July 10, 2024

AMYLYX®

Avexitide: Novel GLP-1 Receptor Antagonist for the Potential Treatment of Hyperinsulinemic Hypoglycemia

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, statements regarding the potential of Avexitide as a treatment for post-bariatric hypoglycemia (PBH) and congenital hyperinsulinism and AMX0035 as a treatment for neurodegenerative diseases; expectations around the timing of a Phase 3 program of Avexitide in PBH; the possibility that results from a phase 3 program could support FDA approval; expectations about the market size for PBH; expectations around interactions with regulatory authorities on potential development plans for Avexitide in PBH; and expectations regarding our longer-term strategy. 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 research, development, and regulatory strategy, regulatory developments, Amylyx’ ability to fund operations, and the impact that the COVID-19 pandemic may have on Amylyx’ 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, 2023, 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.

Avexitide is a Compelling Asset with FDA Breakthrough Therapy Designation

Novel, first-in-class GLP-1 receptor antagonist with the potential to treat hyperinsulinemic hypoglycemia

- Sizable and debilitating orphan indications with no approved treatment options
- Clear match of mechanism of disease (hyperinsulinemic hypoglycemia) and mechanism of potential treatment
- Highly statistically significant and clinically meaningful data with well-tolerated safety profile replicated across five clinical trials of PBH
- Builds on Amylyx' endocrine and neuroscience expertise
- Rapid path to Phase 3 based on outcomes met in Phase 2 and Phase 2b; Plan to utilize FDA-agreed upon primary endpoint in Phase 3

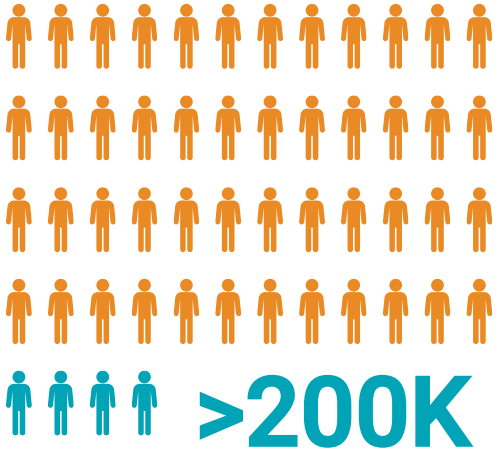
Data from pivotal post-bariatric hypoglycemia (PBH) Phase 3 program expected in 2026, planning for commercial launch in 2027

Bariatric Surgery is a Cornerstone of Weight Loss Therapy

With millions of people having undergone surgery

~2M

people living in the U.S. have received bariatric surgery in the past 10 years[1]



>200K

new procedures are happening annually[1]

Bariatric Surgery Results in Substantial Weight Loss

- **20-30% reduction in bodyweight**, with some participants losing even more[2,3]
  - Higher BMI associated with higher total weight loss[4]
    - Bariatric surgery shows benefits for other conditions including in direct comparison to medical management for **Type 2 diabetes**[5] and **cardiovascular disease**[6,7]

1. Estimate of Bariatric Surgery Numbers, 2011-2022 - American Society for Metabolic and Bariatric Surgery (asmbs.org). Accessed July 9, 2024. **2.** Maciejewski, M. L. et al. *JAMA Surg*. 2016;151(11):1046-1055. doi:10.1001/jamasurg.2016.2317. **3.** O'Brien, P. et al. *Obes Surg*. 2019; 29(1): 3–14. doi:10.1007/s11695-018-3525-0. **4.** Grover, B. T. et al. *Obes Surg*. 2019;29(11), 3493-3499. doi:10.1007/s11695-019-04022-z. **5.** Courcoulas A. et al. JAMA. 2024;27(331):654-664. doi:10.1001/jama.2024.0318. **6.** van Veldhuisen, S. L. et al. *European Heart Journal*. 2022;43(20), 1955–1969. doi:10.1093/eurheartj/ehac071. **7.** Sutanto, A. et al. *Nutrients*. 2021;13(10), 3568. doi.org/10.3390/nu13103568.

Millions of People Have Already Benefited From Bariatric Surgery

Expected to remain a cornerstone of weight loss therapy despite the introduction of GLP-1 receptor agonists for weight loss

Bariatric surgery is likely more effective and more sustainable for weight loss[1,6] and evidence suggest reduced risk of cardiovascular events and MASLD (previously known as NAFLD)[2,3]

Bariatric surgery is cost-effective and covered by insurance[4]

Bariatric surgery and GLP-1 agonists may be combined, especially for people with higher BMIs[5]

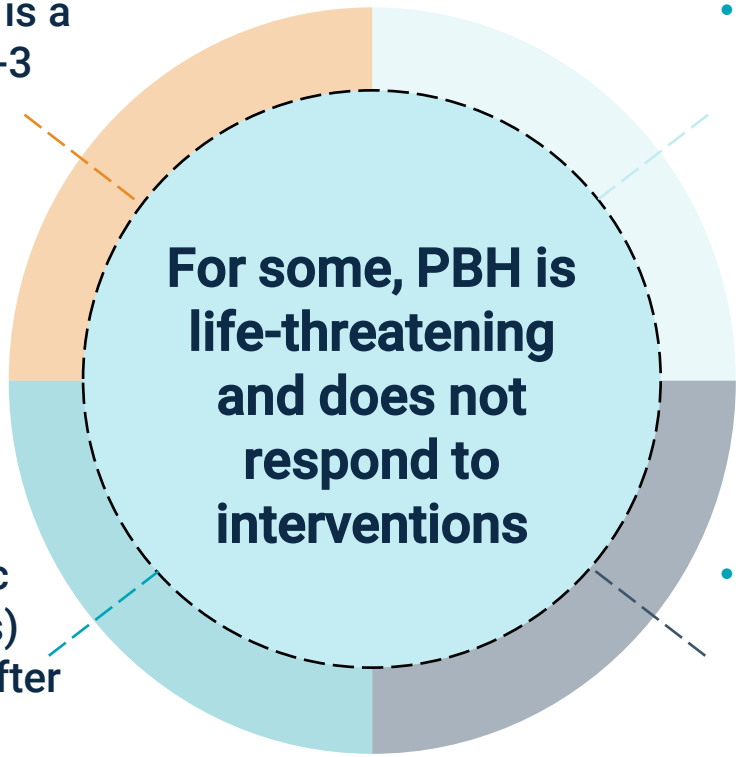
There are already millions of people who have undergone bariatric surgery

MASLD = metabolic dysfunction-associated steatotic fatty liver disease
NAFLD = nonalcoholic fatty liver disease

1. Sarma, S. et al. *Obesity (Silver Spring)*. 2022;30(11):2111-2121. doi:10.1002/oby.23563 **2.** Cohen, E. et al. *The American Journal of Gastroenterology*. 2023;118(10S):p S1237. doi: 10.14309/01.ajg.0000956248.42228.0d **3.** Adekolu, A. et al. *The American Journal of Gastroenterology. 2023;*118(10S):p S971. doi: 10.14309/01.ajg.0000954768.41220.8b4**. 4.** Haseeb, M. et al. *JAMA Netw Open*. 2024;7(4):e246221. doi:10.1001/jamanetworkopen.2024.6221 **5.** Weight-loss drugs are increasingly paired with bariatric surgery, 2023. Axios. **6.** Jenkins, M. et al. (2024, June 9-13). *Effectiveness and durability of common weight loss methods* [Poster]. ASBMS Annual Meeting, San Diego, CA, United States. Link to access.

Post-Bariatric Hypoglycemia is a Condition Affecting People Who Have Undergone Bariatric Surgery

- Post-bariatric hypoglycemia (PBH) is a condition that occurs on average 1-3 years post bariatric surgery[1]



- Characterized by hyperinsulinemic (inappropriately high insulin levels) hypoglycemia (low blood sugar) after a meal (postprandial)[2]

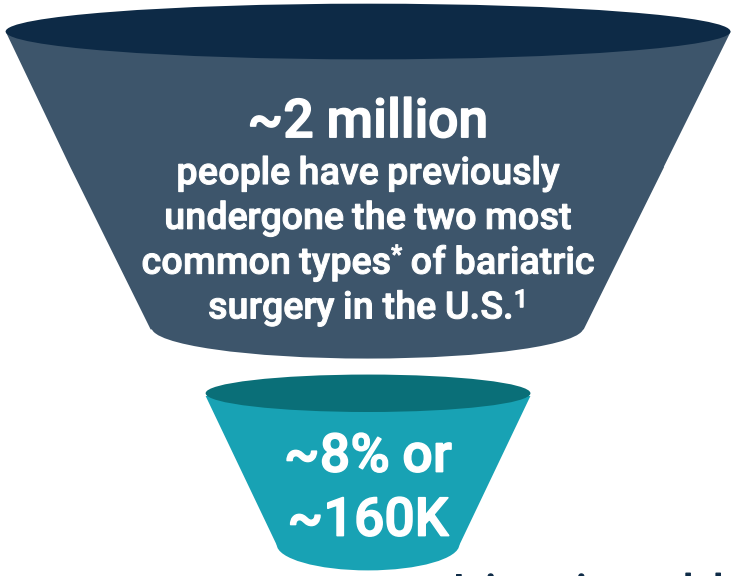
- Symptomatic PBH can have disabling effects
  - > Autonomic and neuroglycopenic symptoms, such as impaired cognition, loss of consciousness, and seizures[3]
  - > Can lead to falls, motor vehicle accidents, and job and income loss[3]

- Current management approaches are insufficient
  - > Symptoms persist for many despite dietary modification and off-label use of acarbose, octreotide, and/or diazoxide[4]
  - > Patient typically managed by endocrinologist/diabetologist

AMYLYX **1.** Hazlehurst, J. et al. *Endocrine Connections.* 2024;13(5), e230285. doi:10.1530/EC-23-0285. **2.** Ostrovosky, V. et al. *NMCD.* 2023;33(6),1197-1205. doi:10.1016/j.numecd.2023.02.012. **3.** Salehi, M. et al. *Journal of Clinical Endocrinology and Metabolism.* 2018;03(8):2815–2826. doi: 10.1210/jc.2018-00528. **4.** Craig, C. M. et al. *The Journal of Clinical Endocrinology and Metabolism.* 2021;106(8):e3235-e3248. doi:10.1210/clinem/dgab103.

Impact of PBH

Prevalence



Estimated that ~8% of people undergoing bariatric surgery will develop *symptomatic* PBH[2,3]

It is estimated that ~160,000 people are currently living with *symptomatic* PBH in the U.S.[1-3]

Characteristics of symptomatic PBH from literature:[2-4]
- Measured glucose value of <54 mg/dL (3.0 mmol/L) after bariatric surgery
- Postprandial neuroglycopenic symptoms: difficulty speaking, blurred vision, confusion, drowsiness, impaired consciousness, coma, seizures, traffic accidents, requiring ER visit or hospitalization

*According to 2022 bariatric surgery estimates from the American Society for Metabolic and Bariatric Surgery (ASMBS), more than 75% of bariatric surgeries in the U.S. are either sleeve gastrectomy (57%) or Roux-en-Y gastric bypass (22%).[1]

Living with PBH

"PBH has affected me physically and mentally."

"I pass out multiple times a week. My lows are averaging 4-5 times a day."

"I lost my driver's license since I am unaware of my lows."

"It affected my ability to work and take care of my family."

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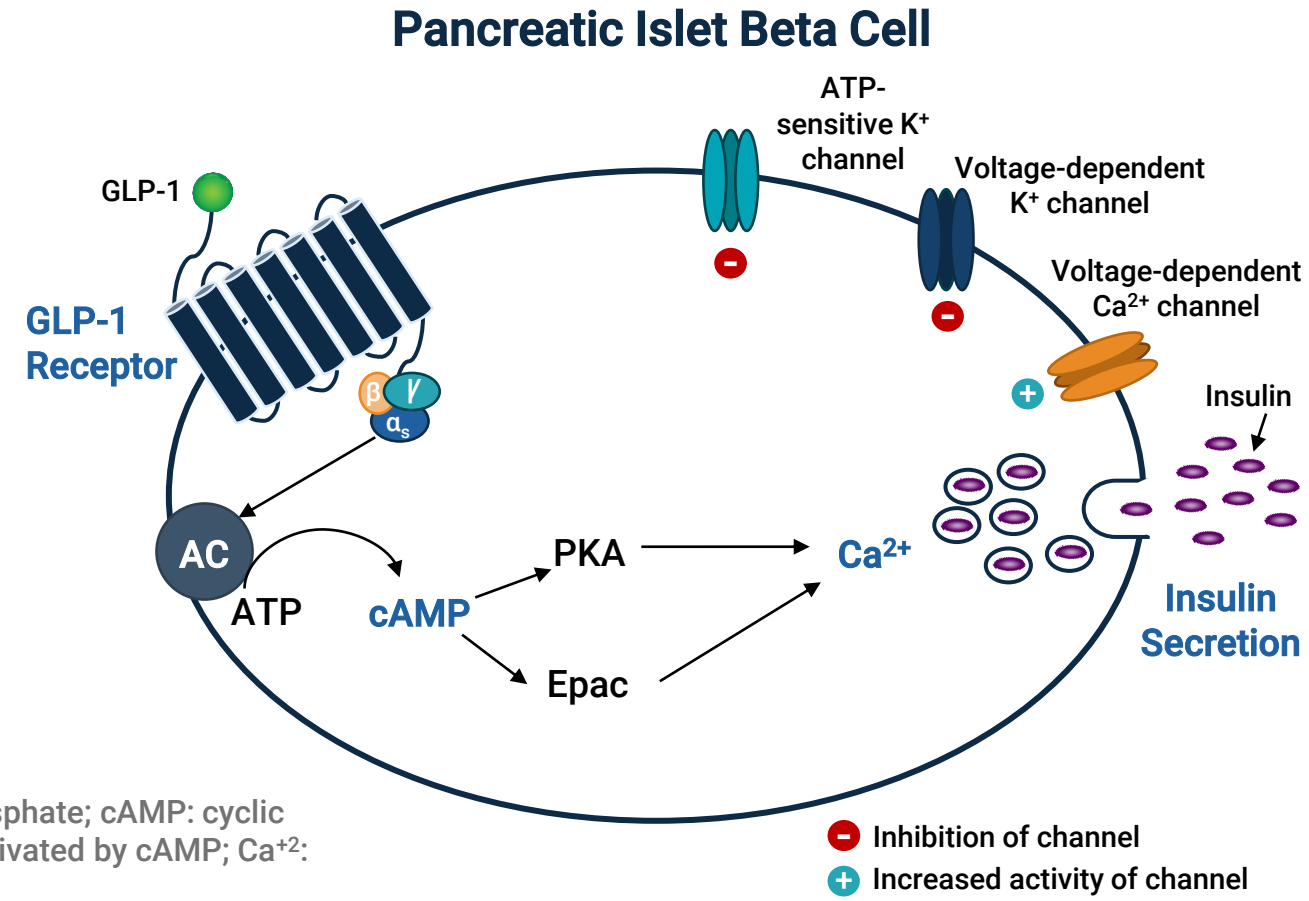
1. Estimate of Bariatric Surgery Numbers, 2011-2022. American Society for Metabolic and Bariatric Surgery (ASMBS). Accessed July 9, 2024. **2.** Raverdy V. et al. *Annals of Surgery.* 2016;264(5):878-885. doi:10.1097/SLA.0000000000001768. **3.** de Heide, L. J. M. et al. *Diabetes, Obesity, & Metabolism.* 2023;25:735-747. doi.org/10.1111/dom.14920. **4.** Hazlehurst, J. et al. Endocrine Connections. 2024;13(5), e230285. doi:10.1530/EC-23-0285.

GLP-1 Receptor Pathway Mediates Blood Glucose Levels via Insulin Secretion

Production of cAMP initiates pathways leading to insulin secretion

GLP-1 Receptor Mediated Insulin Secretion[1,2]

- GLP-1 receptor couples to trimeric G-protein complex, activating adenylyl cyclase (AC)
- Increased production of cAMP
- Activation of PKA and Epac
  - > Inhibition of ATP-sensitive and voltage-dependent potassium channels
  - > Increased activity of voltage-dependent calcium channels
- Increased Ca^{2+} influx
- Insulin secretion



GLP-1: glucagon-like peptide-1; AC: adenylate cyclase; ATP: adenosine triphosphate; cAMP: cyclic adenosine monophosphate; PKA, protein kinase A; Epac: exchange protein activated by cAMP; Ca^{+2}: calcium; K^{+}: potassium.

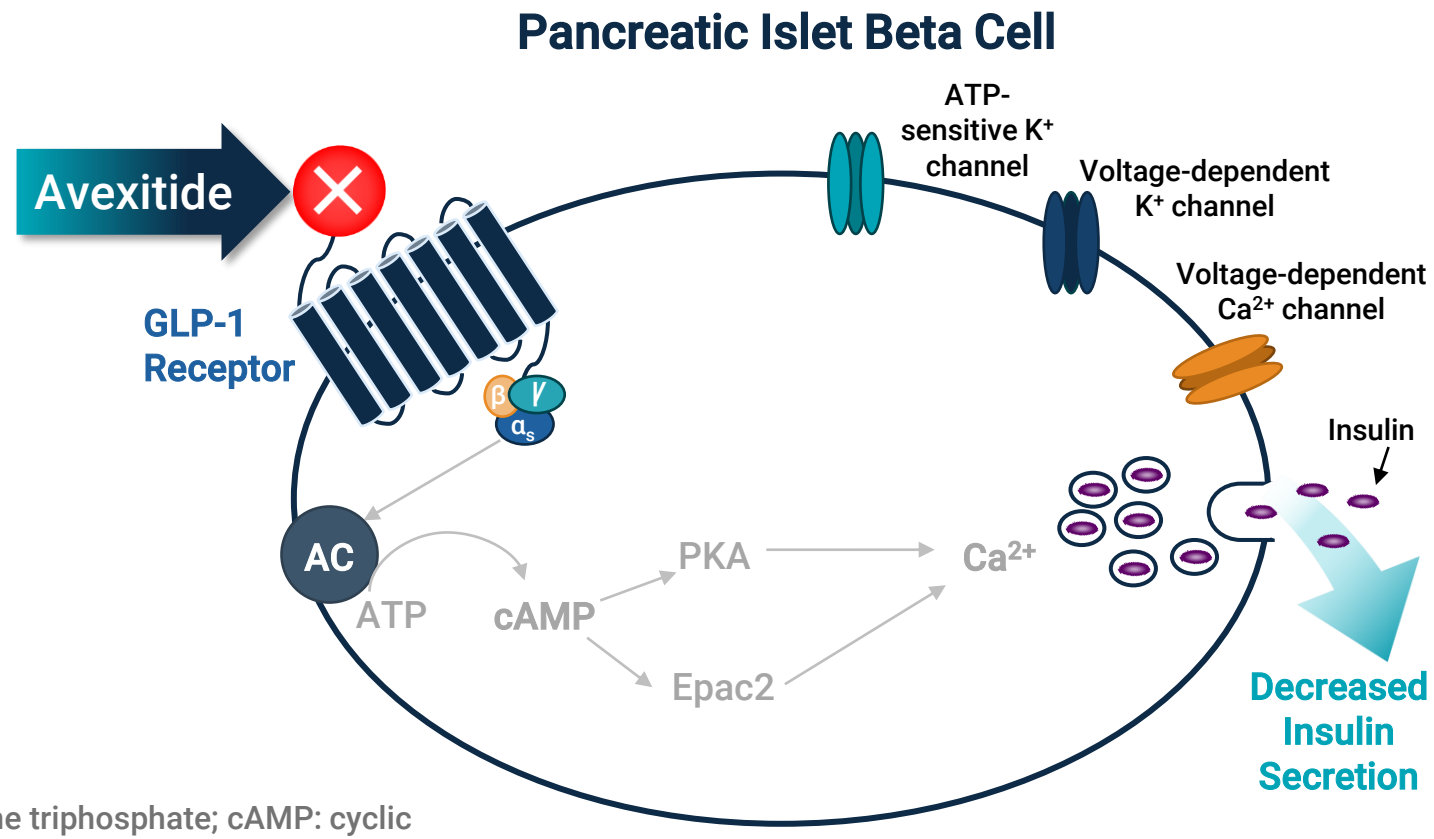
1. Smith, N. K. et al. *Neurochemistry International.* 2019;128:94-105. doi:10.1016/j.neuint.2019.04.010. **2.** Meloni, A. R. et al. *Diabetes, Obesity & Metabolism.* 2013;15(1):15-27. doi.org/10.1111/j.1463-1326.2012.01663.x.

Avexitide: An Investigational GLP-1 Receptor Antagonist

Demonstrated to bind to GLP-1 receptor, decrease insulin secretion, stabilize glucose level

Proposed Mechanism of Action of Avexitide[1-4]

- Binds to GLP-1 receptor (antagonist)
- Lowers cAMP levels
- Decreases insulin secretion
- Stabilizes glucose levels



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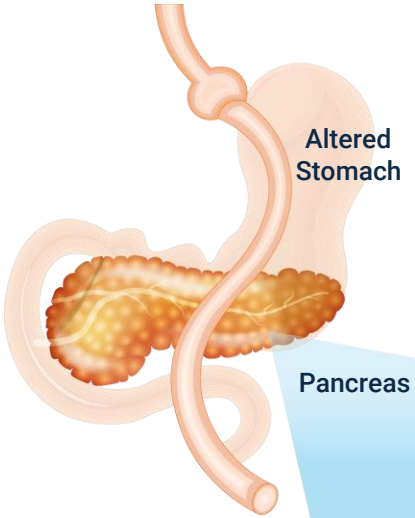
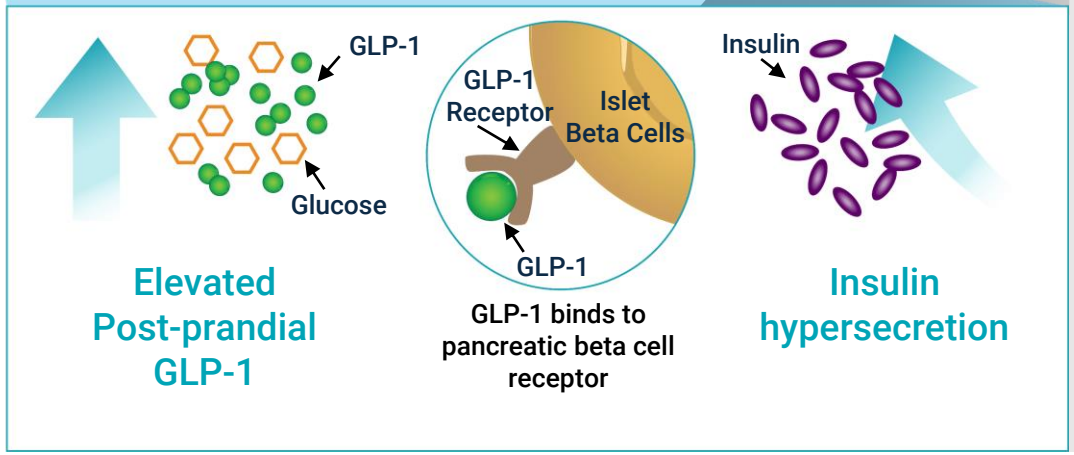
PBH is Believed to be Caused by an Excessive Postprandial GLP-1 Response

Elevated GLP-1 secretion leads to insulin hypersecretion and subsequent hypoglycemia with potentially severe symptoms and consequences[1-7]



Changes Post-Bariatric Surgery[1-3]

- Rapid gastric pouch emptying
- Increased delivery of nutrients to GLP-1 secreting intestinal L cells



Post-bariatric Hypoglycemia (PBH)[1,4-8]

Symptomatic Hypoglycemia

Autonomic Symptoms

- Sweating
- Shaking
- Palpitations
- Anxiety

Neuroglycopenic Symptoms

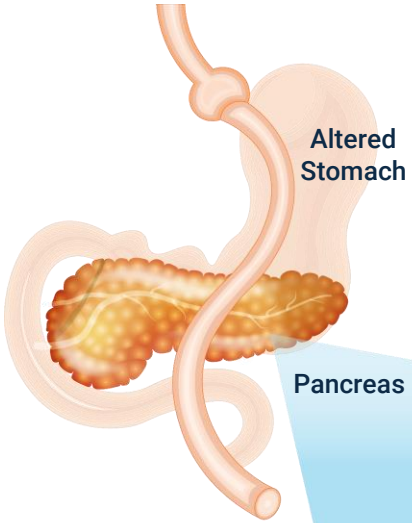
- Blurred Vision
- Confusion
- Drowsiness
- Odd behavior
- Speech difficulty
- Incoordination
- Dizziness
- Weakness
- Loss of consciousness
- Impaired cognition

Potential Consequences

- Hypoglycemia unawareness
- Seizures
- Weight regain
- Motor vehicle accidents
- Cardiac arrythmias
- Missed work
- Decreased quality of life
- Falls

1. Craig, C. M. et al. *Diabetes, Obesity & Metabolism*. 2018;20:352–361. doi.org/10.1111/dom.13078. **2.** Jalleh, R. J. et al. *Reviews in Endocrine and Metabolic Disorders*. 2023;24:1075-1088. doi.org/10.1007/s11154-023-09823-3. **3.** van den Broek, M. et al. *International Journal of Obesity*. 2021;45(3):619-630. doi.org/10.1038/s41366-020-00726-w. **4.** Hazlehurst, J. et al. *Endocrine Connections*. 2024; 13(5):e230285. doi:10.1530/EC-23-0285. **5.** Varma S. et al. *Surgery for Obesity and Related Disorders*.2017;13(10):1728-1734. doi:10.1016/j.soard.2017.06.004. **6.** Patti, M. E. & Goldfine, A. *Gastroenterology*. 2014;146(3):605-608. doi.org/10.1053/j.gastro.2014.01.038. **7.** Athavale, A. & Ganipisetti, V. M. *Postbariatric Surgery Hypoglycemia*. [Updated 2023 Aug 15]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK592417/ **8.** Salehi, M. et al. *The Journal of Clinical Endocrinology and Metabolism*, 2018;03(8):2815–2826. doi.org/10.1210/jc.2018-00528.

Mechanism of Action: Avexitide Proposed to Decrease Insulin Secretion and Stabilize Glucose Levels via GLP-1 Receptor Blockade



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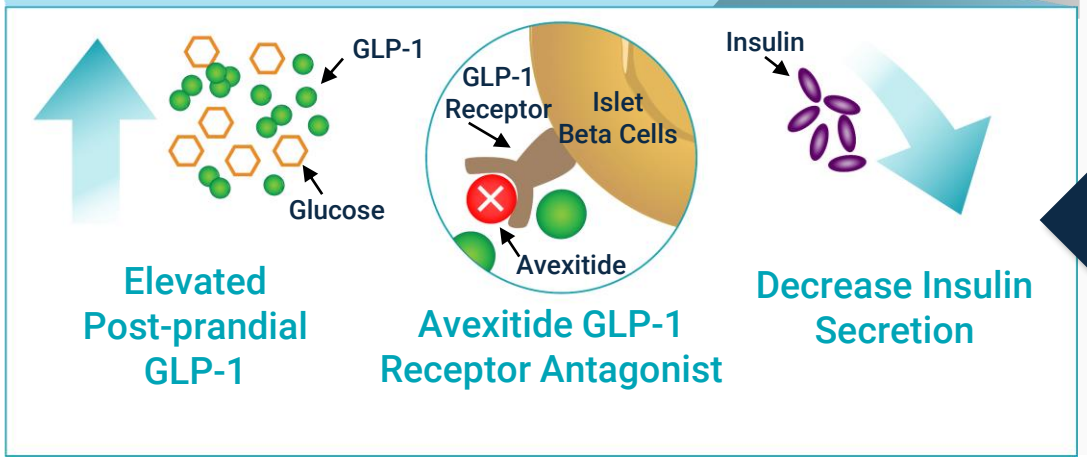


Post-bariatric Hypoglycemia (PBH)[1,4-7]

Symptomatic Hypoglycemia

Autonomic Symptoms
- Sweating
- Shaking
- Palpitations
- Anxiety

Neuroglycopenic Symptoms
- Blurred Vision
- Confusion
- Drowsiness
- Odd behavior
- Speech difficulty
- Incoordination
- Dizziness
- Weakness
- Loss of consciousness

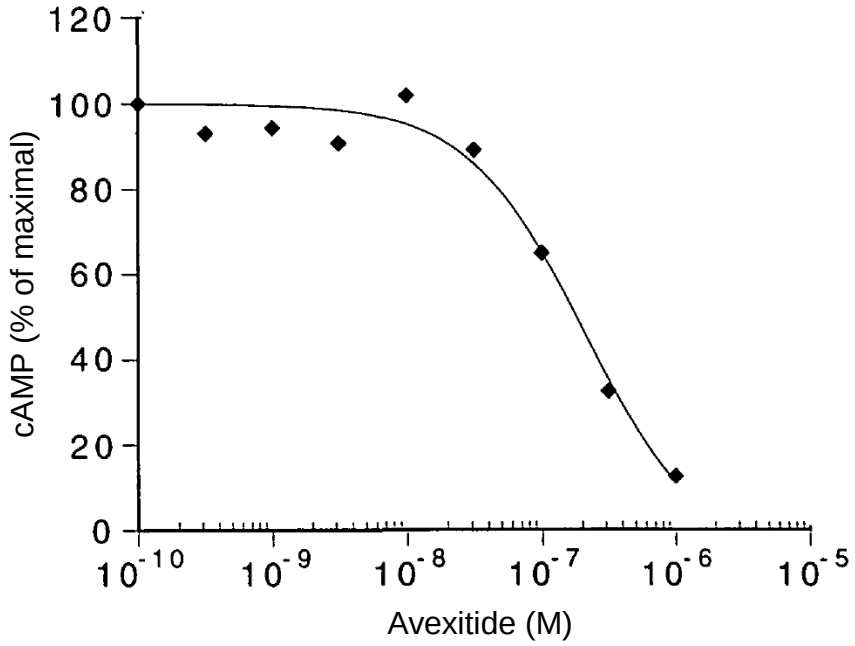
Consequences
- Weight regain
- Motor vehicle accidents
- of life

Stabilized Glucose Levels with Avexitide[1]
GLP-1 Receptor Antagonist

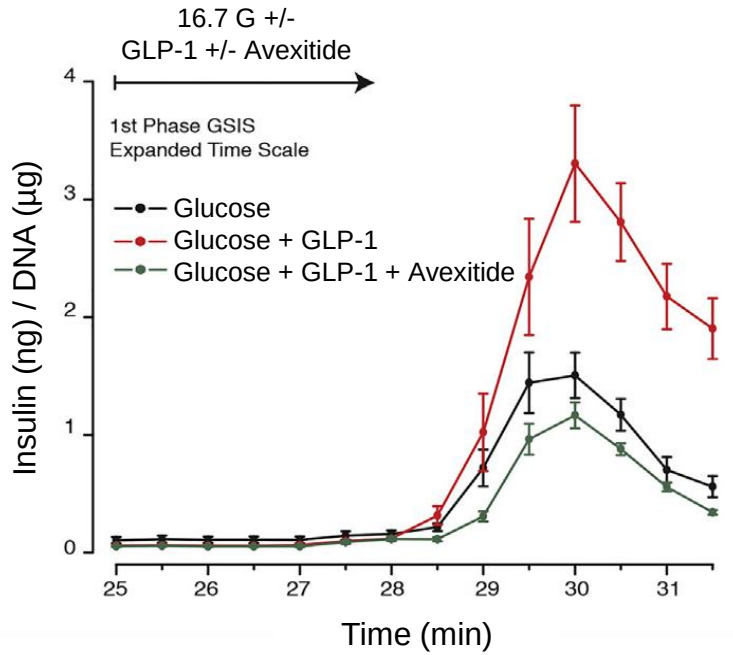
1. Craig, C. M. et al. *Diabetes, Obesity & Metabolism.* 2018;20:352–361. doi.org/10.1111/dom.13078. **2.** Jalleh, R. J. et al. *Reviews in Endocrine and Metabolic Disorders.* 2023;24:1075-1088. doi.org/10.1007/s11154-023-09823-3. **3.** van den Broek, M. et al. *International Journal of Obesity.* 2021;45(3):619-630. doi.org/10.1038/s41366-020-00726-w. **4.** Thorens, B. et al. *Diabetes.*1993;42(11):1678-1682. doi:10.2337/diab.42.11.1678. **5.** Cabrera O. et al. *The Journal of Biological Chemistry.* 2022;298(2):101484. doi:10.1016/j.jbc.2021.101484. **6.** Wang Z. et al. *Journal of Clinical Investigation.* 1995;95(1):417-421. doi:10.1172/JCI117671. **7.** De Leon, D. D. et al. *Journal of Biological Chemistry.* 2008;(283)38: 25786-25793. doi:10.1074/jbc.M804372200.

GLP-1 Receptor Antagonism Lowers cAMP and Insulin Secretion

Dose-dependent antagonism of avexitide in one of the classic GLP-1 agonist cellular assays, wherein blocking the GLP-1 receptor causes a decrease in cyclic AMP (cAMP) in hamster fibroblast cells[1]



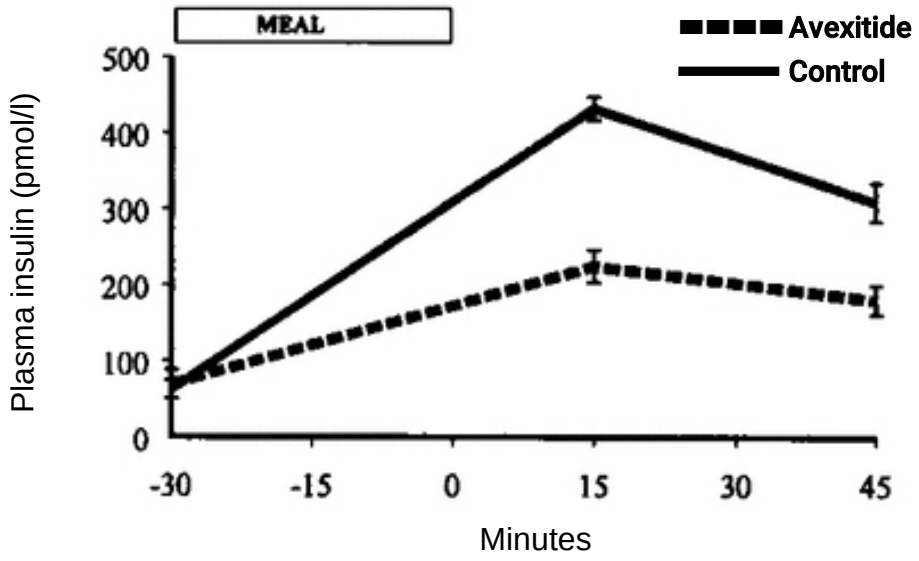
GLP-1 receptor antagonism blocks GLP-1 and decreases insulin response to glucose in rat pancreatic islet cells[2]



1. Thorens, B. et al. *Diabetes*.1993;42(11):1678-1682. doi:10.2337/diab.42.11.1678. **2.** Cabrera O. et al. *The Journal of Biological Chemistry*. 2022;298(2):101484. doi:10.1016/j.jbc.2021.101484.

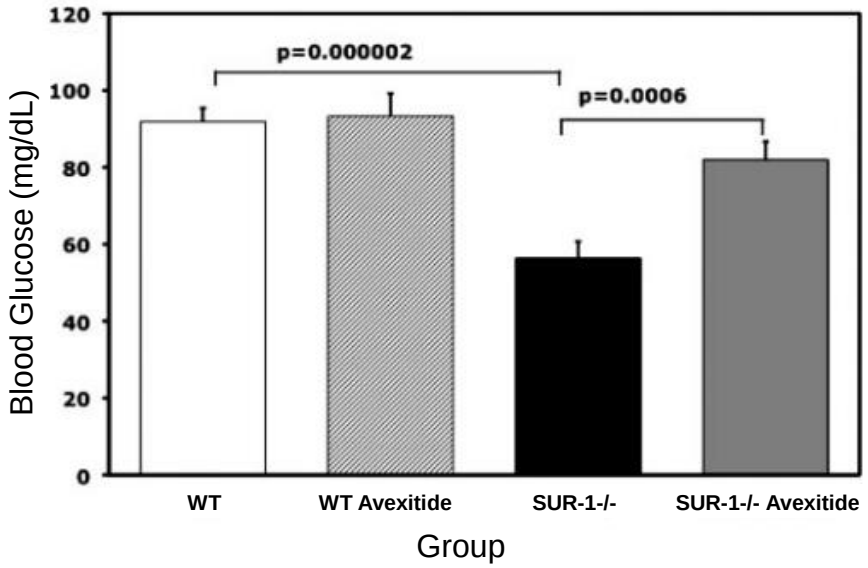
By Inhibiting GLP-1 Activity, Avexitide Decreases Plasma Insulin and Mitigates Hypoglycemia In Vivo Preclinical Models

Avexitide decreased plasma insulin in relevant model[1]



Insulin and glucose concentrations after a meal in conscious trained rats. All rats were injected with pre-meal subcutaneous saline for 10 d beforehand. On the day of the experiment avexitide treated animals (*dotted line*) were given pre-meal subcutaneous avexitide (4.5 nmol/kg) and control animals (*solid line*) received premeal subcutaneous saline. Glucose concentrations were significantly higher ($P < 0.001$) and insulin concentration were reduced in the avexitide treated animals ($P < 0.001$ at 15 min and $P < 0.01$ at 45 min).[1]

Avexitide stabilized blood glucose levels in genetic hypoglycemia model[2]



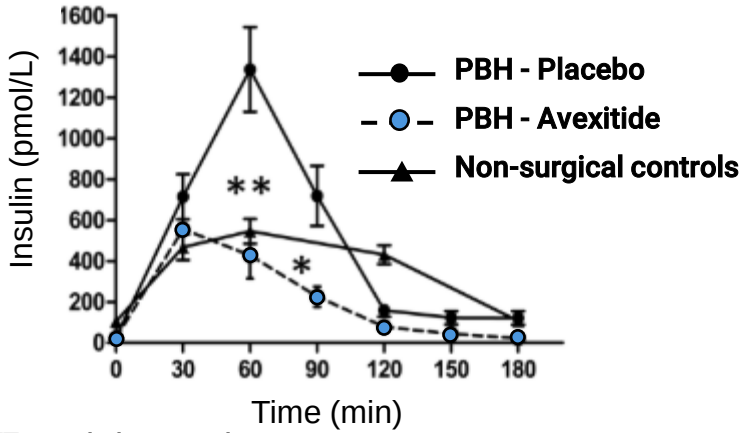
Avexitide stabilized fasting blood glucose levels in SUR-$1^{-/-}$ mice. Blood glucose levels were determined after a 12–16-h fast on day 7. *White bar*, vehicle-treated wild-type littermates (n =13); *hatched bar*, avexitide-treated wild-type littermates(n = 10); *black bar*, vehicle-treated SUR-$1^{-/-}$ mice (n = 11); *gray bar*, avexitide-treated SUR-$1^{-/-}$ mice (n = 11).[2]

1. Wang Z. et al. *Journal of Clinical Investigation*. 1995;95(1):417-421. doi:10.1172/JCI117671. **2.** De Leon, D. D.., et al. *Journal of Biological Chemistry*. 2008;(283)38: 25786-25793. doi:10.1074/jbc.M804372200.

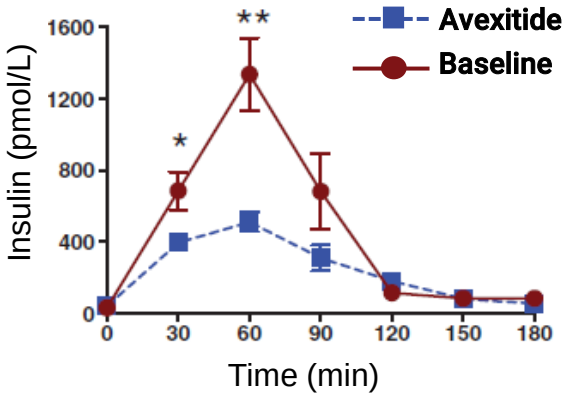
Avexitide Significantly Decreased Post-Meal Insulin Levels

PHASE 1, SAD, MAD

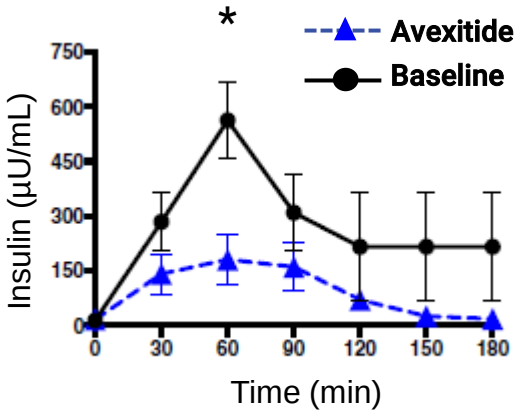
Phase 1, IV infusion[1]
Single Dose, N=8, OGTT



SAD, SC injection[2]
Single Dose, N=8, OGTT



MAD, SC injection[3]
BID Dosing, N=19, OGTT



Consistent and significant decrease in insulin levels across Phase 1, SAD, and MAD trials in people with PBH[1-3]

***p≤0.05, **p≤0.01**

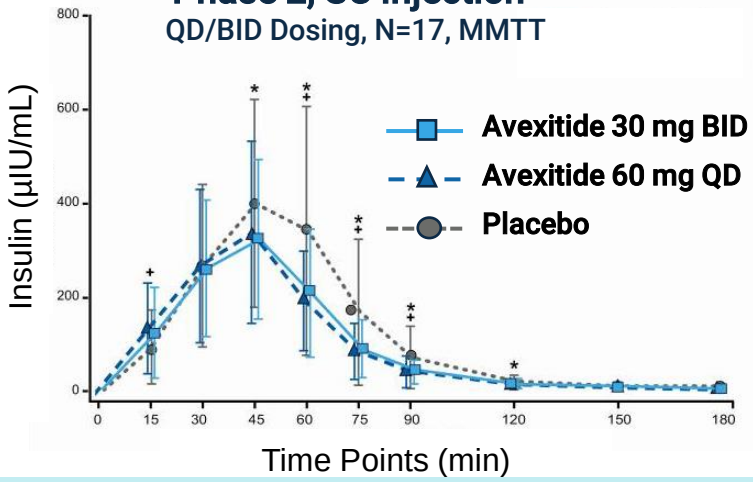
OGTT = oral glucose tolerance test

PHASE 2

PREVENT

For PREVENT (vs placebo)
30 mg BID: *p<0.05
60 mg QD: +p<0.05

Phase 2, SC injection[4]
QD/BID Dosing, N=17, MMTT



Peak insulin was reduced by 23% (p=0.029) and 21% (p=0.042) following avexitide 30 mg BID and 60 mg QD, respectively, compared with placebo in the Phase 2 PREVENT trial in people with PBH[4]

MMTT = mixed meal tolerance test

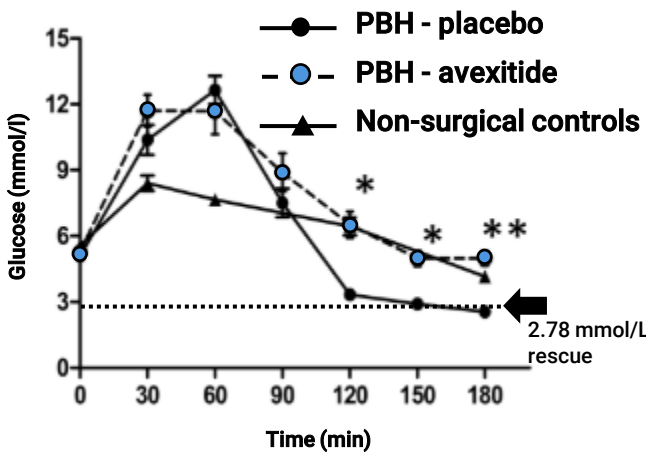
AMYLYX **1.** Craig, C. M. et al. *Diabetologia*. 2017;60(3):531-540. doi:10.1007/s00125-016-4179-x. **2.** Craig, C. M. et al. *Diabetes, Obesity & Metabolism*. 2018;20:352–361. doi.org/10.1111/dom.13078. **3.** Tan, M. et al. *Diabetes, Obesity & Metabolism*. 2020;22(8):1406-1416. doi:10.1111/dom.14048. **4.** Craig, C. M. et al. *The Journal of Clinical Endocrinology & Metabolism*. 2021;106(8):e3235-e3248. doi:10.1210/clinem/dgab103.

Avexitide Significantly Stabilized Post-Meal Glucose Levels

PHASE 1, SAD, MAD

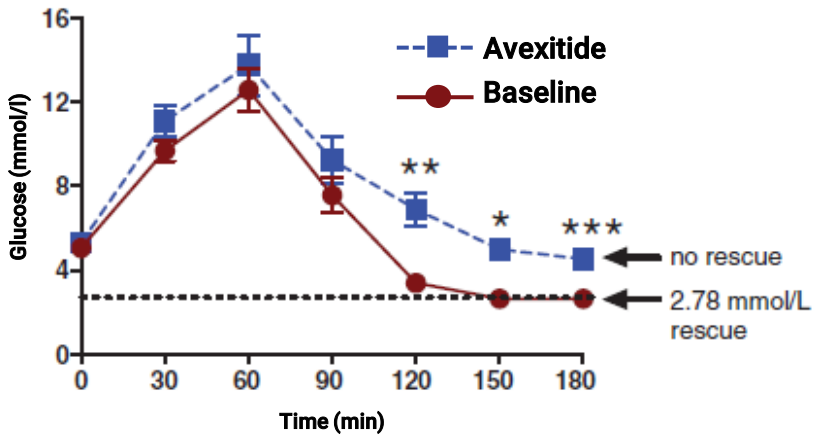
Phase 1, IV infusion[1]

Single Dose, N=8, OGTT



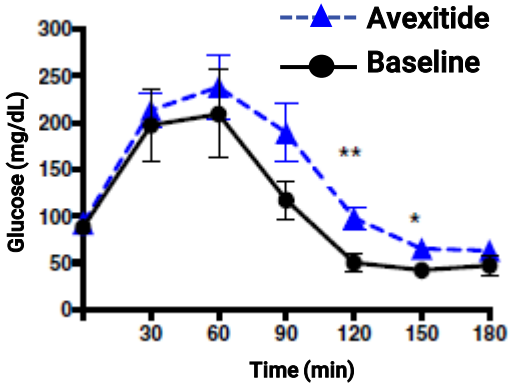
SAD, SC injection[2]

Single Dose, N=8, OGTT



MAD, SC injection[3]

BID Dosing, N=19, OGTT



Consistent and significant stabilization in plasma glucose nadir across Phase 1, SAD, and MAD trials in people with PBH[1-3]

OGTT = oral glucose tolerance test

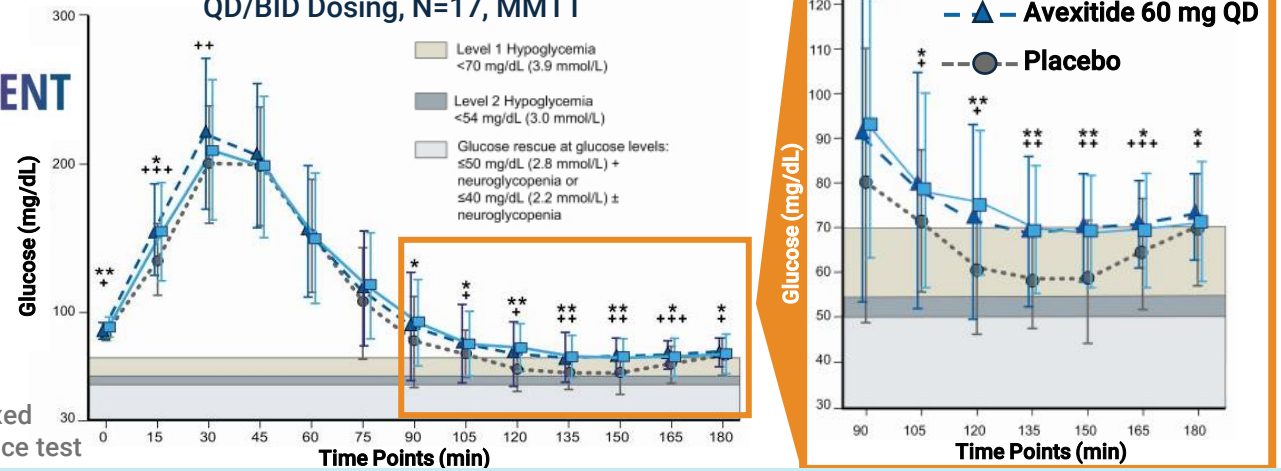
***p≤0.05, **p≤0.01, ***p≤0.001**

PREVENT PHASE 2

Phase 2, SC injection[4]

QD/BID Dosing, N=17, MMTT

PREVENT



MMTT = mixed meal tolerance test

Mean plasma glucose nadir (prespecified primary endpoint) increased by 21% (p=0.001) and 26% (p=0.0002) following avexitide 30 mg BID and 60 mg QD, respectively, compared with placebo in the Phase 2 PREVENT trial in people with PBH[4]

- Corresponded to 50% and 75% fewer participants requiring rescue, respectively

For PREVENT (vs placebo): **30 mg BID:** *p<0.05, **p<0.01, ***p<0.001
60 mg QD: +p<0.05, ++p<0.01, +++p<0.001

AMYLYX **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.

FDA Guidance and Interactions Support Phase 2 and Phase 2b Endpoints as Potential Approvable Phase 3 Primary Endpoint

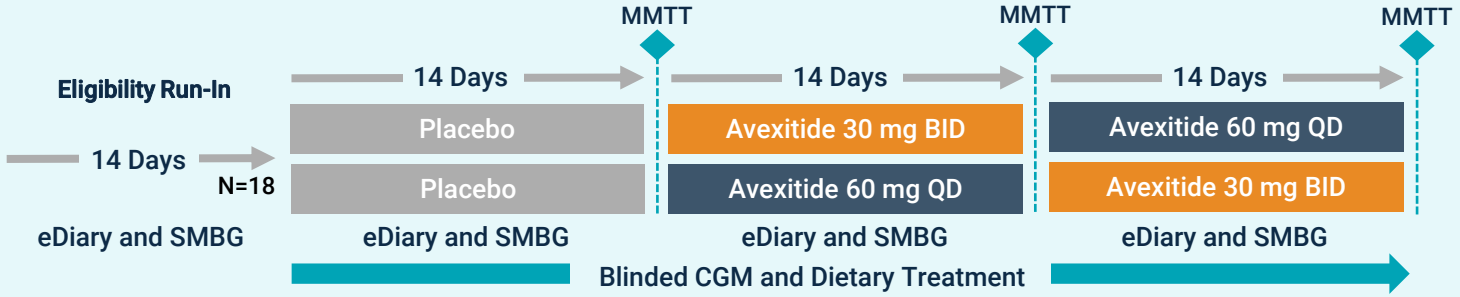
FDA Breakthrough Therapy Designation

- Post-bariatric hypoglycemia (PBH)
- Congenital hyperinsulinism (HI)

- FDA has agreed to primary endpoint expected to be utilized in Phase 3 program:
  - > Composite of Level 2 and Level 3 Hypoglycemia events
    - – FDA guidance for industry for diabetes also supports composite of Level 2 and Level 3 Hypoglycemia events as a potential approvable endpoint[1]
- Phase 2 and Phase 2b study showed avexitide significantly reduced Level 2 and Level 3 events

1. U.S. Food and Drug Administration, FDA-2023-D-0625: Diabetes Mellitus: Efficacy Endpoints for Clinical Trials Investigating Antidiabetic Drugs and Biological Products (2023).

PREVENT Phase 2 Study Met Primary and Secondary Endpoints and Demonstrated Significant Reductions in Hypoglycemic Events



Primary Efficacy Endpoint: Magnitude of postprandial hypoglycemia defined as the **plasma glucose nadir** during MMTT provocation

Participants enrolled had Roux-en-Y gastric bypass

Outcome[a] N=17*	Avexitide 30 mg BID		Avexitide 60 mg QD	
	Improvement vs. Placebo	p value	Improvement vs. Placebo	p value
Post Prandial Glucose Nadir (primary)	**21%** higher	0.001	**26%** higher	0.0002
Peak Insulin Level (secondary)	**23%** lower	0.029	**21%** lower	0.042
Rate of Level 1 Hypoglycemia	**30%** lower	0.072	**61%** lower	0.001
Rate of Level 2 Hypoglycemia	**40%** lower	0.040	**60%** lower	0.004
Rate of Level 3 (Severe) Hypoglycemia	**23%** lower	0.22	**56%** lower	0.014

PREVENT

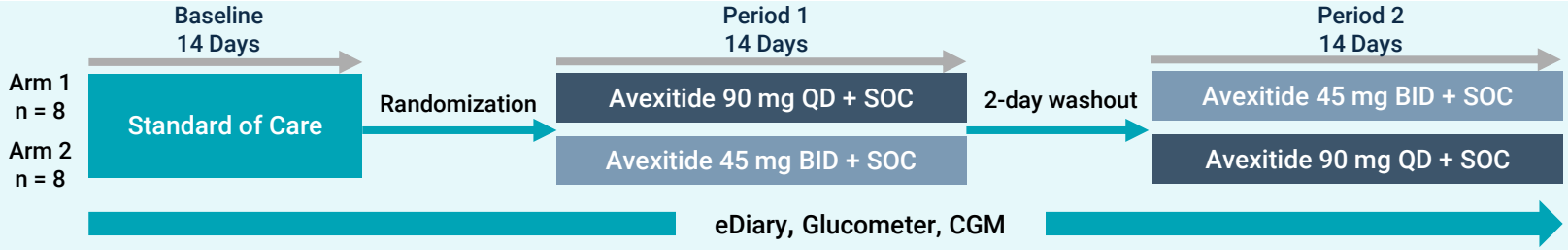
- ✓ **Met Primary Endpoint**
  - Stabilized glucose levels
- ✓ **Met Secondary Endpoint**
  - Decreased post meal insulin levels
- ✓ **Significant reduction in the rate of hypoglycemia events**
  - Events cut by more than half with avexitide 60 mg QD

[a]Level 1 hypoglycemia: self-monitoring of blood glucose (SMBG) <70 mg/dL; Level 2 hypoglycemia: SMBG <54 mg/dL; Level 3 hypoglycemia: a severe event characterized by altered mental and/or physical functioning that requires assistance from another person for recovery. Primary and secondary endpoints were captured during mixed meal tolerance test (MMTT) in Clinical Research Unit. Rates of Levels 1, 2, and 3 hypoglycemia shown were exploratory endpoints captured by SMBG/eDiary in the outpatient setting.

Craig, C. M. et al. *The Journal of Clinical Endocrinology & Metabolism.* 2021;106(8):e3235-e3248. doi:10.1210/clinem/dgab103.

*1 participant was excluded from analysis due to a major protocol deviation (glycemic rescue was not administered as indicated per protocol during the Period 1 placebo MMTT).

A Phase 2b Study of Higher Dose Avexitide in Broader Population Also Demonstrated Significant Reductions in Hypoglycemic Events



Primary efficacy endpoint:
Rate of daytime Level 2 hypoglycemia by CGM (glucose <54 mg/dL)

Participants enrolled had Roux-en-Y gastric bypass, vertical sleeve gastrectomy, esophagectomy, Nissen fundoplication, or gastrectomy

eDiary and SMBG Outcome N=16	Avexitide 45 mg BID		Avexitide 90 mg QD	
	Decrease from Baseline	p value	Decrease from Baseline	p value
Rate of Level 1 Hypoglycemia	**54%** lower	0.003	**68%** lower	0.0005
Rate of Level 2 Hypoglycemia	**57%** lower	0.003	**53%** lower	0.004
Rate of Level 3 (Severe) Hypoglycemia	**68%** lower	0.0003	**66%** lower	0.0003

- Avexitide also significantly decreased % time in hypoglycemia <70 mg/dL and <54 mg/dL

- ✓ **Second placebo-controlled study**
- ✓ **Met primary endpoint**
  - Stabilized glucose levels leading to fewer daytime level 2 hypoglycemia events as measured by CGM
- ✓ **Significant reduction in the *rate* of severe Level 3 hypoglycemia**
- ✓ **Significant reduction of *time* in hypoglycemia**

1. Craig, C. M. et al. *Journal of the Endocrine Society*. 2022;6(1):A349. 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 was Generally Well-Tolerated with a Favorable Safety Profile Across Both Phase 2 Trials

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 withdrawals	No participant withdrawals

No clinically relevant increases were observed in fasting or peak postprandial plasma glucose levels (i.e., no hyperglycemia observed)

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.

Participant Testimonials in Phase 2b Study Support Meaningful Benefit

AVEXITIDE STUDY TEAM	STUDY PARTICIPANTS
Termeh Shamloo Stanford University School of Medicine	*"My husband noted I'm in a much better mood, and my nocturnal hypoglycemia was all gone."*
Dalia Perelman, RD Stanford University School of Medicine	*"Experience was amazing…"*
	"I felt great and normal after a very long time - very happy."
Colleen Craig, MD Eiger BioPharmaceuticals, Inc.	*"I'm back to practicing as a [professional] with full cognitive functioning."*
Tracey McLaughlin, MD, MS Stanford University School of Medicine	*"Feeling protected, mood is much better, the explosive behavior has been much better."*
	"Memory loss and recall improved."
	"I feel like myself again after a very long time."

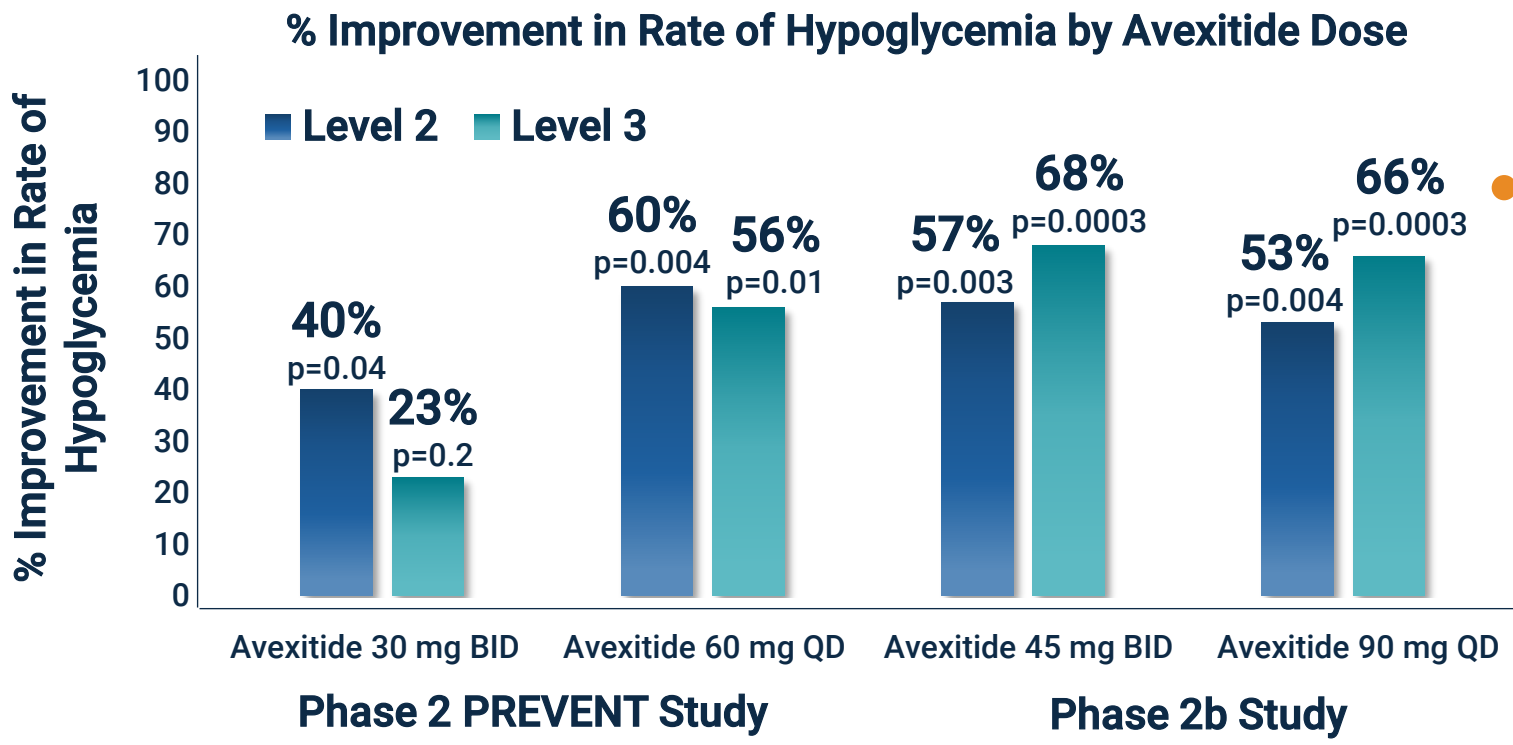
Stanford MEDICINE

EIGER BIOPHARMACEUTICALS

These are individual experiences and not necessarily representative of all clinical trial participants.

Image source: 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 Significantly Reduced Rates of Hypoglycemia in Two Phase 2 Clinical Trials in People with PBH

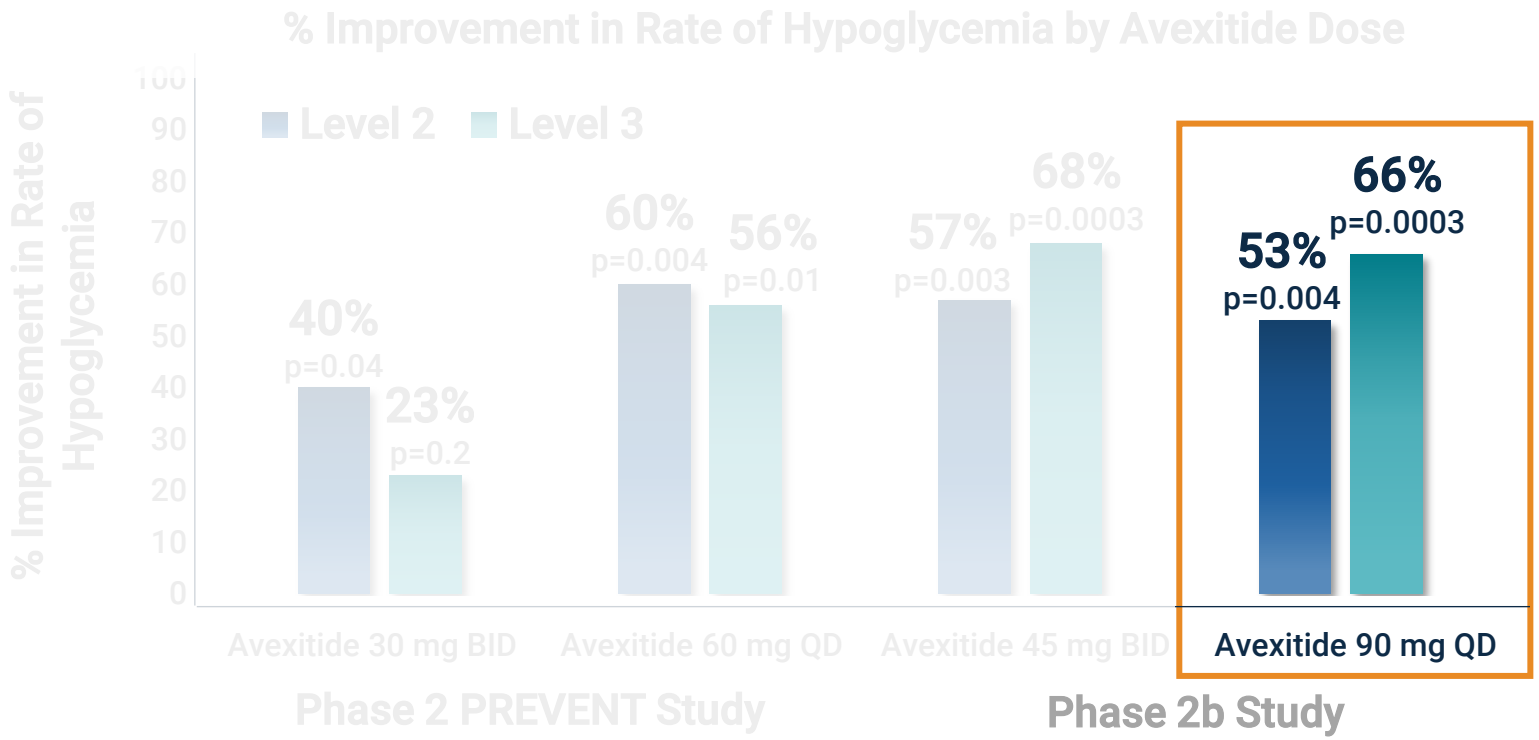


Avexitide cuts rates of hypoglycemia events by **>50%**

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.

Planned Phase 3 Designed To Leverage Success from Phase 2 and Phase 2b

Consistent, dose-dependent effects enable dose selection for evaluation in planned Phase 3 program in PBH

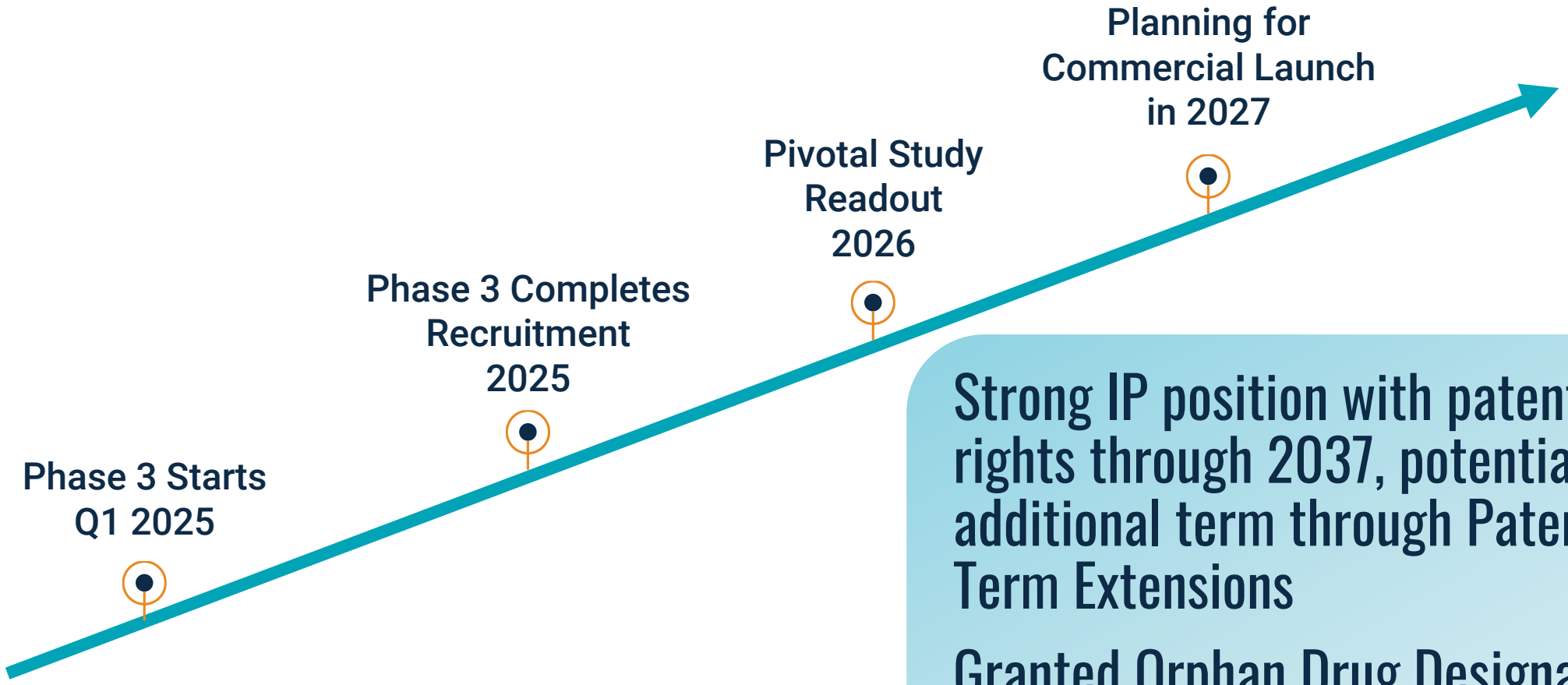


Phase 3 program will evaluate 90 mg QD in people living with PBH

FDA-agreed upon primary endpoint: Composite of Level 2 and Level 3 Hypoglycemia events

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 3 to Begin Q1 2025, Readout in 2026



Strong IP position with patent rights through 2037, potential for additional term through Patent Term Extensions

Granted Orphan Drug Designation and positioned for NCE exclusivity

Financial Terms for Acquisition of Avexitide

Up Front Payment	• **$35.1M using cash on hand***
Future Royalties	• **3% royalty on future sales of avexitide in PBH**

$373.3M in cash, cash equivalents, and short-term investments as of 3/31/24

AMYLYX *On July 9, 2024, Amylyx completed the acquisition of substantially all of the rights, title and interests in, to and under those assets and interests used by the seller in the development, manufacture and commercialization of avexitide from Eiger BioPharmaceuticals for $35.1 million plus the aggregate amount of determined cure costs and assumed liabilities.

A Growing Pipeline of Therapies to Serve Communities with High Unmet Needs

AVEXITIDE GLP-1 RECEPTOR ANTAGONIST	PRECLINICAL	IND-ENABLING STUDIES	PHASE 1	PHASE 2	PHASE 3	COMMERCIAL	EXPECTED UPCOMING MILESTONE(S)
Post-Bariatric Hypoglycemia (PBH)	FDA BREAKTHROUGH DESIGNATION						Phase 3 program begins in Q1 2025; Completes recruitment in 2025; Readout 2026, Planning for Commercial Launch in 2027
Congenital Hyperinsulinism (HI)	FDA BREAKTHROUGH DESIGNATION						Engaging physician and community experts in discussions around next steps for clinical development

AMX0035 SODIUM PHENYLBUTYRATE (PB) AND TAURURSODIOL (TURSO, ALSO KNOWN AS URSODOXICOLTAURINE)	PRECLINICAL	IND-ENABLING STUDIES	PHASE 1	PHASE 2	PHASE 3	COMMERCIAL	EXPECTED UPCOMING MILESTONE(S)
Wolfram Syndrome							FDA Feedback; Report 24-week topline data in Fall 2024
Progressive Supranuclear Palsy (PSP)							Data from interim analysis expected in mid-2025

AMX0114 ANTISENSE OLIGONUCLEOTIDE	PRECLINICAL	IND-ENABLING STUDIES	PHASE 1	PHASE 2	PHASE 3	COMMERCIAL	EXPECTED UPCOMING MILESTONE(S)
Amyotrophic Lateral Sclerosis (ALS)							Initiate multiple ascending dose clinical trial in people with ALS in second half of 2024

Avexitide is a Compelling Asset with FDA Breakthrough Therapy Designation

Novel, first-in-class GLP-1 receptor antagonist with the potential to treat hyperinsulinemic hypoglycemia

- Sizable and debilitating orphan indications with no approved treatment options
- Clear match of mechanism of disease (hyperinsulinemic hypoglycemia) and mechanism of potential treatment
- Highly statistically significant and clinically meaningful data with well-tolerated safety profile replicated across five clinical trials of PBH
- Builds on Amylyx' endocrine and neuroscience expertise
- Rapid path to Phase 3 based on outcomes met in Phase 2 and Phase 2b; Plan to utilize FDA-agreed upon primary endpoint in Phase 3

Data from pivotal post-bariatric hypoglycemia (PBH) Phase 3 program expected in 2026, planning for commercial launch in 2027

AMYLYX®

Q&A Session