AMYLYX®

MAY 2026

We have an audacious mission to develop novel therapies for diseases with high unmet needs, with a focus on serious and fatal endocrine conditions and neurodegenerative diseases.

Maggie, a mom and advocate living with post-bariatric hypoglycemia (PBH).

Pancreatic islet cells

DISCLAIMER

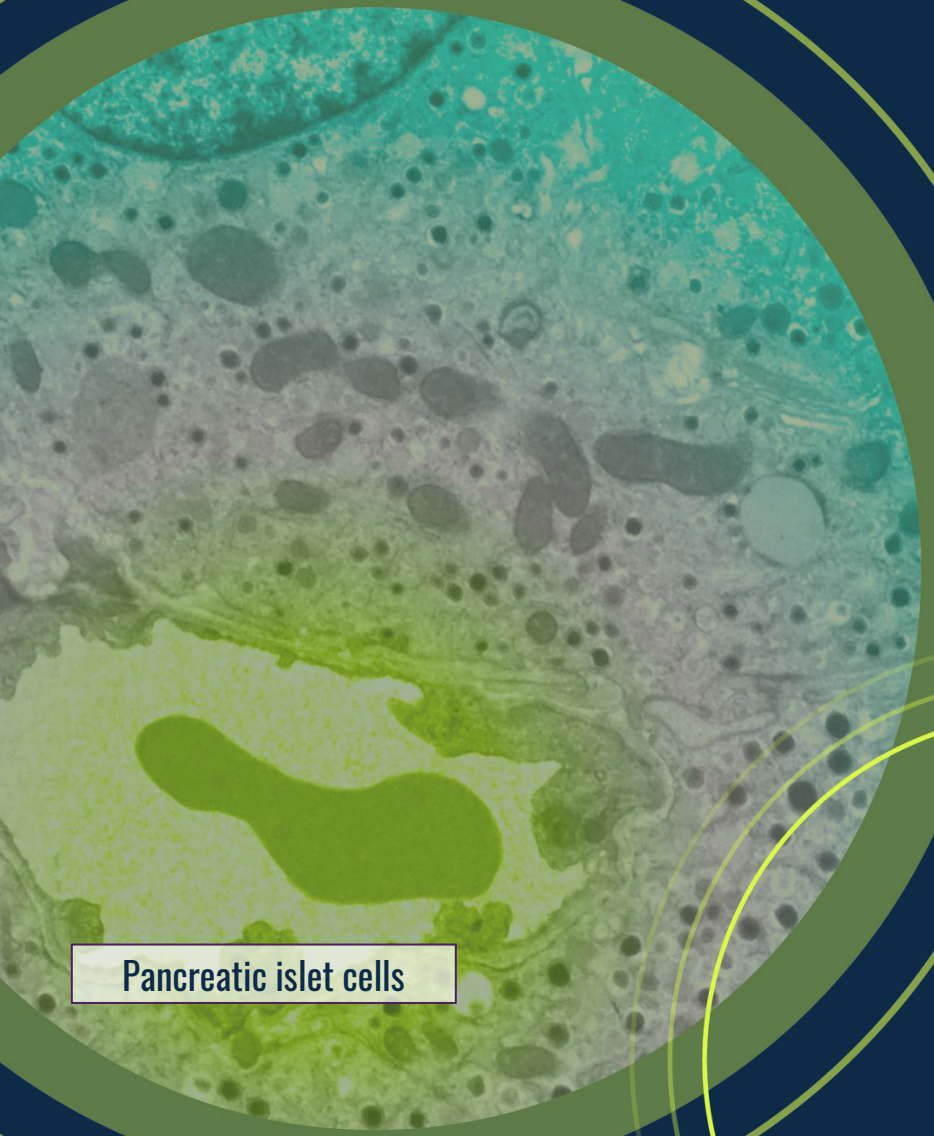
Statements contained in this presentation regarding matters that are not historical facts are “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Such statements include, but are not limited to, the Company’s plans to explore the use of avexitide as a treatment for post-bariatric hypoglycemia (PBH) and congenital hyperinsulinism, AMX0035 for Wolfram syndrome, AMX0114 for ALS, and AMX0318 for PBH and other rare diseases; statements regarding the timing of clinical trials for PBH, Wolfram syndrome and/or ALS; expectation for regulatory action; and expectations regarding our longer-term strategy and expected cash runway. 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’s program development activities, including ongoing and planned clinical trials, Amylyx’s ability to execute on its development and regulatory strategy, regulatory developments, Amylyx’s cash runway and ability to fund operations, as well as the risks and uncertainties set forth in Amylyx’s United States Securities and Exchange Commission (SEC) filings, including Amylyx’s Annual Report on Form 10-K for the year ended December 31, 2025, 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.

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

Led by an experienced team with a proven track record of commercialization in rare diseases

ASO=antisense oligonucleotide; FDA=U.S. Food and Drug Administration; GLP-1=glucagon-like peptide-1; IND=investigational new drug; SAE=serious adverse events.

AMYLYX



Pancreatic islet cells

AVEXITIDE

Investigational, First-in-Class GLP-1 Receptor Antagonist with FDA Breakthrough Therapy Designation

lucidity

Avexitide: Investigational, First-in-Class GLP-1 Receptor Antagonist

- FDA Breakthrough Therapy Designation and Orphan Drug Designation in hyperinsulinemic hypoglycemia
- Phase 3 LUCIDITY trial is evaluating the FDA-agreed upon primary outcome of reduction in the composite of Level 2 and Level 3 hypoglycemic events in PBH following RYGB surgery
  - > Completed enrollment in LUCIDITY in March 2026
- Prior clinical studies generated highly statistically significant reductions in hypoglycemic events
- PBH is an orphan condition that is often life-altering; ~160,000 prevalent patients
- Strong IP position with patent rights through 2037 and potential for patent term extension

EXPECTED MILESTONES

Q3 2026

Topline data from avexitide Phase 3 trial in PBH

2027

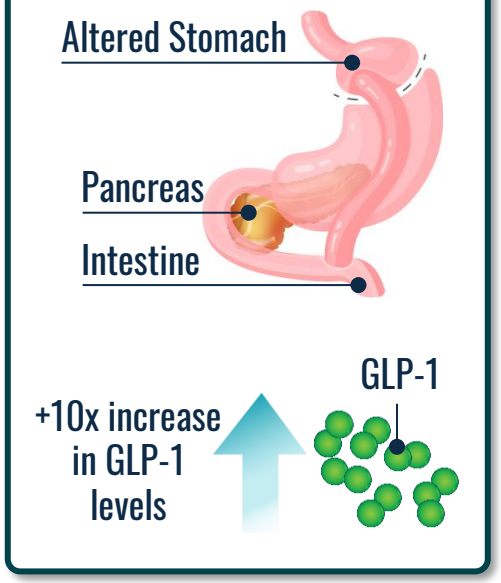
Commercial launch of avexitide in 2027, if approved

FDA=U.S. Food and Drug Administration; GLP-1=glucagon-like peptide-1; IND=Investigational New Drug; IP=intellectual property; PBH=post-bariatric hypoglycemia; RYGB=Roux-en-Y gastric bypass.

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

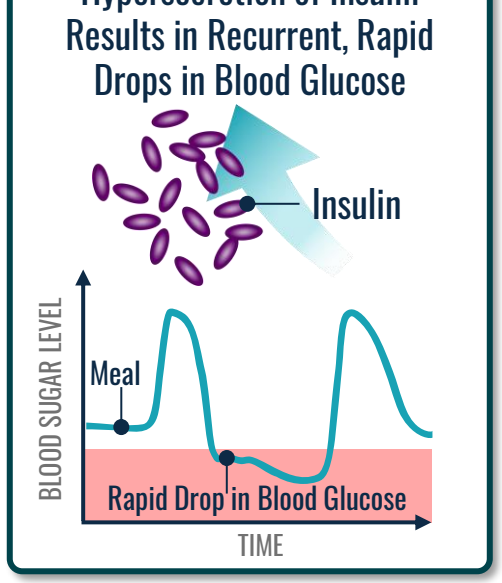
GLP-1 Receptor Antagonism

1



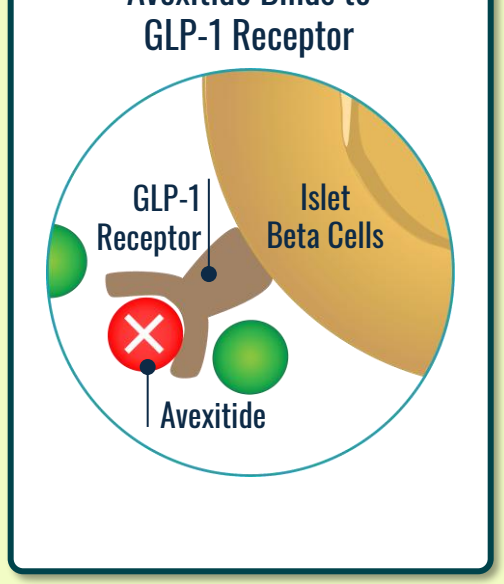
Altered nutrient transit due to anatomical changes associated with bariatric surgery (e.g., Roux-en-Y gastric bypass) leads to **exaggerated GLP-1 secretion** in people with PBH

2



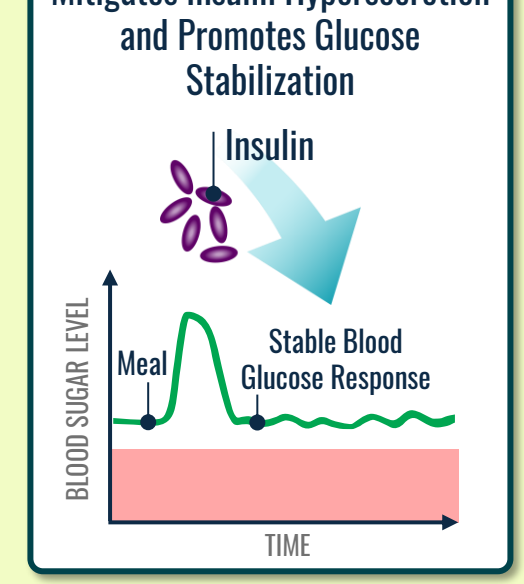
This exaggerated GLP-1 secretion leads to abnormally high insulin levels in the bloodstream, and subsequent hypoglycemia

3



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

4

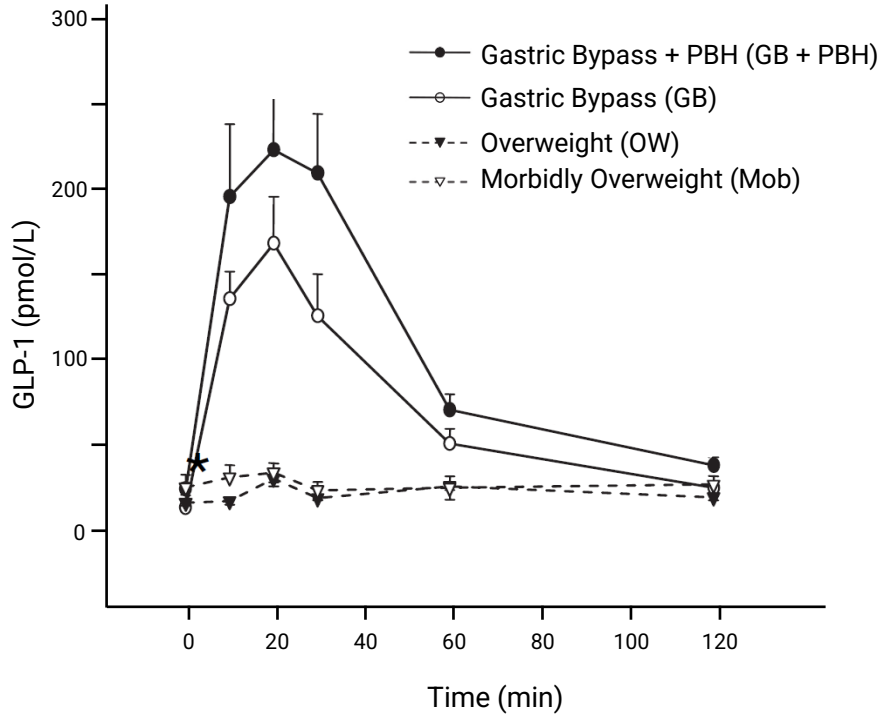


Decreased insulin secretion and stabilized glucose levels resulting from inhibition of the effect of exaggerated GLP-1

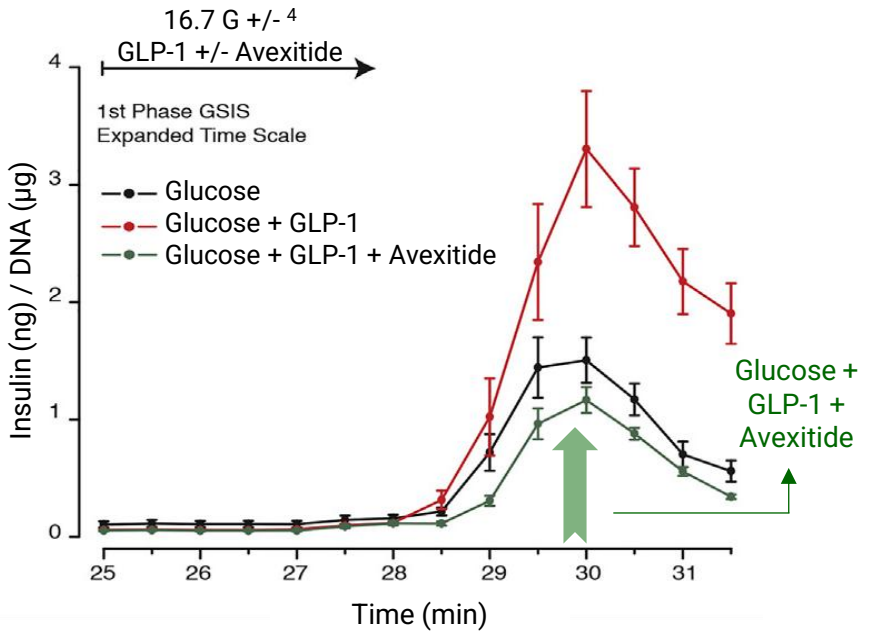
GLP-1=glucagon-like peptide-1; PBH=post-bariatric hypoglycemia; **1.** Sheehan A, Patti ME. *Diabetes Metab Syndr Obes*. 2020;13:4469-4482; **2.** Craig CM, et al. *Diabetes Obes Metab*. 2017; 1-10. **3.** Thorens B,. et al. *Diabetes*.1993;42(11):1678-1682. **4.** Craig CM, et al. *Diabetes Obes Metab*. 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.

Targeted Approach to Inhibit Effects of Excessive GLP-1 in PBH to Mitigate Hypoglycemia

GLP-1 levels observed to be more than 10-fold higher in PBH than in Nonsurgical Controls, resulting in **dysregulated secretion of insulin** and subsequent hypoglycemia



Avexitide inhibits GLP-1 receptor activity and **decreases the insulin response** to glucose in rat pancreatic islet cells[1,2,3]

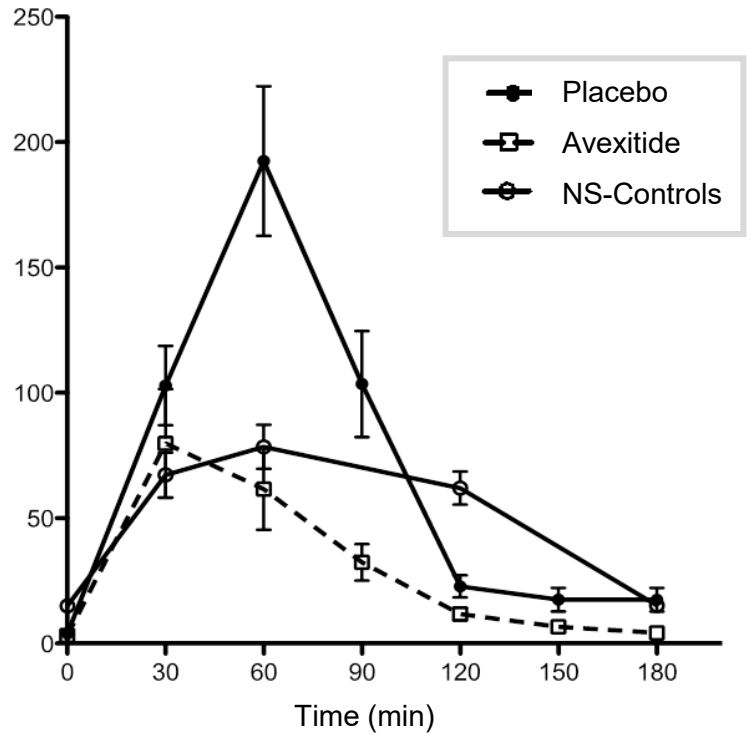


GLP-1=glucagon-like peptide-1; GSIS=glucose-stimulated insulin secretion; PBH=post-bariatric hypoglycemia; **1.** Goldfine A. B. et al. *J Clin Endocrinol Metab. 2007;* 92(12):4678–4685. doi.org/10.1210/jc.2007-0918. **2.** Cabrera O. et al. *The Journal of Biological Chemistry*. 2022;298(2):101484. doi:10.1016/j.jbc.2021.101484; **3.** Averaged data from five independent experiments; **4.** 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

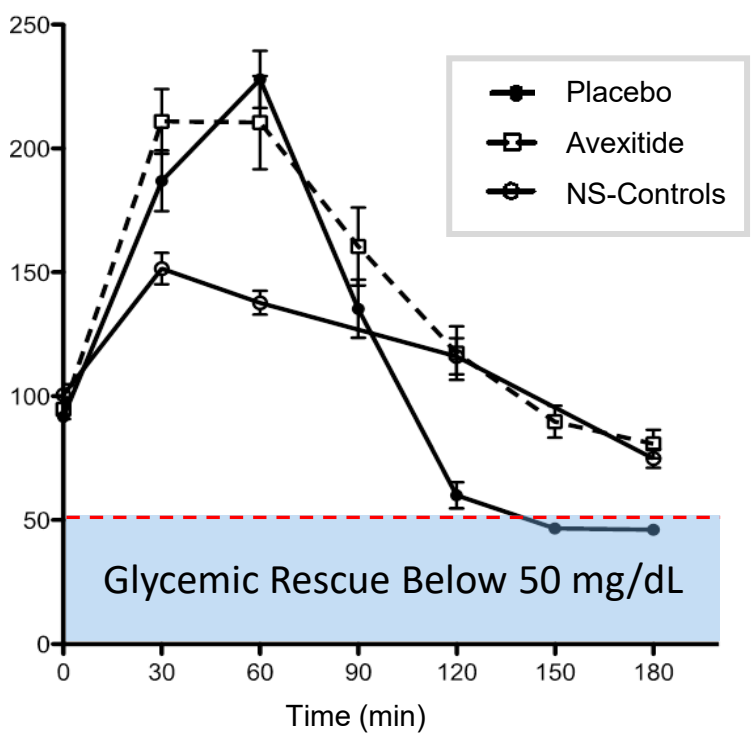
Insulin

(μU/mL, mean ± SEM)



Glucose

(mg/dL, mean ± SEM)

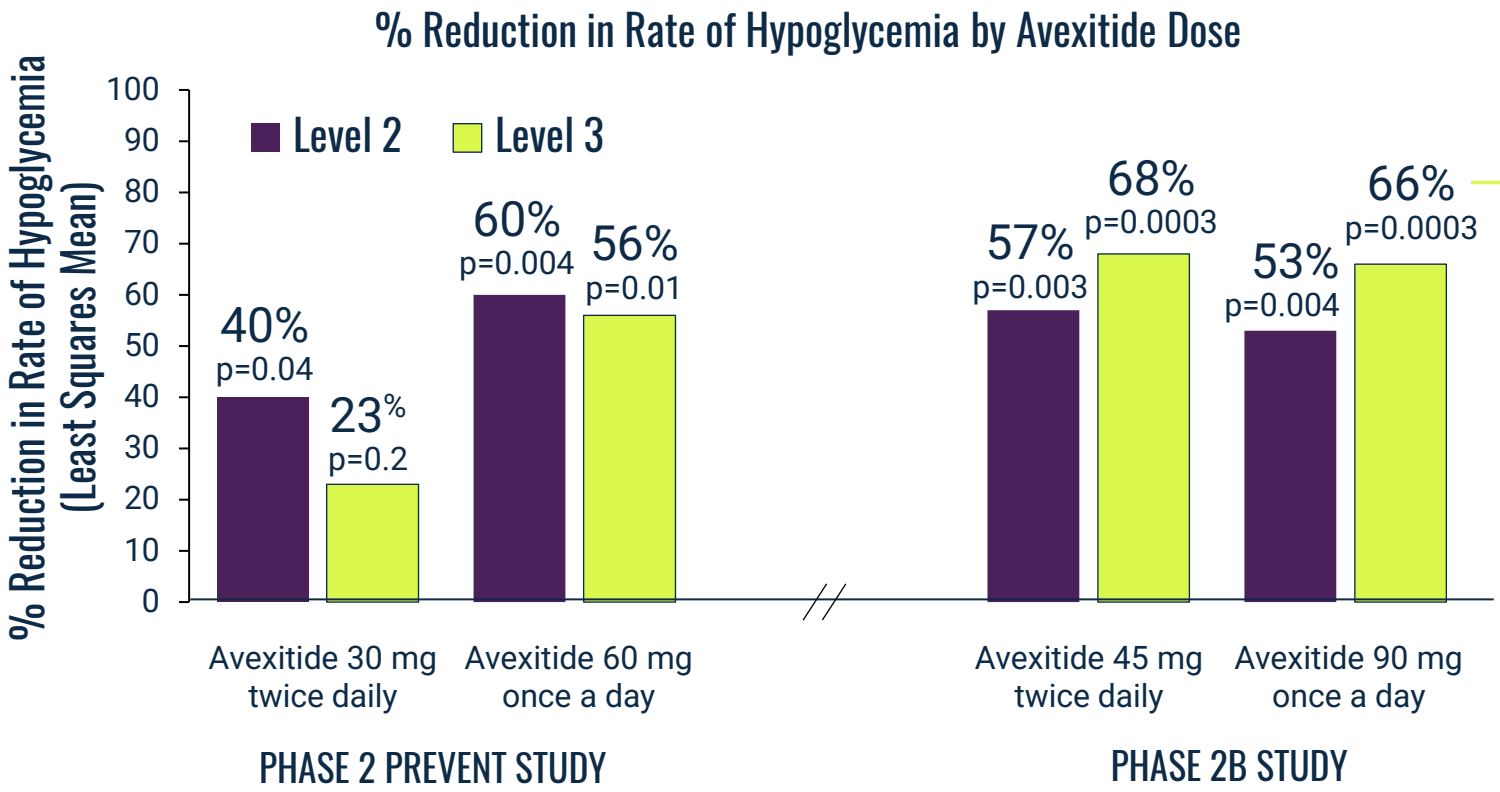


Proof of Concept in People with PBH (N=8) Demonstrated:

- 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; SEM=standard error of the mean; Craig et al. *Diabetologia* 2017.

Avexitide Significantly Reduced Rates of Hypoglycemia in Two Phase 2 Clinical Trials in PBH



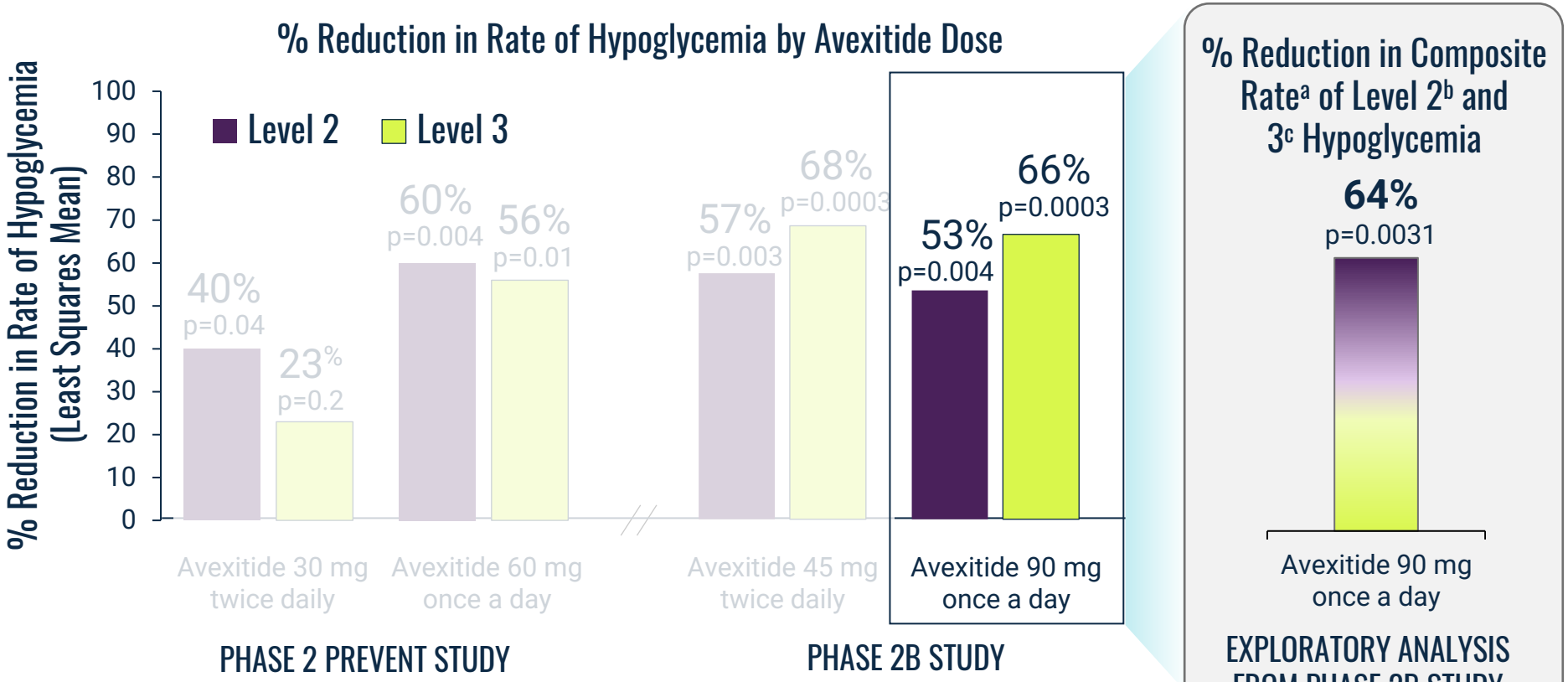
Avexitide cut rates of hypoglycemic events by

>50%

Treatment effect supported by consistent, dose-dependent effects across Phase 1, SAD, and MAD trials in PBH

MAD=multiple ascending dose; PBH=post-bariatric hypoglycemia; SAD=single ascending dose; **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 Significantly Reduced Rates of Composite Level 2 and 3 Hypoglycemia in Exploratory Analysis



FDA Breakthrough Therapy Designation

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

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

All dose regimens demonstrated consistent reductions in composite rate of Level 2 and Level 3 hypoglycemic events

ENDO 2025 PRESENTATION

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. [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.

Exploratory Analysis of Prior Trials Showed Statistically Significant Results Using the Phase 3 LUCIDITY Primary Endpoint Model

Table 1. Reduced Rates of Composite Level 2 and 3 Hypoglycemia in Phase 2 PREVENT Study[1]

	Screening Period (28 days) [2] n=17	Run-In Period (14 days) n=17	Placebo n=17	Avexitide 30 mg Twice Daily n=17	Avexitide 60 mg Daily n=17
Composite Weekly Rate of Level 2&3 Hypoglycemia					
Mean (SD)	1.37 (1.244)	2.19 (2.144)	1.47 (1.049)	0.89 (1.101)	0.66 (0.609)
Median	1.04	1.50	1.50	0.50	0.50
Rate Ratio *(over placebo of hypoglycemia during treatment period)* [3]					
LS Mean (SE)	N/A	N/A	N/A	0.61 (0.245)	0.45 (0.224)
95% CI	N/A	N/A	N/A	0.374, 1.003	0.288, 0.709
P-Value	N/A	N/A	N/A	0.0514	0.0009

Table 2. Reduced Rates of Composite Level 2 and 3 Hypoglycemia in Phase 2b Study

	Run-In Period N=16	Avexitide 45 mg Twice Daily N=16	Avexitide 90 mg Daily N=16
Composite Weekly Rate of Level 2&3 Hypoglycemia			
Mean (SD)	1.39 (1.908)	0.51 (0.719)	0.59 (1.604)
Median	0.93	0.25	0
Rate Ratio *(over run-in of hypoglycemia during treatment period)*			
LS Mean (SE)	N/A	0.38 (0.298)	0.36 (0.325)
95% CI	N/A	0.206, 0.687	0.187, 0.694
P-Value	N/A	0.0021	0.0031

Key Takeaways

- LUCIDITY model for Primary endpoint analysis (negative binomial regression) applied to PREVENT and Phase 2b datasets demonstrates significant reduction in composite of Level 2 and Level 3 hypoglycemia
- 90 mg once daily dose reduced weekly events from 1.39 to 0.59 (mean) and 0.93 to 0 (median) compared with run-in
- 90 mg once daily dose led to highly statistically 64% reduction in composite events (p=0.0031)
- LUCIDITY trial is estimated to be ≥90% powered to detect a 35% relative improvement over placebo even with up to a 50% placebo effect

1. Table 1 is updated from Poster SUN-627 at ENDO 2025 Annual Meeting (“ENDO Poster”).
2. ENDO Poster displayed this information as Run-in Period. The values represented event rate normalized to the 28-day Screening Period, including the 14-day Eligibility Run-In Period.
3. Updated model from ENDO Poster utilizing 14-day Run-In Period instead of the 28-day Screening Period for the run-in event rate covariate.

CONSISTENT RESULTS IN PBH CLINICAL TRIALS

Avexitide Reproducibly Improved Insulin and Glucose Responses 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 BID SC injection (n=5)	Avexitide 30 mg BID SC injection (N=17)[5]	Avexitide 60 mg QD 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)

BID=twice daily; IV=intravenous; MAD=multiple ascending dose; PBH=post-bariatric hypoglycemia; QD=once daily; 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 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 discontinuations	No participant discontinuations

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

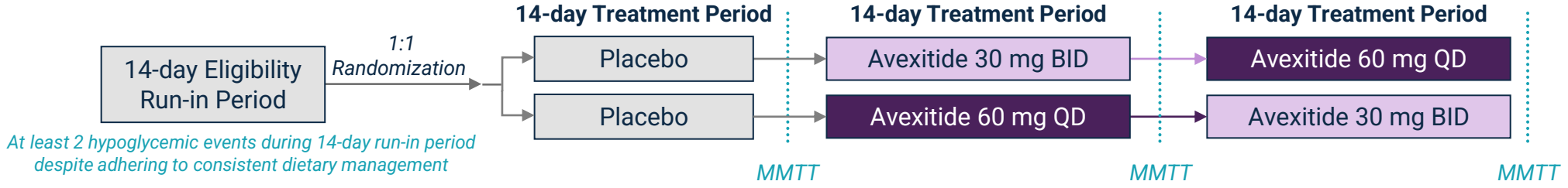
*Injection site reactions generally mild and transient with no grade 3 events or resulting discontinuations

AE=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.

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

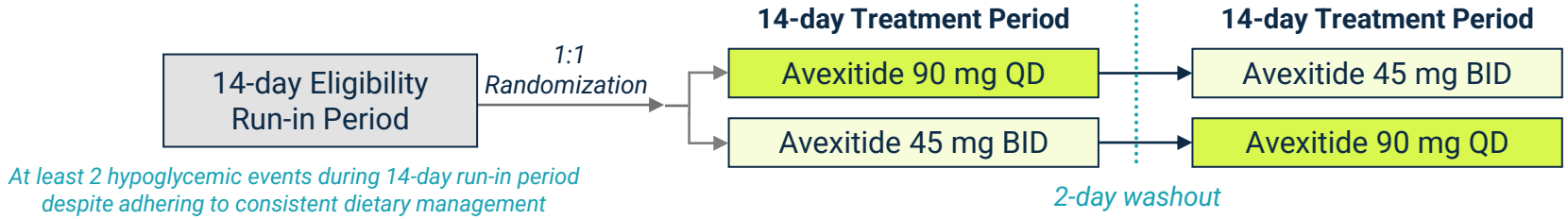
PHASE 2 PREVENT TRIAL DESIGN - 28-day, randomized, placebo-controlled crossover trial (N=18)

Participants enrolled had Roux-en-Y gastric bypass (RYGB)



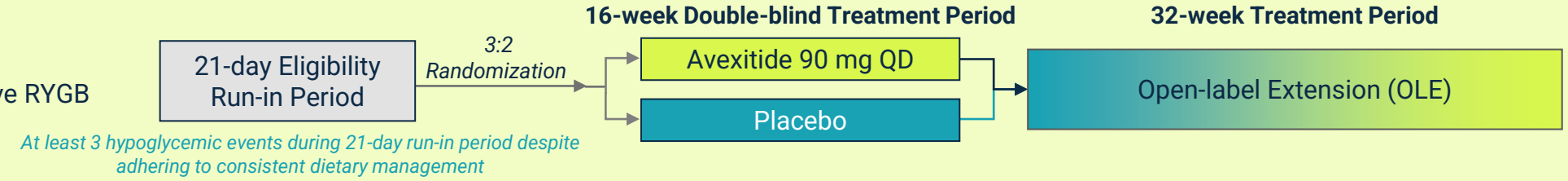
PHASE 2B TRIAL DESIGN - 28-day, open-label, investigator-initiated, crossover trial (N=16)

Participants enrolled had RYGB, vertical sleeve gastrectomy, esophagectomy, Nissen fundoplication, or gastrectomy



PHASE 3 LUCIDITY TRIAL DESIGN - Multicenter, randomized, double-blind, placebo-controlled trial (N=78)

Enrollment complete. Participants enrolled have RYGB



BID=twice daily; MMTT=mixed meal tolerance testing; PBH=post-bariatric hypoglycemia; QD=once daily.

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; PBH=post-bariatric hypoglycemia; QD=once daily; RYGB=Roux-en-Y gastric bypass; OLE=open-label extension.

Post-Bariatric Hypoglycemia (PBH) is Believed to be Caused by Excessive GLP-1 Response that Leads to Hyperinsulinemic Hypoglycemia Post-Meal

Hypoglycemia from PBH is Often Dangerous and Life-Altering

- General fatigue, confusion, difficulty speaking, blurred vision
- Risk of falls, seizures, vehicle accidents
- Job and income loss

~160,000 people

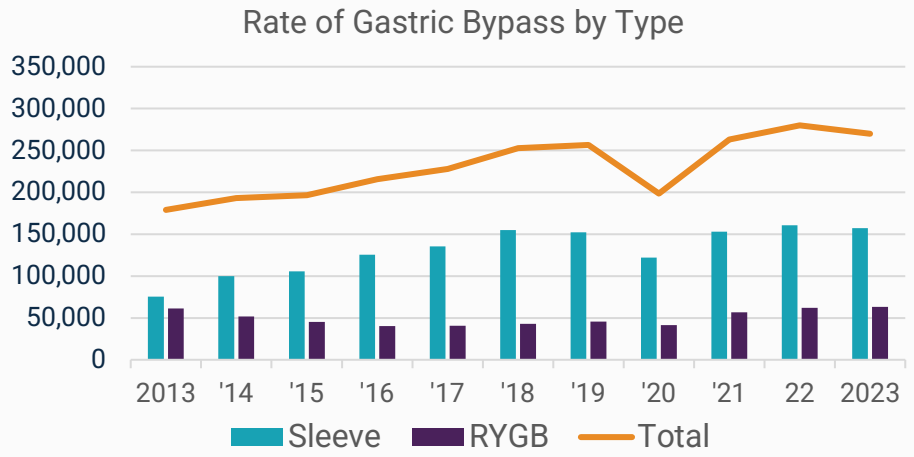
Currently living with PBH in the U.S.[1-3]

No approved treatment options

~200K new procedures

occur annually[1]

PBH develops on average 1-3 years post surgery



BETWEEN 2013-2023

Sleeve.....~1.4 million

RYGB.....~0.6 Million

Total.....~2.5 Million

LIVING WITH PBH

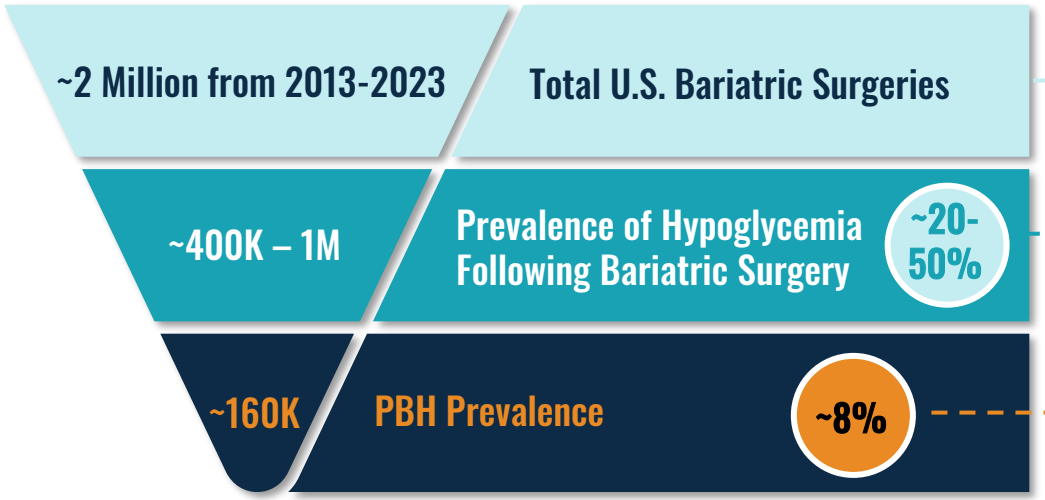
"It affected my ability to work and take care of my family."

"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."

PBH=post-bariatric hypoglycemia; RYGB=Roux-en-Y gastric bypass; **1.** Estimate of Bariatric Surgery Numbers, 2013-2023. American Society for Metabolic and Bariatric Surgery (ASMBS). Accessed May 6, 2026. **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.

~160K People Live With PBH in U.S.



Source	Finding
ASMBS Registry of Bariatric Surgery[1a]	2.5M bariatric surgeries of which 2M were either sleeve gastrectomy (SG) or Roux-en-Y gastric bypass (RYGB)
8-Study Meta-Analysis (N=280)[2]	56.1% prevalence of hypoglycemia in studies specifically examining RYGB and 54.3% in those examining SG
Prospective, Longitudinal Cohort (N=1,448)[3]	43.2% prevalence of post-RYGB hypoglycemia symptoms
Prospective 1-Year Study (N=186)[4]	32.8% of participants had at least one OGTT (oral glucose tolerance test)-related hypoglycemic event after laparoscopic sleeve gastrectomy
Prospective 2-Year Study (N=281)[5]	32.6% showed post-challenge hypoglycemia after RYGB; 22.6% after SG
Retrospective Survey (N=341)[6]	29% with new-onset hypoglycemia symptoms post-RYGB or SG
Retrospective Study (N=120)[7]	Of 107 individuals with PBH treated with acarbose, 37% had persistent/unacceptable frequency of hypoglycemic events [**Note**: Equates to ~8-16% of total bariatric surgery population[b]]
Retrospective Study (N=1,206)[8]	13.1% met criteria for PBH 5 years post-op and 5% of those with PBH had severe symptoms[c]
Prospective, Longitudinal Cohort (N=177)[9]	7.9% met criteria for PBH 5-years post-RYGB
Prospective, Longitudinal Cohort (N=1,448)[3]	Symptoms of PBH requiring hospitalization or ER visit occurred in 2.6-3.6% of people who underwent RYGB after 5 years

Additional Corroborating Data

1

Preliminary data from multiple industry-leading medical claims providers align with current literature understanding of ~160K prevalent population[10]

2

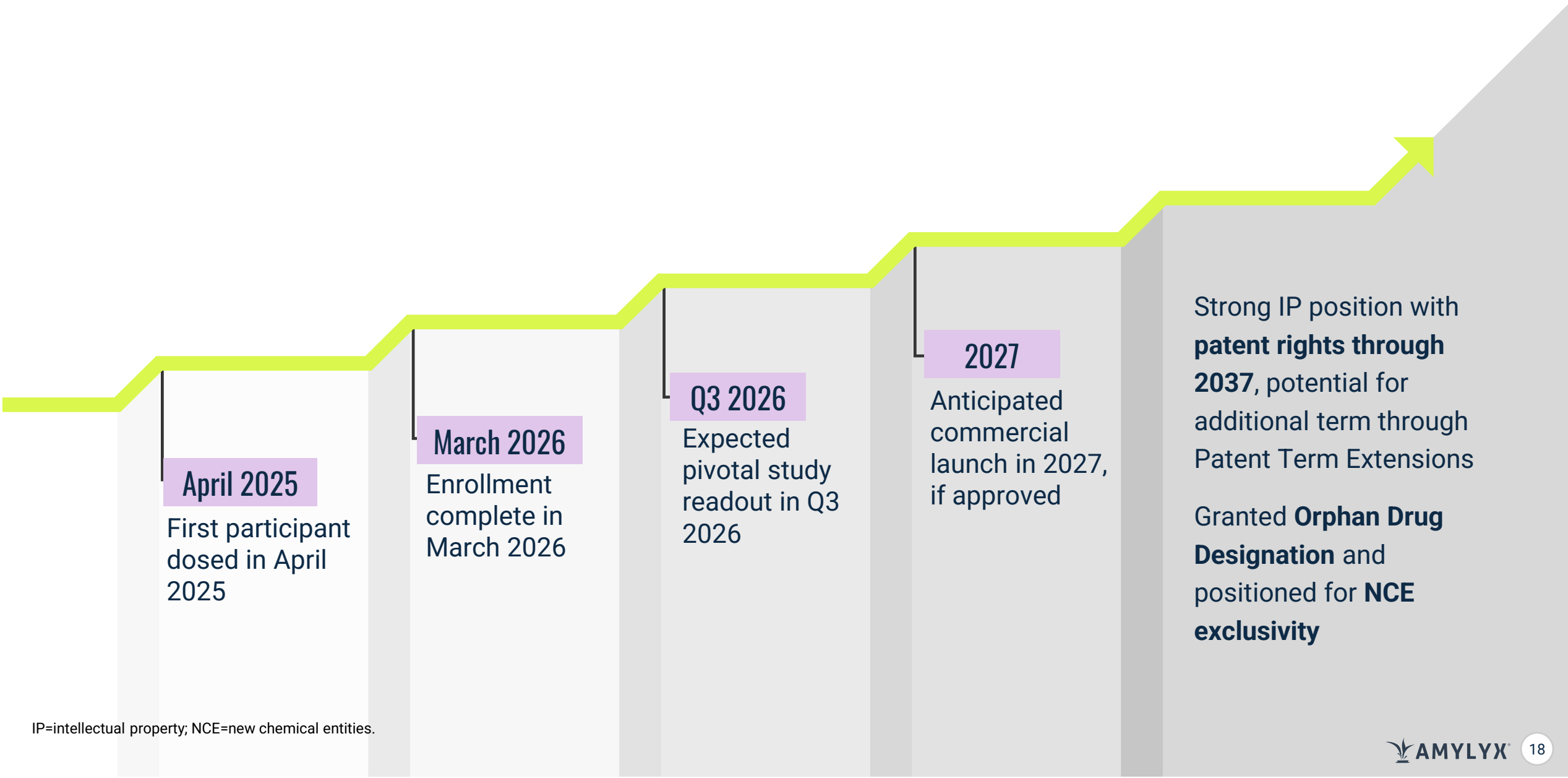
Data from a Recent Academic Review[12d]:

	Incidence		Prevalence		
	RYGB	SG	RYGB	SG	Total
Any PBH • *>3 hypoglycemia symptoms* • *Neuroglycopenia* • *Need for assistance* ***or*** • *Glucose ≤54 mg/Dl*	27.3%	10.3%	275,717	111,370	387,087
Medically-Important PBH *Visit to inpatient or outpatient facility*	11.8%	4.4%	118,843	48,026	**166,869**

[a]The ASMBS total bariatric procedure numbers are based on the best estimation from available data (BOLD,ACS/MBSAQIP, National Inpatient Sample Data and outpatient estimations) [b] Assumes 20-40% post-surgical hypoglycemic symptom prevalence; [c]Severe symptoms defined as glucose <40 mg/dL or emergency room/hospital visit; [d]Analysis incorporated historical census data dating back to 1993, life expectancy estimates, and disease-state modeling to inform projections

1. Estimate of Bariatric Surgery Numbers, 2013-2023. American Society for Metabolic and Bariatric Surgery (ASMBS). Accessed May 6, 2026. **2.** Lupoli R, et al. *Nutr Metab Cardiovasc Dis.* 2022;32(1):32-39. **3.** Fischer LE, et al. *Surg Obes Relat Dis.*2021;17(10):1787-1798. **4.** Belilgoli A, et al. *Obes Surg.* 2017;27:3179-3186 797-802.**5.** Brix JM, et al. *Obes Facts.* 2019;12:397-406. **6.** Lee CJ, et al. *Surg Obes and Relat Dis*. 2018;14(6):797-802. **7.** de Heide LJM, et al. *Diabetes Obes Metab*.2023;25:735-747.**8.** Lee CJ, et al. *Obesity*.2016.24(6):1342-1348. **9.** Raverdy V, et al. *Annals Surg.* 2016.264(5):878-885.**10.** Data on file. **11.** Hazelhurst J, et al. *Endocr Connect.* 2024;13(5):e230285. **12.** McLaughlin, T et al. (2025, July 12-15). *Prevalence of Post-bariatric Hypoglycemia in the United States*, [Poster presentation]. ENDO 2025.

Phase 3 LUCIDITY Trial Underway, Readout Expected in Q3 2026



IP=intellectual property; NCE=new chemical entities.

Raquel, a college student and martial artist living with Wolfram syndrome.

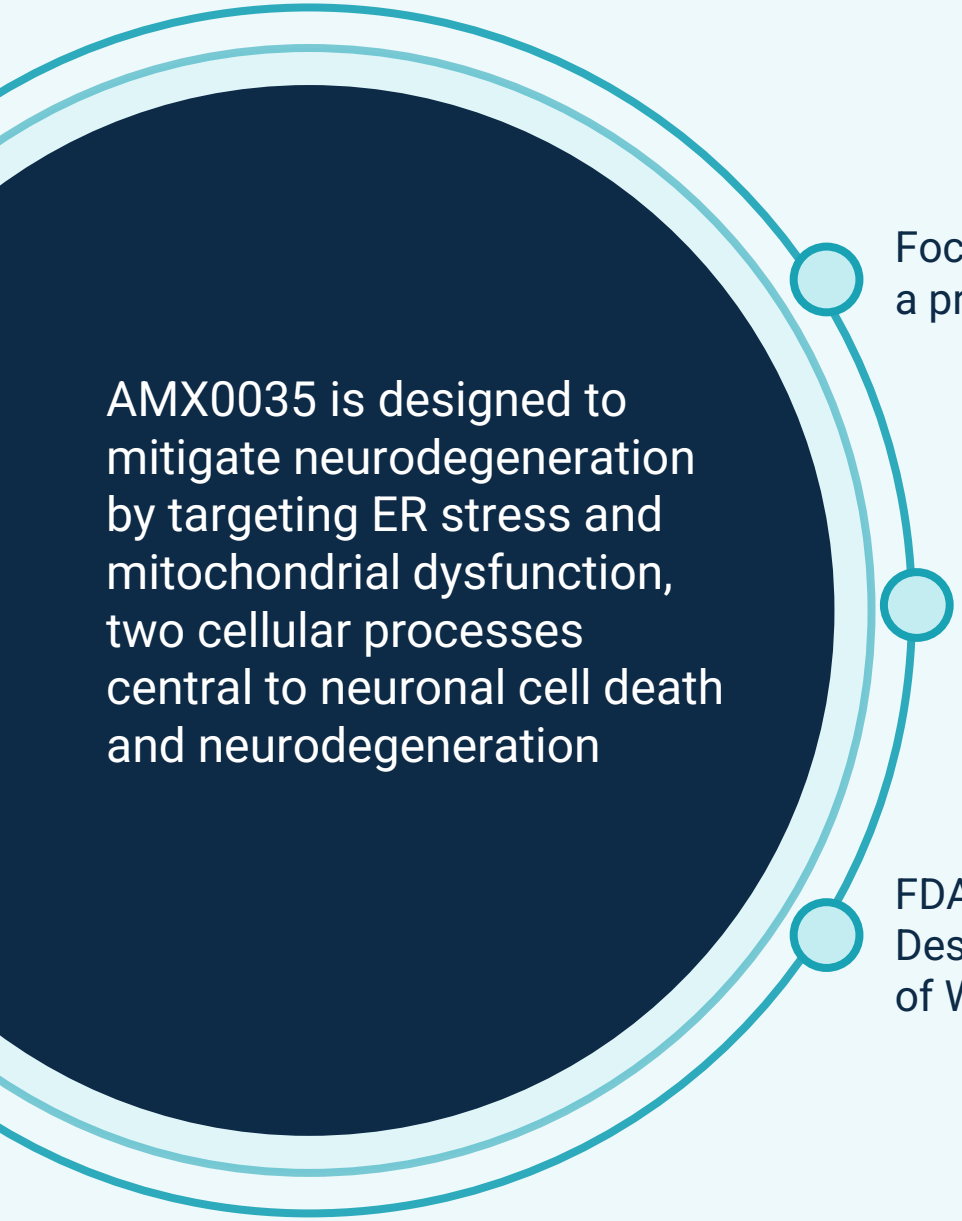
Retinal ganglion cells

AMX0035

Fixed-Dose Combination of Sodium Phenylbutyrate and Taurursodiol Designed to Slow or Mitigate Neurodegeneration

HELIOS

AMX0035 for the Potential Treatment of Wolfram Syndrome



- Focused on studying AMX0035 in Wolfram syndrome, a prototypical ER stress disorder
- Primary efficacy outcome of improvement in pancreatic function at Week 24 met in Phase 2 HELIOS trial; treatment with AMX0035 from Week 24 to Week 48 showed continued stabilization or improvement in multiple outcomes related to disease progression, including pancreatic function, glycemic control, vision, and overall symptom burden
- FDA Orphan drug designation and EU Orphan Drug Designation granted to AMX0035 for the treatment of Wolfram syndrome

ER=endoplasmic reticulum.

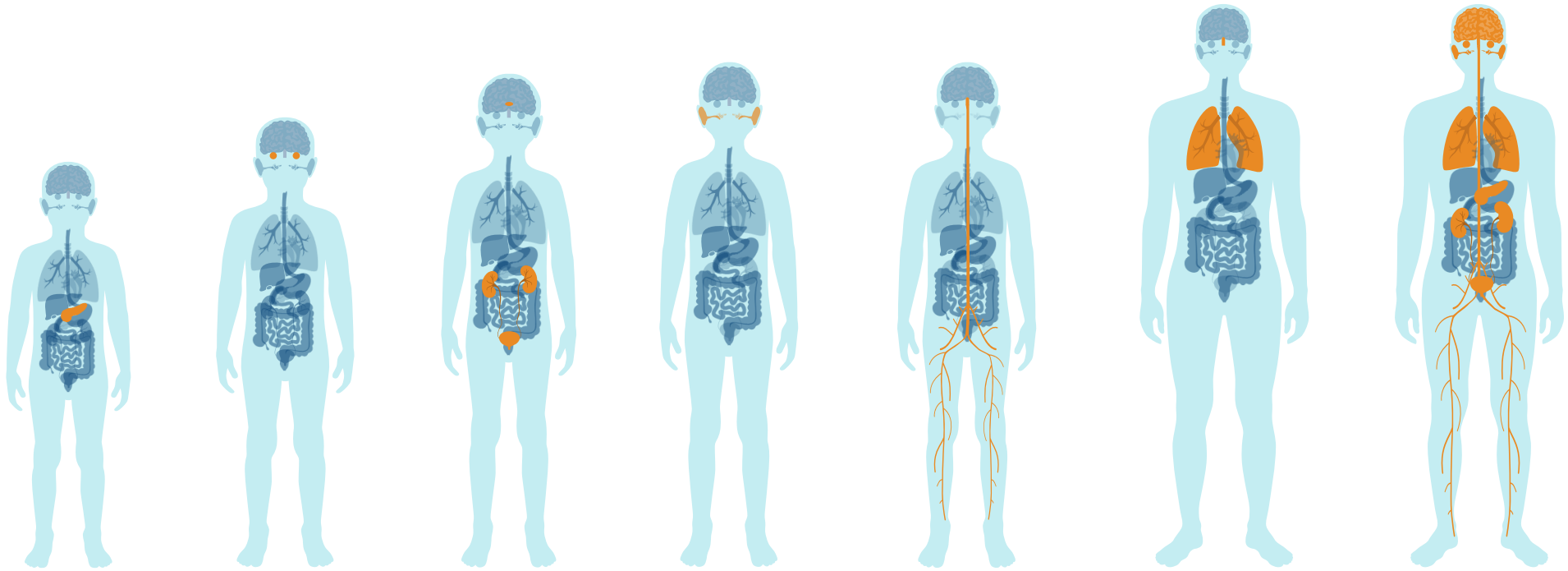
Wolfram Syndrome is a Rare, Fatal, Monogenic, Progressive Disorder[1-5]

WFS1 GENE MUTATION → PROGRESSIVELY IMPACTS MULTIPLE ORGANS AND SYSTEMS[1-5]

~3,000 people

Living with Wolfram Syndrome in the U.S.[1,2]

No approved therapies for Wolfram syndrome[6]



Childhood-onset Diabetes Mellitus
Elevated blood sugar levels from insulin-producing beta cell death

Gradual Loss of Vision Leading to Blindness
Optic nerve cell death

Diabetes Insipidus
Kidneys produce too much urine from a faulty pituitary gland

Hearing Loss
From cranial nerve damage

Balance and Coordination Difficulty
Ataxia from cerebellum damage

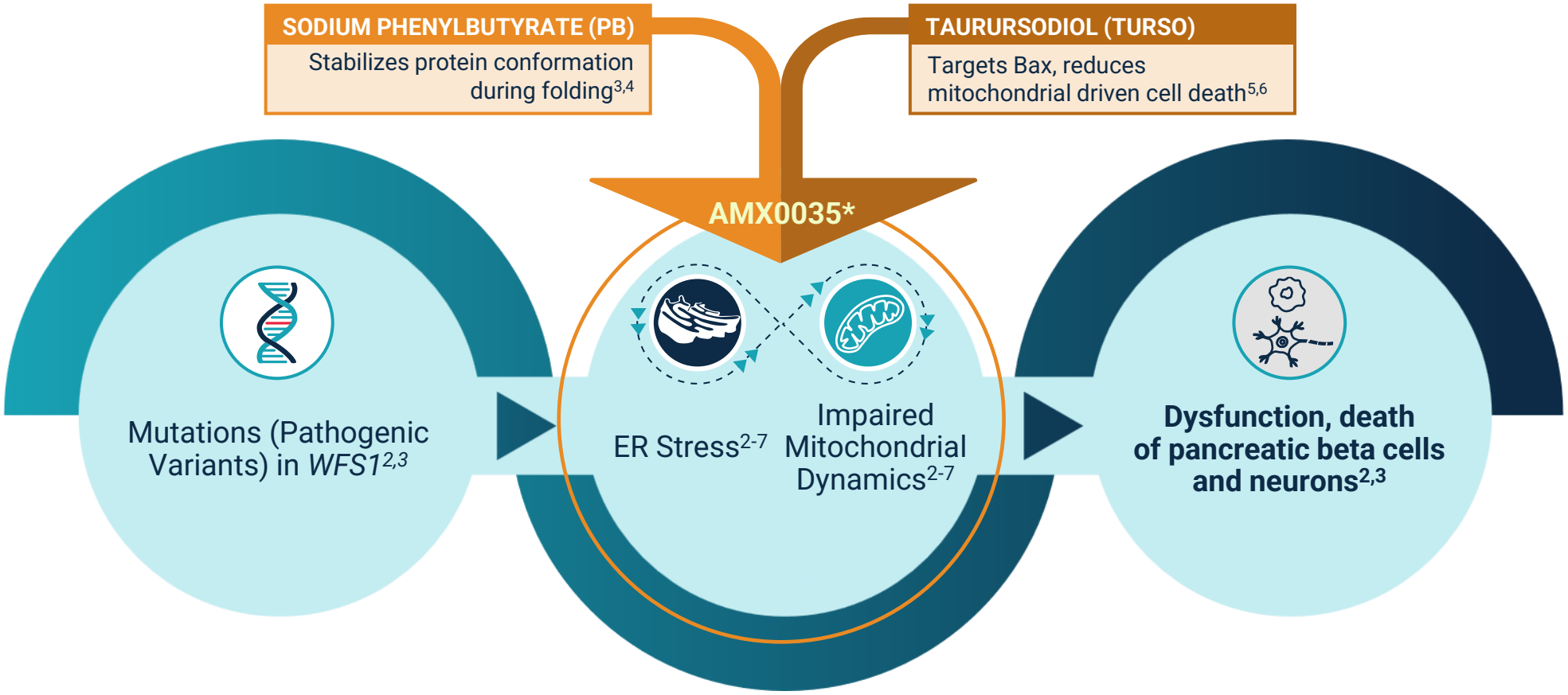
Difficulty Breathing
From brain stem damage

Death occurs at a median age of 30 years (range 25-49 years), **mainly from respiratory failure**

WFS1=Wolfram syndrome type 1 gene; **1.** Urano, F. *Diabetes*. 2014;63(3):844-846. **2.** Pallotta MT, et al. *J Transl Med*. 2019;17:238. **3.** Lee, E., et al. *Front Genet*. 2023;14:1198171. **4.** Leslie, M. *Science*. 2021;371(6530):663-665. **5.** Matsunage et al. *Plos One*. 2014;9(9):106906. **6.** Urano, F. *Curr Diab Rep*. 2016;16(1):6.

Wolfram Syndrome is a Prototypical Endoplasmic Reticulum (ER) Stress Disorder[1]

AMX0035 targets ER stress and related mitochondrial dysfunction pathways



Clear Link of Mechanism of Disease and Mechanism of AMX0035

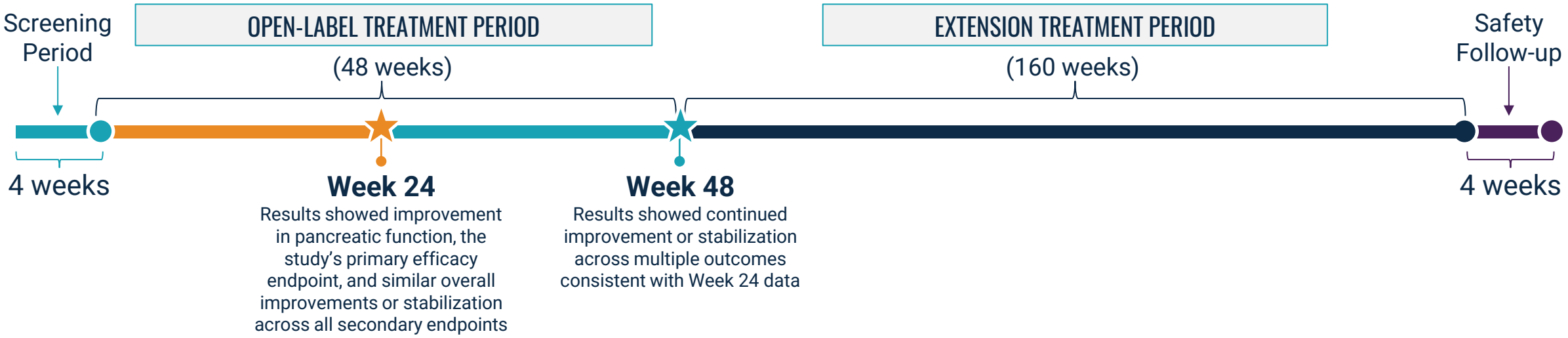
JCI insight

AMX0035 has been extensively studied in Wolfram models including patient-derived cells and mouse model

WFS1=Wolfram syndrome type 1 gene; * Results for AMX0035 are synergistic relative to PB or TURSO alone. Supported by data on file with Amylyx & Cohen. J., et al. Clinical trial design for a phase II, randomized, placebo-controlled trial of AMX0035 in amyotrophic lateral sclerosis (CENTAUR). Poster presented at: 28th International Symposium for ALS/MND; December 4–10, 2017; Boston, MA; **1.** Urano, F. *Diabetes*. 2014;63(3):844-846. **2.** Sarmara A, et al. Orphanet J Rare Dis. 2019; 14(1):279. **3.** Pallotta MT, et al. *J Transl Med*. 2019;7(1):238-249. **4.** Shang L, et al. *Diabetes*. 2014;63(3):923-933. **5.** Zhou W. *J Biol Chem*. 2011;286(17):14941-14951. **6.** Rodrigues CM, Steer CJ. *Expert Opin Investig Drugs*. 2001;10(7):1243-1253. **7.** Mishra R, et al. *Ther Adv Rare Dis*. 2021:2:26330040211039518.

HELIOS Study Design

Open-label, single-arm clinical trial of AMX0035 in people with Wolfram syndrome, enrolling up to 12 participants



PRIMARY OBJECTIVES

- To assess the safety and tolerability of AMX0035 administered orally for up to 208 weeks
- To evaluate the effect of AMX0035 on residual beta cell function over 24 weeks by monitoring C-peptide levels

KEY TRIAL ENTRY CRITERIA[1,2]

- Aged ≥17 years
- Definite diagnosis of Wolfram syndrome defined by documented pathogenic mutations in *WFS1* gene*
- Stimulated C-peptide level of ≥0.2 ng/mL at screening
- Insulin-dependent diabetes mellitus due to Wolfram syndrome
- No current GLP-1 agonist use

GLP-1=glucagon-like peptide-1; *WFS1*=Wolfram syndrome type 1 gene; *Documented functionally relevant recessive mutations on both alleles of the *WFS1* gene based on historical test results (if available) or from a qualified laboratory at screening; **1.** ClinicalTrials.gov identifier: NCT05676034. Updated November 21, 2023. Accessed April 9, 2024. https://www.clinicaltrials.gov/ct2/show/NCT05676034.
2. Urano, F. et al. (2025, May 10-13). *48-Week Results from the HELIOS Trial: A Phase 2, Open-Label Study Evaluating an Oral, Fixed-Dose Combination of Sodium Phenylbutyrate and Taurursodiol in Wolfram Syndrome* [Poster presentation]. Joint Congress of ESPE and ESE 2025.

Long-Term Data Suggest Potential Benefit of AMX0035 in Wolfram Syndrome Across Multiple Outcomes Related to Disease Progression

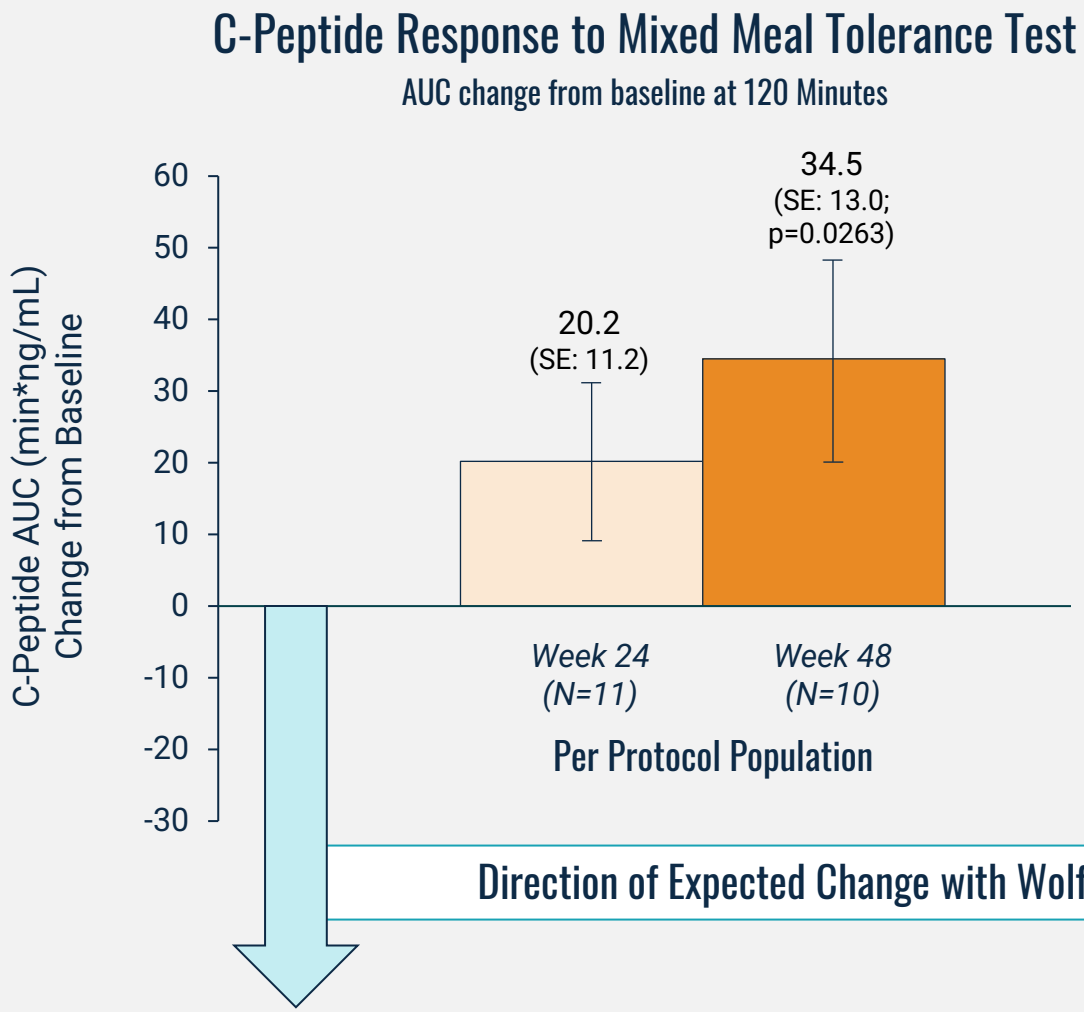
HELIOS

	Expected Progression of Wolfram Syndrome	Trend Baseline to Week 24	Trend Baseline to Week 48	
C-Peptide Response AUC	↓ Progressive Decline	↑ Partial Reversal in C-Peptide Phenotype	↑ Partial Reversal in C-Peptide Phenotype	Diabetic Measures
Δ C-Peptide	↓ Progressive Decline[1]	↑ Increase in Beta Cell Responsiveness	↑ Increase in Beta Cell Responsiveness	
HbA1c	Progressively More Difficult to Maintain[2]	↓ Improved Glycemic Control	↓ Improved Glycemic Control	
Time in Target Glucose Range (70-180 mg/dL)	Progressively More Difficult to Maintain	↑ Improved Glycemic Control	↑ Improved Glycemic Control	
Visual Acuity	↓ Progressive Decline[3]	↑ Improved or Stable Acuity	↑ Improved or Stable Acuity	Visual Measure
CGI-C and PGI-C	↓ Progressive Decline	↑ Participant and Clinician Reported Improvement or Stabilization	↑ Participant and Clinician Reported Improvement or Stabilization	Symptom Burden
		Safety Profile was Consistent with Prior Safety Data[4]	Safety Profile was Consistent with Prior Safety Data[4]	

AUC=area under the curve; CGI-C=clinician-reported global impression of change ; HbA1c=glycated hemoglobin A1c; PGI-C=patient-reported global impression of change; Urano, F. et al. (2025, May 10-13). *48-Week Results from the HELIOS Trial: A Phase 2, Open-Label Study Evaluating an Oral, Fixed-Dose Combination of Sodium Phenylbutyrate and Taurursodiol in Wolfram Syndrome* [Poster presentation]. Joint Congress of ESPE and ESE 2025. **1.** Recent natural history study demonstrated C-peptide levels progressively decline in people with Wolfram syndrome. **2.** Recent natural history study demonstrated that average HbA1c increases and time in target glucose range declines in people with Wolfram syndrome. **3.** Recent natural history study demonstrated visual acuity progressively worsens in people with Wolfram syndrome. **4.** AMX0035 was generally well-tolerated. All adverse events (AEs) were mild or moderate, and there were no serious AEs related to AMX0035 treatment.

Primary Endpoint: Improvement in C-Peptide Response Observed

Overall increase in mean C-peptide production from 0-120 minutes during MMTT*



Improvement in C-Peptide Response Observed Compared to Screening

WS NATURAL HISTORY EXPECTATIONS:
C-peptide progressively **decreases**

JOINT CONGRESS OF

ESPE European Society for Paediatric Endocrinology

European Society of Endocrinology The voice for endocrinology

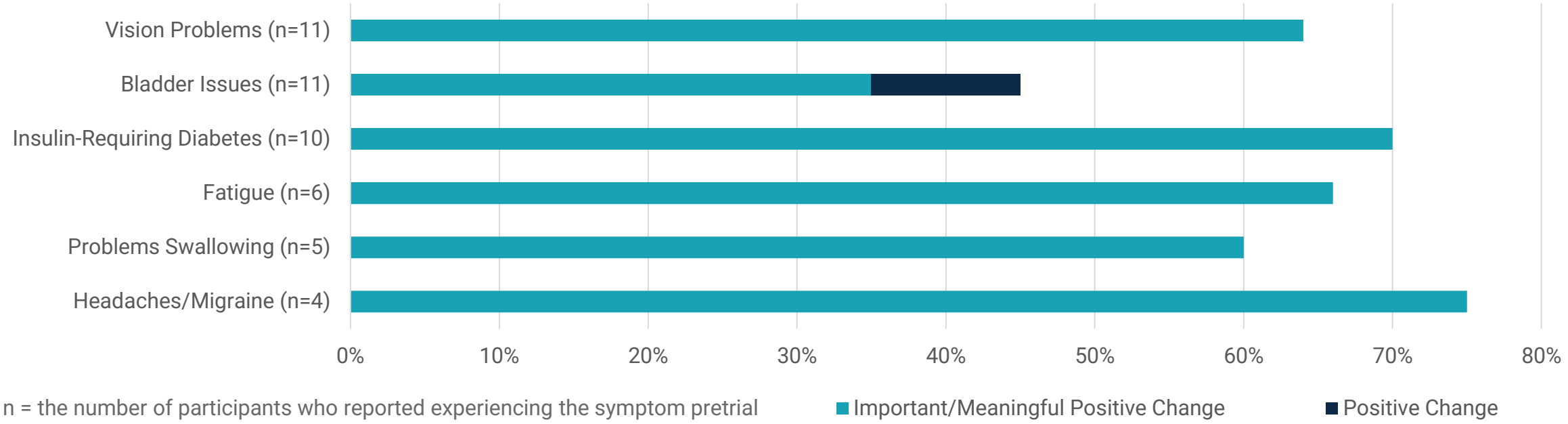
48-Week Results from the HELIOS Trial: A Phase 2, Open-Label Study Evaluating an Oral, Fixed-Dose Combination of Sodium Phenylbutyrate and Taurursodiol in Wolfram Syndrome

*In non-diabetic individuals, C-peptide peaks after a meal at approximately ~30 minutes; in Wolfram syndrome, peak is slower but generally was at or before 120 minutes in HELIOS. AUC over 120 minutes after meal challenge reflects beta cell response to a meal. Amylyx is currently planning to focus on 120-min AUC as the C-peptide measure for future studies. AUC=Area under the curve; ITT=Intent to Treat; Min=Minute; MMTT=mixed meal tolerance testing; ng/mL=Nanograms per milliliter; SE=Standard error; WS=Wolfram syndrome; Urano, F. et al. (2025, May 10-13). *48-Week Results from the HELIOS Trial: A Phase 2, Open-Label Study Evaluating an Oral, Fixed-Dose Combination of Sodium Phenylbutyrate and Taurursodiol in Wolfram Syndrome* [Poster presentation]. Joint Congress of ESPE and ESE 2025.

AMX0035 Reduced Overall Symptom Burden at Week 24 and Week 48

Qualitative on-study interview results support potential positive impact of AMX0035 on symptom burden

Positive Changes in Wolfram Syndrome-Related Symptoms by Participant Report in On-Study Interviews



In on-study interviews after at least 24 weeks of treatment, 9 of 11 participants reported improvements in ≥1 Wolfram syndrome-related symptom with all noting the change being meaningful in at least one symptom

Data on File. Urano, F. et al. (2025, May 10-13). *48-Week Results from the HELIOS Trial: A Phase 2, Open-Label Study Evaluating an Oral, Fixed-Dose Combination of Sodium Phenylbutyrate and Taurursodiol in Wolfram Syndrome* [Poster presentation]. Joint Congress of ESPE and ESE 2025.

AMX0035 Safety and Tolerability in HELIOS

- AMX0035 was **generally well tolerated**
  - > Diarrhea was the most common TEAE (58.3%); all cases were of mild severity
  - > All TEAEs were graded mild or moderate
- **No new safety signals** were identified
- Nearly all participants reported ≥1 TEAE during the trial
  - > Most did not lead to modification or interruption of AMX0035 dosing and **none led to drug discontinuation**

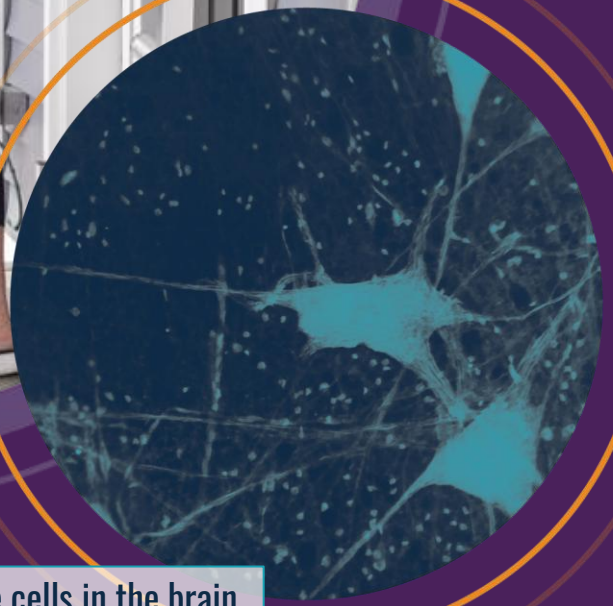
Summary of Treatment Emergent Adverse Events (TEAEs)

	AMX0035 (N=12)* n (%)
Participants with ≥1 TEAE	11 (91.7)
TEAE related to study drug**	10 (83.3)
Serious adverse events	0 (0)
Drug interrupted owing to TEAE	3 (25.0)
Dose reduced owing to TEAE	3 (25.0)
Drug discontinued owing to TEAE	0 (0)

*All available safety data as of January 10, 2025 included
**Includes those with TEAEs considered at least possibly related to treatment

Urano, F. et al. (2025, May 10-13). *48-Week Results from the HELIOS Trial: A Phase 2, Open-Label Study Evaluating an Oral, Fixed-Dose Combination of Sodium Phenylbutyrate and Taurursodiol in Wolfram Syndrome* [Poster presentation]. Joint Congress of ESPE and ESE 2025.

In memory of Mick, a husband and father, who was a gifted tattoo artist and musician.



Nerve cells in the brain

AMX0114

Potent Antisense Oligonucleotide (ASO) Targeting Calpain-2

AMX0114: Antisense Oligonucleotide (ASO) Targeting Knockdown of Calpain-2 for the Potential Treatment of ALS

- ALS leads to deteriorating muscle function, inability to move and speak, respiratory paralysis, and death[1,2]
- ALS affects as many as 30,000 adults in the U.S.[3]
  - >90% of people have no family history of disease
- Calpain-2 (*CAPN2*), a protein involved in neurofilament biology, plays an essential role in axonal degeneration, a critical effector in the progression of ALS
- In preclinical studies, treatment with AMX0114 resulted in potent, dose-dependent, and durable reduction in *CAPN2* mRNA and calpain-2 protein levels in disease-relevant cell models of axonal degeneration
- Phase 1 LUMINA trial will evaluate the safety and biological activity of AMX0114 in people living with ALS
- Early data from LUMINA show AMX0114 was generally well-tolerated for participants enrolled in Cohort 1 (n=12), with no treatment-related SAEs
- The FDA granted Fast Track Designation to AMX0114 in May 2025 providing eligibility for Priority Review if relevant criteria continue to be met

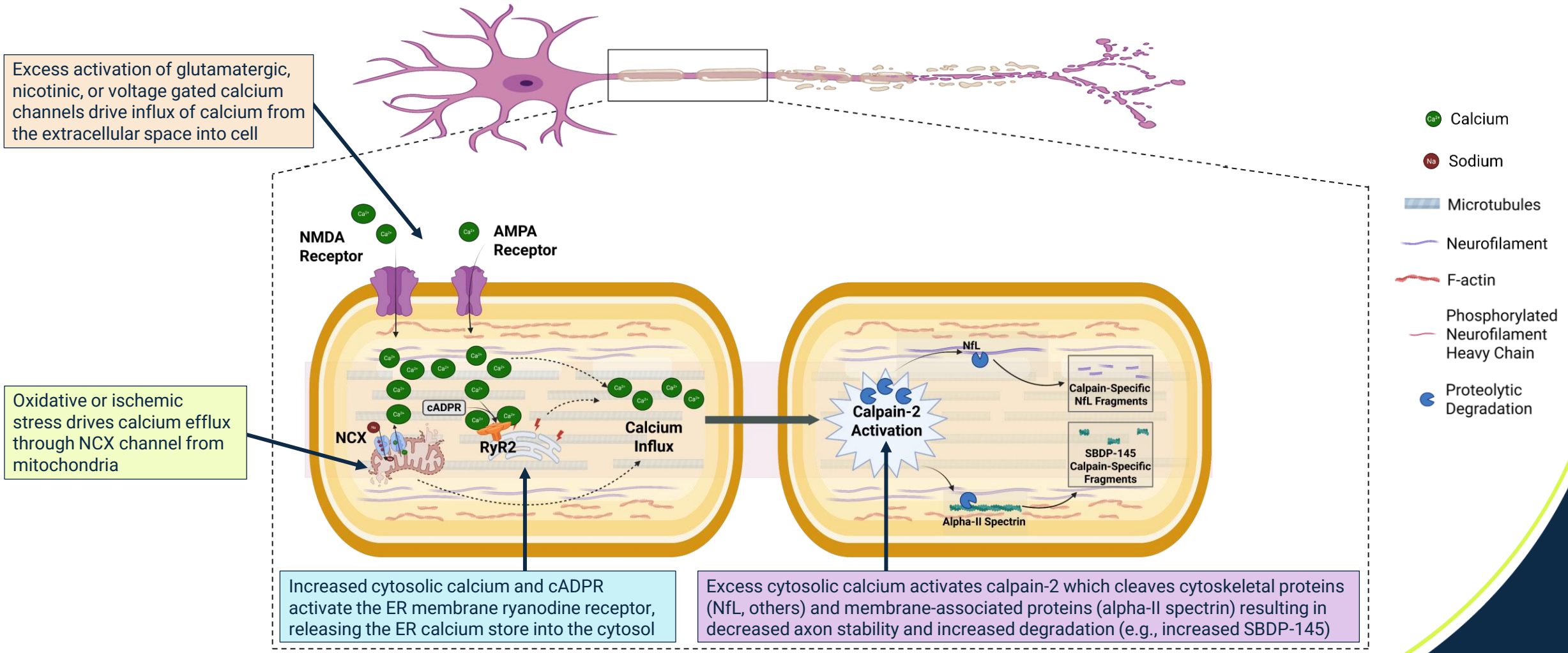
EXPECTED MILESTONES

September 2025 (Complete)	Fully enrolled Cohort 1 (n=12) of the Phase 1 LUMINA trial
December 2025 (Complete)	Early safety and tolerability data presented at medical meeting; began enrolling Cohort 2 (n=12) in Canada
March 2026 (Complete)	Fully enrolled Cohort 2 (n=12)
1H 2026	Present Cohort 1 biomarker data at a medical meeting

ALS=amyotrophic lateral sclerosis; mRNA=messenger ribonucleic acid; SAE=serious adverse event; **1.** Brown, R. H., Al-Chalabi A. *N Engl J Med*. 2017;377(2):162-172; **2.** Al-Chalabi, A., et al. *Lancet Neurol*. 2016;15(11):1182-1194; **3.** Mehta, P., et al. *Amyotroph Lateral Scler Frontotemporal Degener*. 2023:1-7. doi: 10.1080/21678421.2023.2245858.

Axonal Degeneration Disrupts Neural Connectivity and is a Key Early Contributor to the Pathogenesis of ALS

Mechanisms of Axonal Degeneration



AMPA=α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid; cADPR=cyclic adenosine diphosphate ribose; ER=endoplasmic reticulum; NCX=sodium-calcium exchanger; NfL=neurofilament light chain; NMDA=N-methyl-D-aspartate; RyR2=ryanodine receptor 2; SBDP-145=alpha-II spectrin breakdown product 145 kDa; Created in BioRender. Fontaine, R. (2026).

Calpain-2, a Protein Involved in Neurofilament Biology, Plays an Essential Role in Axonal Degeneration, a Critical Effector in the Progression of ALS

Evidence for Targeting Calpain-2 in ALS[1-4]

Multiple injury paradigms and hypotheses of axonal degeneration converge on calpain-2

- Calpain-2 levels are elevated in people with ALS
- Calpain-2 inhibition increases overall survival and delays disease onset in ALS mouse model
- Calpain-2 substrates include neurofilament and TDP-43
- AMX0114 has shown efficacy in preclinical ALS models

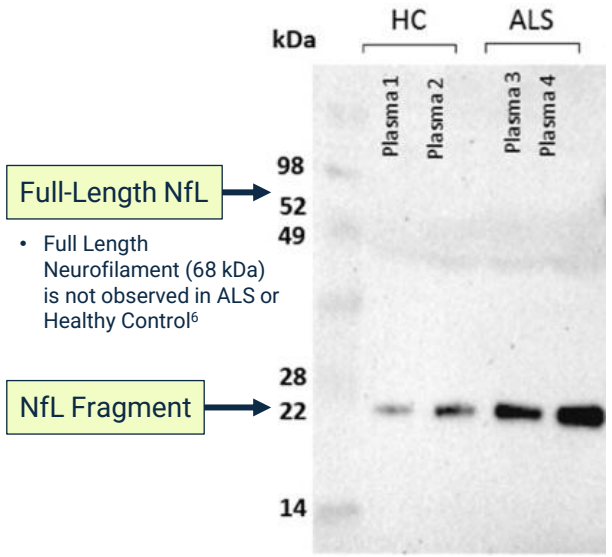
Genetic Support for Calpain-2 as a Target

Calpain-2 genetic variant found to be associated with ALS

~30K data set

(~20K with ALS / ~10K controls)[7]

NfL is Cleaved by Calpain-2, with Increased NfL Fragments Seen in ALS

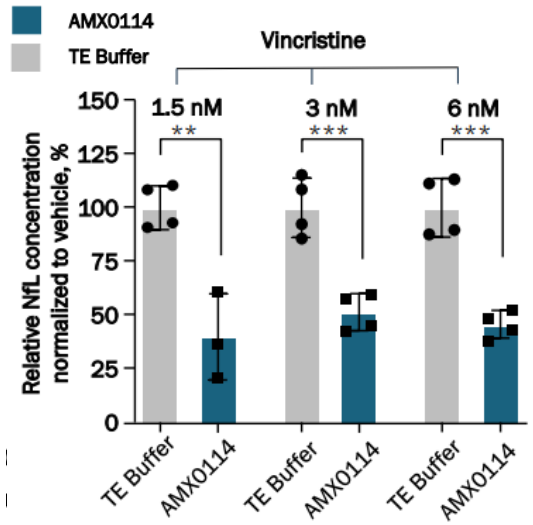


- Full Length Neurofilament (68 kDa) is not observed in ALS or Healthy Control[6]

ALS=amyotrophic lateral sclerosis; **1.** Ueyama H et al. *J Neurol Sci*. 1998;155(2):163-169. **2.** Yamashita T et al. *Nat Commun*. 2012;3:1307. **3.** Rao MV, et al. *J Neurochem*. 2016;137(2):253-65. **4.** Ma M, et al. *Neurobiol Dis*. 2013;56:34-46. **5.** Asakawa, K., Handa, H., Kawakami, K. Multi-phaseted problems of TDP-43 in selective neuronal vulnerability in ALS. *Cell Mol Life Sci*. 2021;78(10):4453-4465. doi:10.1007/s00018-021-03792-z **6.** Lombardi, V., Carassiti, D., Giovannoni, G. *et al. Sci Rep* 10, 97 (2020). doi:10.1038/s41598-019-54310-y; **7.** Hop et al. *Nat Genet* (2026). doi:10.1038/s41588-026-02535-9.

AMX0114 Reduces Extracellular NfL Levels in Multiple Models of Trigger-Induced Neuronal Injury and Improves Survival in Relevant Models

Pretreatment with AMX0114 Reduces Extracellular NfL in Vincristine Treated Neurons



Similar NfL Reduction in Rotenone and Colchicine iPSC models

Bars represent mean (SD) Nfl concentrations relative to vehicle. Overlying symbols represent individual replicate values. NS= P>.05.

* = P<.05.

** = P<.01,

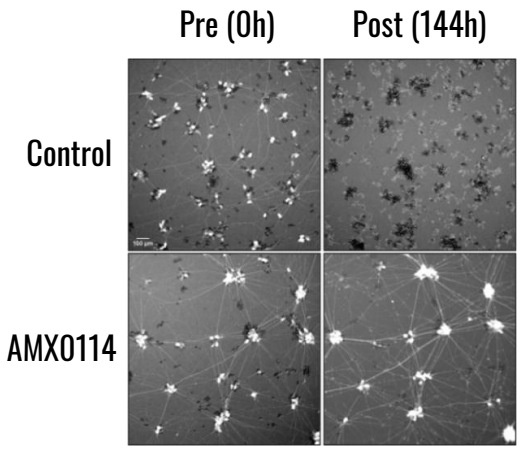
*** = P<.001,

**** = P<.0001.

NfL, neurofilament light chain; NS, not significant; TE, tris ethylenediaminetetraacetic acid.

Pretreatment with AMX0114 improves motor neuron survival following oxidative stress (or H_2O_2 exposure)

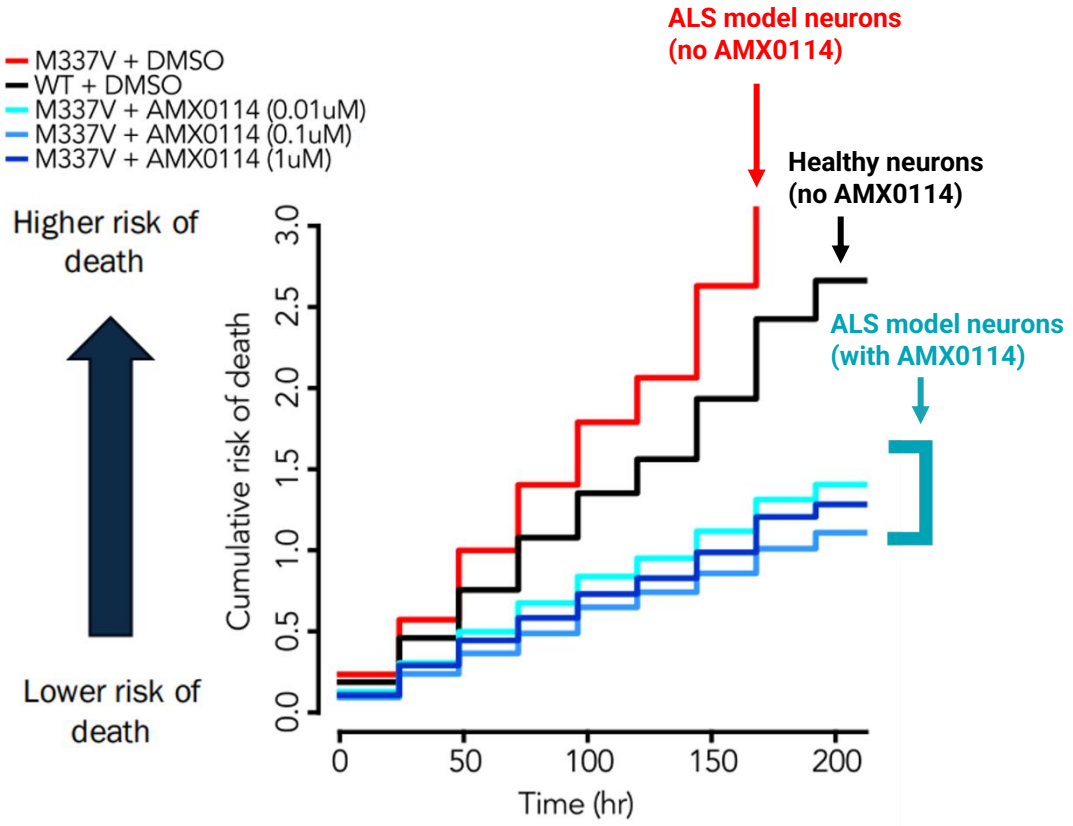
Representative Images of Motor Neurons Pre- and Post-Exposure to H_2O_2



Presented at ALS ONE

AMX0114 Treatment Improves Motor Neuron Survival in TDP43 ALS iPSC Model

TDP-43 ALS Model



Induced pluripotent stem cell (iPSC)-derived motor neurons were exposed to varying concentrations of the neurotoxic compounds vincristine, rotenone, and colchicine after pretreatment with AMX0114.

ALS=amyotrophic lateral sclerosis; NfL=neurofilament light chain; Data on File. Amylyx Pharmaceuticals Inc. 2024; Survival analyses performed in the lab of Dr. Sami Barmada at the University of Michigan Medical School by Dr. Michael Bekier.

LUMINA: Phase 1 Clinical Trial of AMX0114 in ALS

LUMINA

PRIMARY OBJECTIVE: To assess the safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) of AMX0114 in people living with ALS

- Will assess ALS biomarkers, including change from baseline in neurofilament light (NfL) levels

DOSING AND ADMINISTRATION

Intrathecal administration every 4 weeks for a total of up to 4 doses per cohort (N=48)

Cohort 4 (Planned dose level 4)
AMX0114 (n=9) Placebo (n=3)

Open-Label Extension[1]

Cohort 3 (Planned dose level 3)
AMX0114 (n=9) Placebo (n=3)

Cohort 2 (25 mg)
AMX0114 (n=9) Placebo (n=3)
(Fully Enrolled)

Cohort 1 (12.5 mg)
AMX0114 (n=9) Placebo (n=3)
(Fully Enrolled)

All participants in Cohort 1 have completed all 4 doses of AMX0114 or placebo. AMX0114 was generally well-tolerated with no treatment-related SAEs or serious neurological adverse events[2] as of the data cut-off[3].

Screening Period (up to 4 week)	Treatment Period (up to 13 week)	Safety Follow-Up Period (up to 8 week)

COHORT 1 BIOMARKER DATA EXPECTED IN 1H 2026

ALS=amyotrophic lateral sclerosis; SBDP-145=spectrin breakdown product-145.
1. The open-label extension may be implemented if safety and efficacy data support a positive benefit-risk profile; **2.** Porcari G et al. *Neurol Genet*. 2025;11(1):e200229; **3.** As of March 11, 2026.

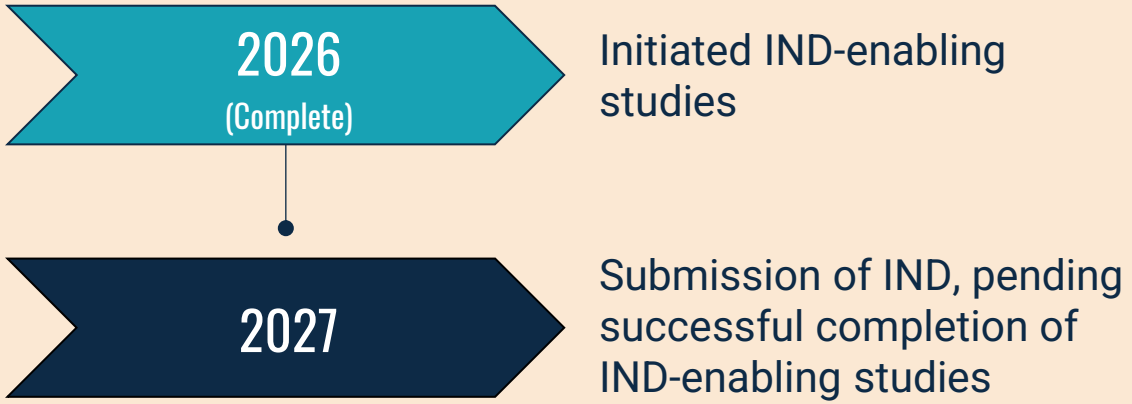
AMX0318

Novel, Long-Acting GLP-1 Receptor Antagonist

AMX0318: A Novel, Long-Acting Glucagon-Like Peptide-1 (GLP-1) Receptor Antagonist

- Entered into a collaboration with Gubra A/S in December 2024 to develop a long-acting GLP-1 receptor antagonist and in January 2026, AMX0318 was nominated as a development candidate
- AMX0318 completed an extensive preclinical evaluation in collaboration with Gubra A/S
- In preclinical studies, AMX0318 met key preclinical criteria for a long-acting GLP-1 receptor antagonist, including:
  - > Robust chemical stability profile
  - > High solubility
  - > Strong *in vitro* potency
  - > Evidence of *in vivo* activity and tolerability
  - > Favorable pharmacokinetic profile consistent with a long-acting peptide

EXPECTED MILESTONES



IND=investigational new drug.

Key Corporate Highlights

Advancing Novel Therapies for Diseases with High Unmet Needs

Focus on diseases with well-defined mechanistic rationale, clear clinical outcomes and biomarkers, and rigorous preclinical data

AVEXITIDE — First-in-class GLP-1 receptor antagonist with FDA Breakthrough Therapy and Orphan Drug designations

AMX0035 — Oral, fixed-dose combination of two small molecules, sodium phenylbutyrate and taurursodiol

AMX0114 — Antisense oligonucleotide designed to target calpain-2, a protein involved in axonal degeneration & neurofilament biology with FDA Fast Track Designation

AMX0318 — Novel, long-acting GLP-1 receptor antagonist

Expected Upcoming Milestones

Q3 2026	**Avexitide**	PBH	Clinical	Phase 3 LUCIDITY topline data anticipated in Q3 2026
2027	**Avexitide**	PBH	Regulatory	Commercial launch, if approved, anticipated in 2027
1H 2026	**AMX0114**	ALS	Clinical	Phase 1 LUMINA trial Cohort 1 (n=12) biomarker data to be presented at a medical meeting expected in 1H 2026
2027	**AMX0318**	PBH & Rare Diseases	Preclinical	IND-enabling studies underway with an IND filing targeted for 2027

ALS=amyotrophic lateral sclerosis; GLP-1=glucagon-like peptide-1; PBH=post-bariatric hypoglycemia.

Avexitide, AMX0035, and AMX0114 are Protected by Robust Global IP Portfolio

AVEXITIDE

>200 granted patents and over 40 pending applications worldwide*

- Granted US patent rights through 2037
  - > **Additional patent term potentially available through patent term extension**
- Positioned for NCE exclusivity
- Granted Orphan Drug Designation for the treatment of hyperinsulinemic hypoglycemia

AMX0035

>80 granted patents and over 50 pending applications worldwide

- Granted US patent rights through 2040
- Granted Orphan Drug Designation for the treatment of Wolfram syndrome

AMX0114

Pending composition of matter patent provides potential patent term through 2043 if granted

- Positioned for NCE exclusivity

FISH.
FISH & RICHARDSON

* Includes in-licensed patents

NCE=new chemical entities.

CASH RUNWAY EXPECTED INTO 2028

THROUGH THE POTENTIAL APPROVAL AND LAUNCH OF AVEXITIDE IN 2027

As of March 31, 2026

- $279.8M in cash, cash equivalents, and short-term investments
- ~111M shares outstanding

Team

Leadership Team Tenured in Rare Disease with Commercial and Clinical Development Capabilities

Joshua Cohen, BSE
Co-CEO and Director

Co-Founded Amylyx, Co-CEO since 2013, led preclinical, clinical and commercial development of RELYVRIO as well as IPO and ~$1B in financing

Justin Klee, ScB
Co-CEO and Director

Co-Founded Amylyx, Co-CEO since 2013, led preclinical, clinical and commercial development of RELYVRIO as well as IPO and ~$1B in financing

Jim Frates
Chief Financial Officer

22-year CFO at Alkermes; grew to >$1B in annual revenue and >2,000 employees worldwide

Camille L. Bedrosian, MD
Chief Medical Officer

Nearly 30 years of experience within the biotech industry; Former CMO at Ultragenyx, Alexion, and ARIAD

Dan Monahan
Chief Commercial Officer

20+ years of commercial leadership experience; Former commercial lead for multiple industry-leading medicines at Otsuka, Novartis, and Sanofi

Tom Holmes
Chief Technical Operations Officer

More than 25 years of biotech experience; Former Head of Global External Manufacturing at Biogen

Gina M. Mazzariello
Chief Legal Officer and General Counsel

20+ years of corporate and commercial legal experience within the healthcare industry, including at Boehringer Ingelheim

Linda Arsenault
Chief Human Resources Officer

25+ years of global HR experience at multibillion-dollar life sciences and technology companies, including at Sumitomo Pharma America Holdings (SMPA)

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