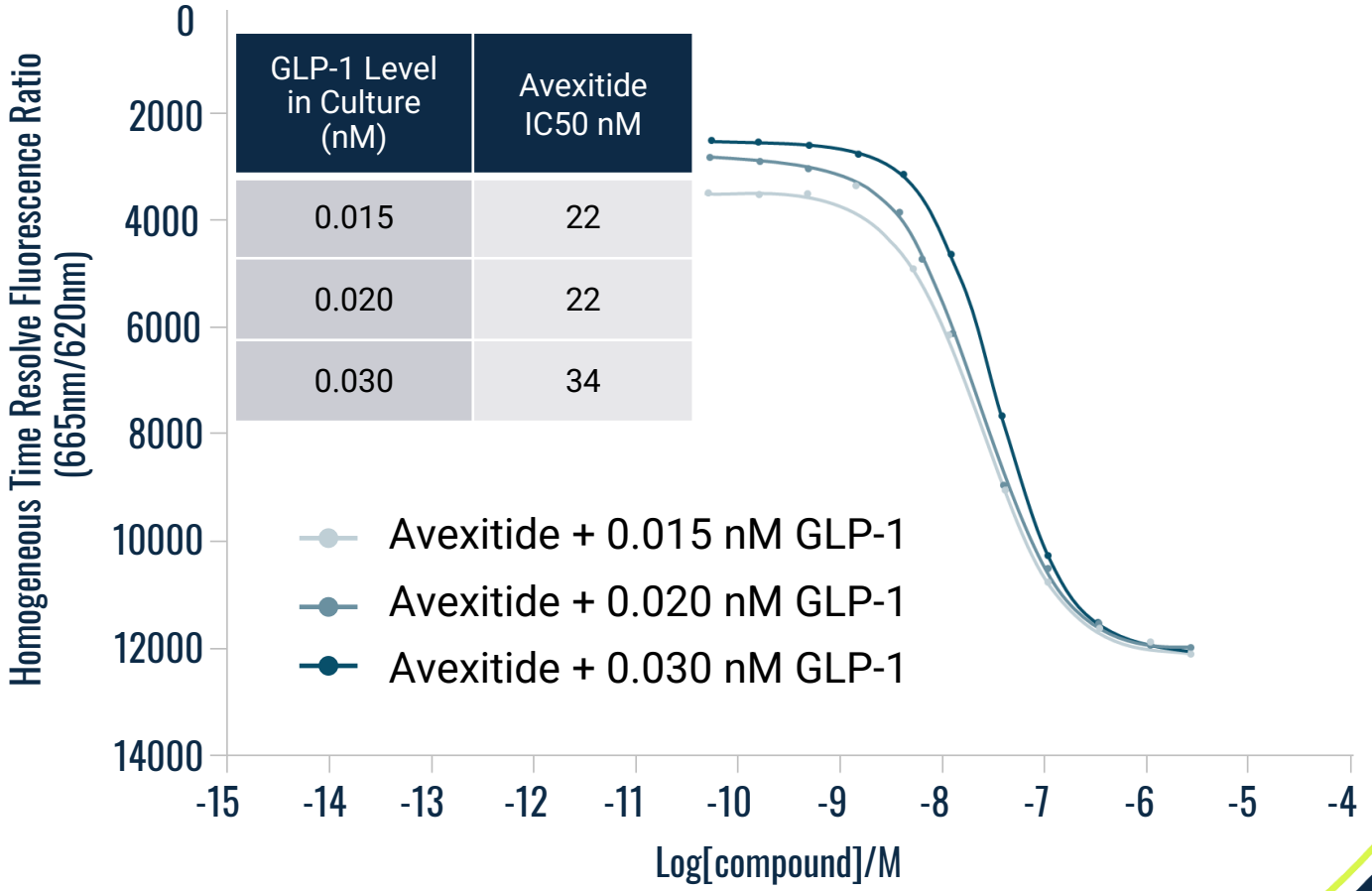
GLP-1=Glucagon-like peptide-1; PBH=post-bariatric hypoglycemia; Craig, C. et al. (2025, July 12-15). *Population PK (PopPK) and Pharmacokinetic/Pharmacodynamic (PK/PD) Analysis of Avexitide in Individuals with Post-Bariatric Hypoglycemia* [Poster presentation]. ENDO 2025.

Consistent Inhibition of GLP-1 Activity in PBH-Relevant *in Vitro* Potency Studies

- **At clinically relevant GLP-1 levels, avexitide demonstrated target inhibition** with an IC50 of ~20-30 nM (70-100 ng/mL)
- **Avexitide maintained its inhibitory activity** even as GLP-1 concentrations increased
- Data underscore **avexitide's potential to inhibit excessive GLP-1** in people living with PBH

Avexitide *In Vitro* Potency Screen

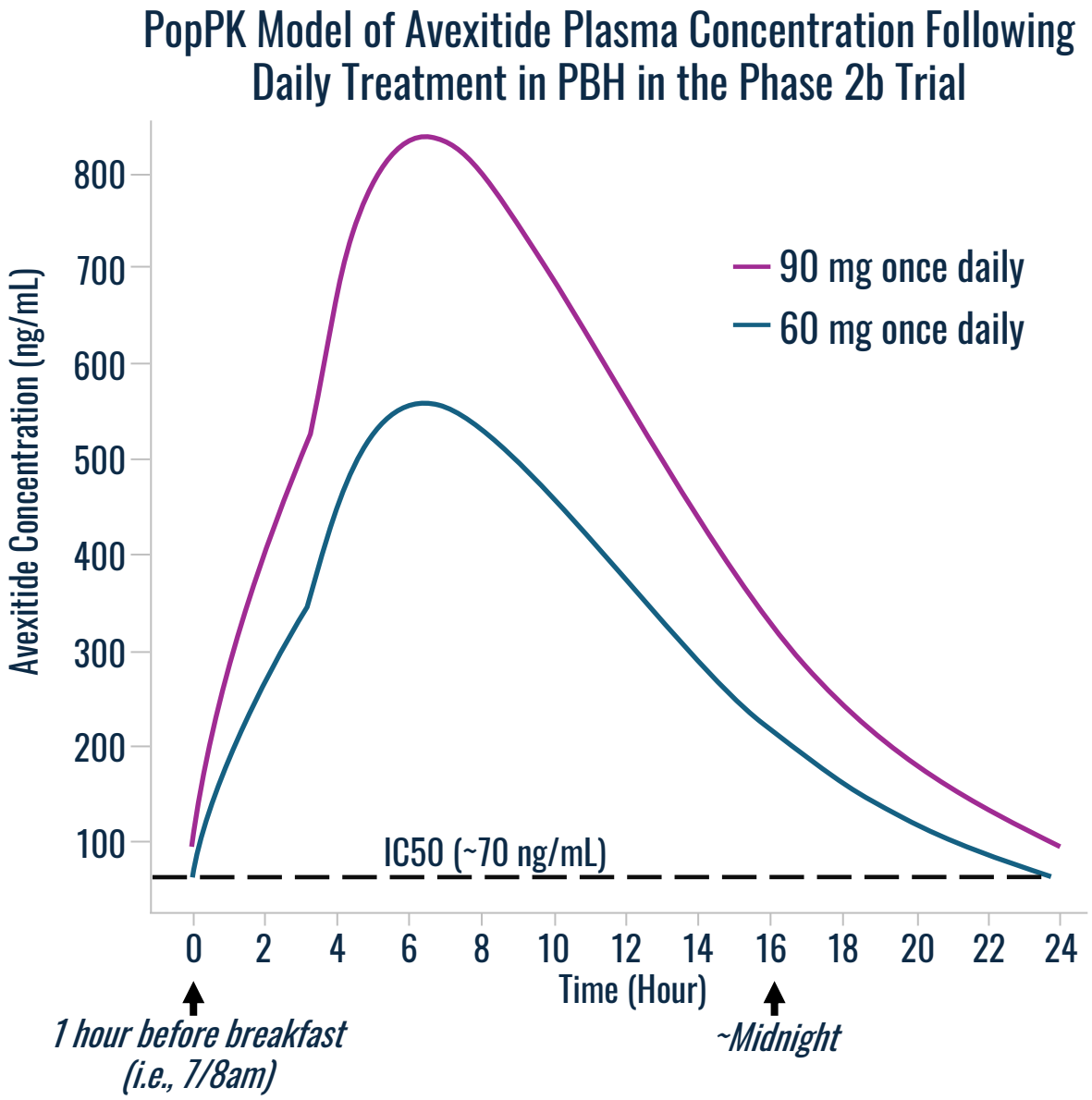
GLP-1 Level in Culture (nM)	Avexitide IC50 nM
0.015	22
0.020	22
0.030	34



GLP-1=Glucagon-like peptide-1; IC50=half-maximal inhibitory concentration; PBH=post-bariatric hypoglycemia; Craig, C. et al. (2025, July 12-15). *Population PK (PopPK) and Pharmacokinetic/Pharmacodynamic (PK/PD) Analysis of Avexitide in Individuals with Post-Bariatric Hypoglycemia* [Poster presentation]. ENDO 2025.

We gratefully acknowledge Gubra for their valuable data contributions and scientific collaboration that supported the *in vitro* potency analysis

Avexitide 90 mg Once Daily Exceeded IC50 for 24 Hours



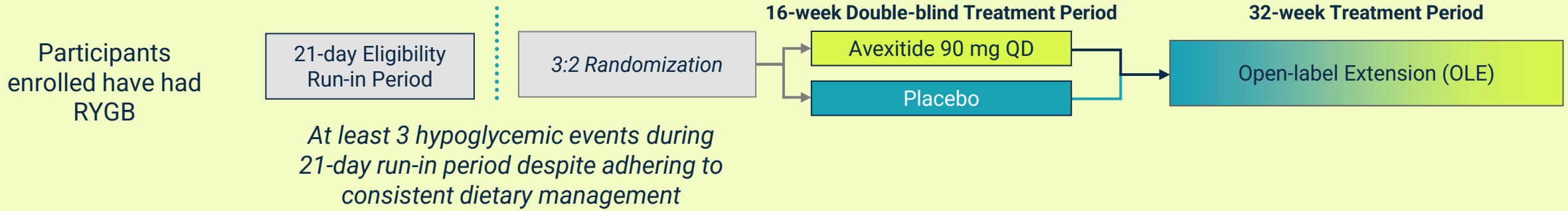
- Avexitide 90 mg once daily demonstrated a half-life of ~3 hours, with a time to peak concentration (Tmax) ranging from 6-9 hours, and therapeutic exposure through 24 hours
- Avexitide 90 mg once daily resulted in Cmin above IC50
- Results provide evidence that avexitide 90 mg once daily can have continued biological effect between doses

IC50=half-maximal inhibitory concentration; PBH=post-bariatric hypoglycemia; Craig, C. et al. (2025, July 12-15). *Population PK (PopPK) and Pharmacokinetic/Pharmacodynamic (PK/PD) Analysis of Avexitide in Individuals with Post-Bariatric Hypoglycemia*[Poster presentation]. ENDO 2025.

LUCIDITY is a Pivotal Phase 3, U.S., Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial for the Treatment of PBH

PHASE 3 LUCIDITY TRIAL DESIGN

Multicenter, randomized, double-blind, placebo-controlled trial (N=~75)



- U.S.-only study ~20 sites
- Evaluating the FDA-agreed upon primary endpoint: composite of Level 2 and Level 3 hypoglycemic events

FDA Breakthrough Therapy and Orphan Drug Designations

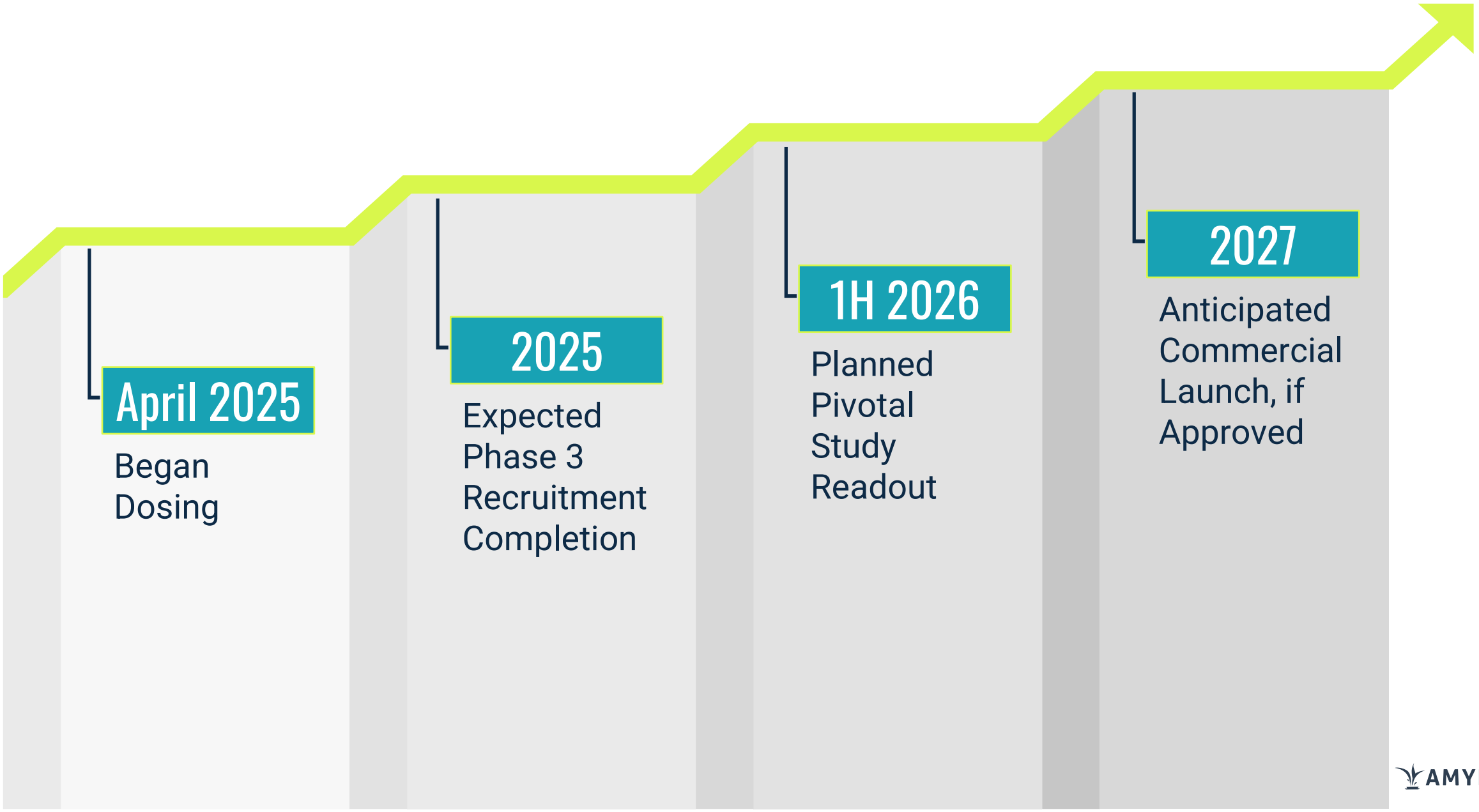
FDA=U.S. Food and Drug Administration; PBH=post-bariatric hypoglycemia; QD=once daily; RYGB=Roux-en-Y Gastric Bypass.

Phase 3 LUCIDITY Trial Designed to be Consistent with Phase 2 PREVENT and Phase 2b Trials Evaluating Avexitide for the Treatment of PBH

Study Design Elements	Phase 2 PREVENT	Phase 2b	Phase 3 LUCIDITY
Study Population: Surgery	**RYGB**	**RYGB** Sleeve gastrectomy, Esophagectomy, Nissen fundoplication, Gastrectomy	**RYGB**
Study Population: Diet	**Hypoglycemic events despite dietary management**	**Hypoglycemic events despite dietary management**	**Hypoglycemic events despite dietary management**
Run-In Hypoglycemic Event Rate	**At least one per week**	**At least one per week**	**At least one per week**
Avexitide Dose	30 mg BID/60 mg QD	45 mg BID/**90 mg QD** (90 mg QD administered as 2 sequential injections)	**90 mg QD** (90 mg QD administered as 2 sequential injections during double blind treatment period and OLE Part A and as 1 injection during OLE Part B)
Endpoints	**Exploratory:** **Level 2** hypoglycemic events **Level 3** hypoglycemic events	**Secondary:** **Level 2** hypoglycemic events **Level 3** hypoglycemic events	**Primary:** Composite of **Level 2 and Level 3** hypoglycemic events

BID=twice daily; MMTT=mixed meal tolerance testing; PBH=post-bariatric hypoglycemia; QD=once daily; RYGB=Roux-en-Y Gastric Bypass.

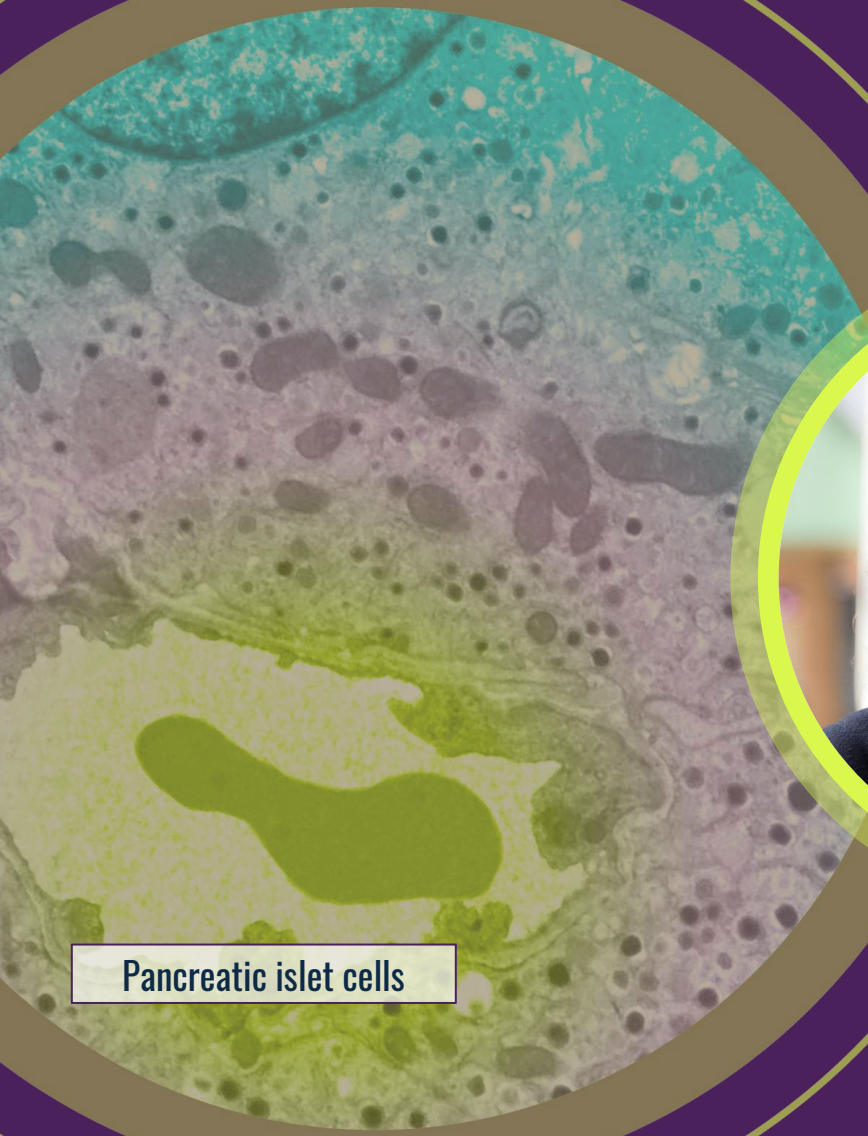
Phase 3 LUCIDITY Trial Underway, Readout in First Half of 2026



Closing Remarks

Josh Cohen

Co-Chief Executive Officer & Co-Founder of Amylyx



Pancreatic islet cells

Q&A

MODERATED BY

Camille Bedrosian, MD

Chief Medical Officer of Amylyx

Speakers' Bios

Helen Lawler, MD

Investigator on the LUCIDITY Clinical Trial, Co-Lead Investigator of the Phase 2 PREVENT Clinical Trial, and Associate Professor of Medicine in Endocrinology at University of Colorado at Denver School of Medicine

Colleen Craig, MD

Co-lead Investigator of Proof-of-Concept and First-in-Human Studies of Avexitide in PBH, Leader of Avexitide Development Program During Phase 2 PREVENT Clinical Trial, and Scientific Advisor and Consultant for Amylyx

Marilyn Tan, MD, FACE

Principal Investigator of the LUCIDITY Clinical Trial, Co-Lead Investigator of the Phase 2 PREVENT Clinical Trial, and Clinical Associate Professor of Medicine at Stanford University School of Medicine

Jamie Timmons, MD

Vice President, Medical Affairs at Amylyx

Thank you!

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