AMYLYX®

Investor Presentation

January 2024

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

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 approval of AMX0035 for the treatment of ALS in countries other than Canada and the United States; statements regarding intentions to seek approval in Europe; the potential of AMX0035 as a treatment for ALS and the Company’s plans to explore the use of AMX0035 for other neurodegenerative diseases, including progressive supranuclear palsy (PSP) and Wolfram syndrome (WS); statements regarding the timing of clinical trials for PSP and/or WS; the potential market acceptance and market opportunity for RELYVRIO®; as well as access to and coverage for RELYVRIO; 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 successfully market RELYVRIO in the United States, Amylyx’ ability to execute on its commercial and regulatory strategy, regulatory developments, expectations regarding the timing of EMA review of AMX0035 for the treatment of ALS, Amylyx’ 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, 2022, 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.

Amylyx Highlights

1st Strong Launch in ALS in United States and Canada

- RELYVRIO® is the first and only FDA approved ALS therapy to show benefit on function and survival
- Approved with conditions in Canada as ALBRIOZA™
- Strong launch with ~3,900 people on therapy in U.S. as of 9/30/23; generated $272.3M of revenue in first three full quarters of U.S. launch

relyvrio® (sodium phenylbutyrate and taurursodiol) for oral suspension 3 g/1 g

Pr albrioza™ sodium phenylbutyrate and ursodoxicoltaurine powder for suspension

Strong Global IP Position

- Composition of matter patents issued
- NCE and orphan drug exclusivity received

Global Opportunity in ALS

- ~200,000 people living with ALS worldwide
- Evaluating opportunities to bring RELYVRIO to people with ALS globally

Research Priorities Focused on Neurodegenerative Diseases

- RELYVRIO has potential across other neurodegenerative diseases
- Evaluating RELYVRIO in Progressive Supranuclear Palsy and Wolfram syndrome

ALS – Amyotrophic lateral sclerosis

FDA – U.S. Food and Drug Administration

Our Mission is to end the suffering caused by neurodegenerative diseases

BUILDING A ROBUST PIPELINE TO TRANSFORM THE LIVES OF PEOPLE LIVING WITH NEURODEGENERATIVE DISEASES

Amyotrophic Lateral Sclerosis (ALS)

Program	Program Indication	Preclinical	IND-Enabling Studies	Phase 1	Phase 2	Phase 3	Approved
RELYVRIO®/ALBRIOZA™/ AMX0035 Sodium Phenylbutyrate (PB) and Taurursodiol (TURSO, also known as Ursodoxicoltaurine)	Treatment of ALS in Adults in the U.S.						
	Treatment of ALS in Canada						
	Treatment of ALS in Europe						
AMX0114	ALS and Additional Neurodegenerative Diseases						
Bax and Bak protein inhibitors	ALS and Additional Neurodegenerative Diseases						

Progressive Supranuclear Palsy (PSP)

Program	Program Indication	Preclinical	IND-Enabling Studies	Phase 1	Phase 2	Phase 3	Approved
RELYVRIO®/ALBRIOZA™/ AMX0035 Sodium Phenylbutyrate (PB) and Taurursodiol (TURSO, also known as Ursodoxicoltaurine)	Treatment of PSP in Adults						

Wolfram Syndrome (WS)

Program	Program Indication	Preclinical	IND-Enabling Studies	Phase 1	Phase 2	Phase 3	Approved
RELYVRIO®/ALBRIOZA™/ AMX0035 Sodium Phenylbutyrate (PB) and Taurursodiol (TURSO, also known as Ursodoxicoltaurine)	Treatment of WS in Adults						

Alzheimer's Disease (AD)

Program	Program Indication	Preclinical	IND-Enabling Studies	Phase 1	Phase 2	Phase 3	Approved
RELYVRIO®/ALBRIOZA™/ AMX0035 Sodium Phenylbutyrate (PB) and Taurursodiol (TURSO, also known as Ursodoxicoltaurine)	Treatment of AD in Adults						

AMYLYX

Key Value Drivers

Commercial launch of RELYVRIO® in ALS

Phase 3 PHOENIX Trial and Additional Data in ALS

Research Pipeline Focused on Neurodegenerative Diseases

In memory of Beth, a wife and mother, who was a community leader and avid gardener.

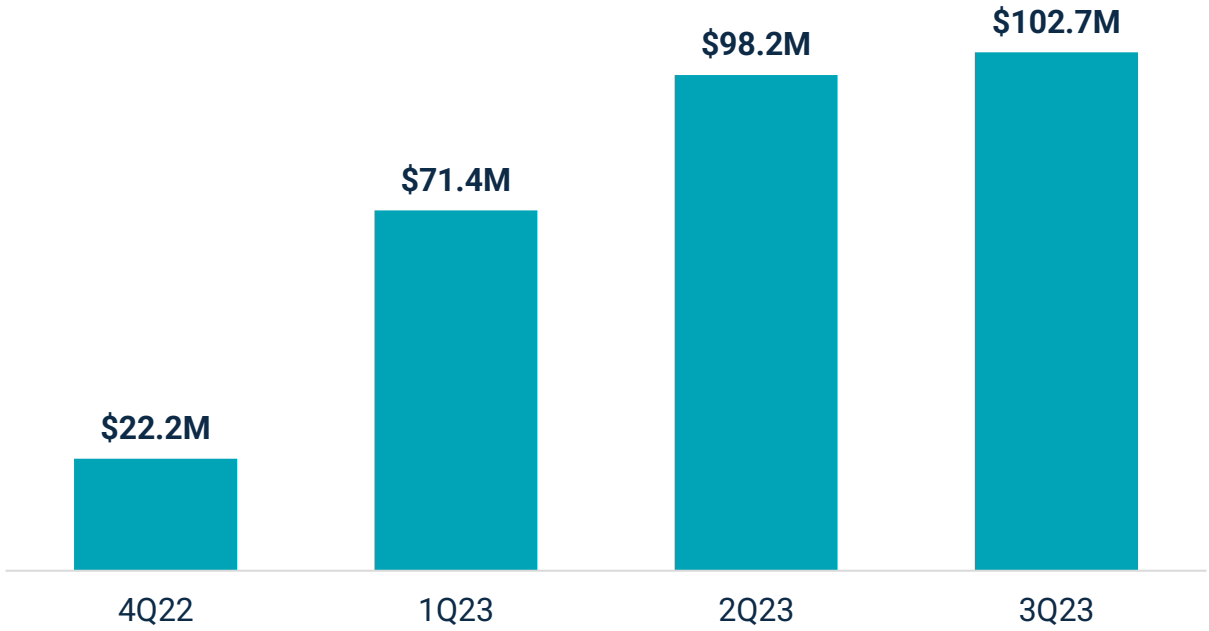
Commercial Launch of RELYVRIO® in ALS

Strong Commercial Launch in ALS

Launched in U.S and Canada

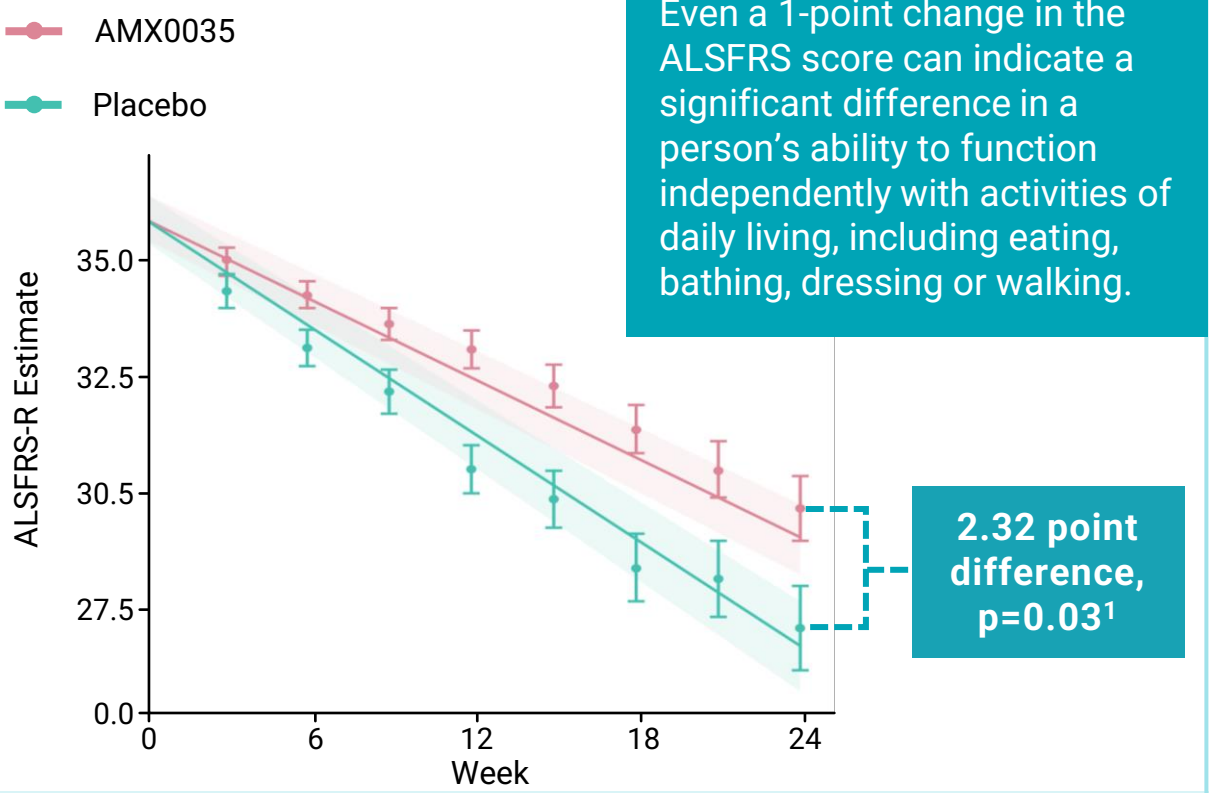
- ~3,900 people on RELYVRIO® in the U.S. at the end of 3Q23
- Vast majority of U.S. insurers provide broad access; coverage in place for vast majority of publicly-insured lives in Canada
- People with ALS able to access therapy quickly

Generated $272.3M of net product revenue in first three full quarters of U.S. launch



Phase 2 CENTAUR Trial Results

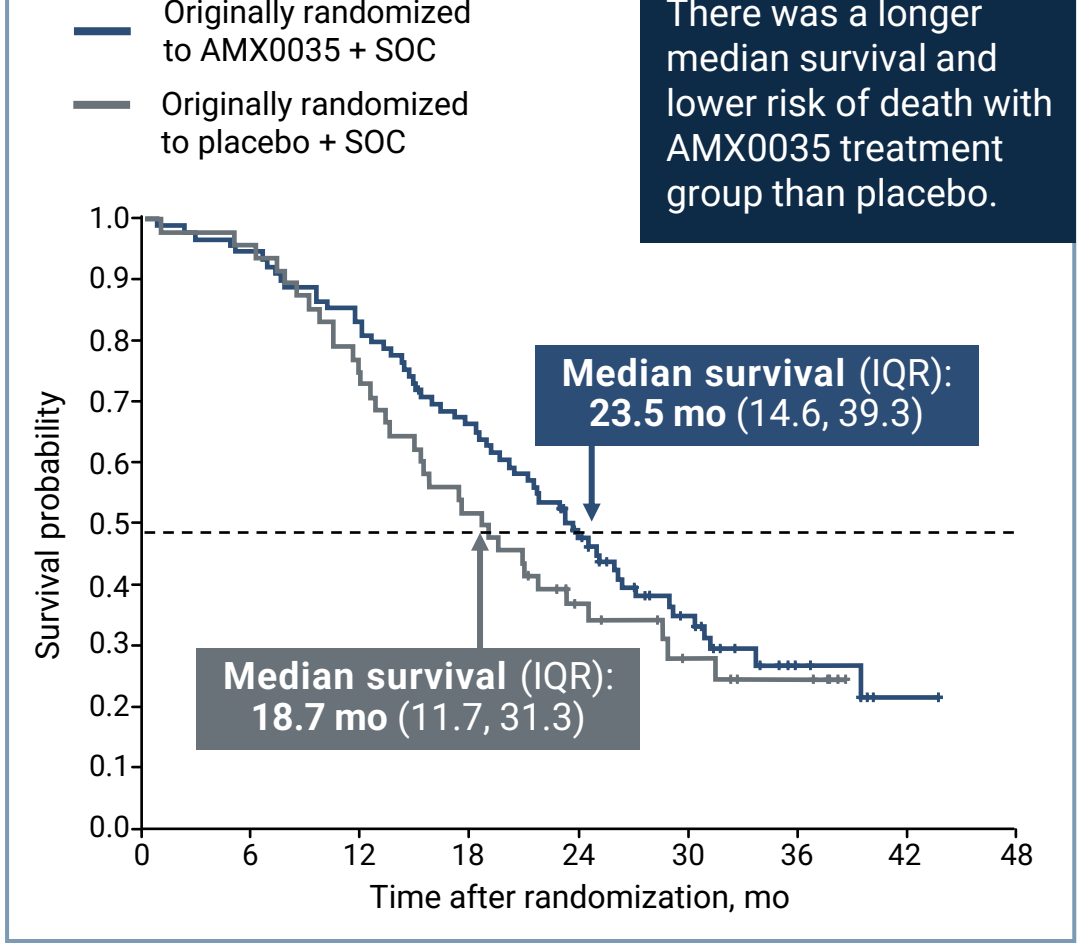
The First Randomized Controlled Trial to Show Benefit on Function and Survival



Even a 1-point change in the ALSFRS score can indicate a significant difference in a person's ability to function independently with activities of daily living, including eating, bathing, dressing or walking.

2.32 point difference, p=0.03[1]

No. of Participants										
	AMX0035	87	84	79	79	75	70	67	68	64
	Placebo	48	48	44	44	44	43	39	38	37



There was a longer median survival and lower risk of death with AMX0035 treatment group than placebo.

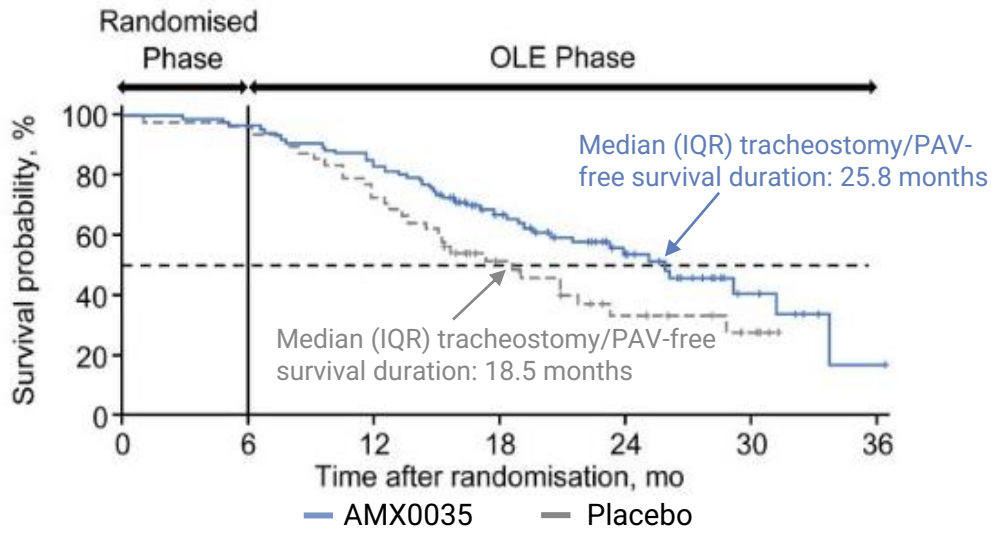
1. Two participants did not have follow-up efficacy assessments and were not included in the efficacy population (modified intention to treat n=135).

Phase 2 CENTAUR Trial Results

AMX0035 Delayed Initiation of Tracheostomy/PAV and Delayed First Hospitalization

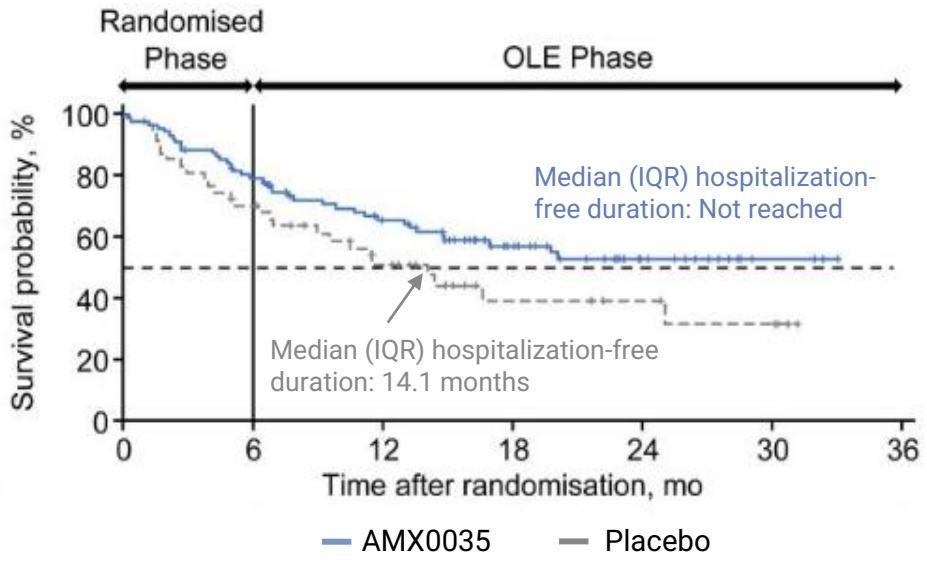
In pre-specified analyses, randomization to AMX0035 resulted in:

- 49% lower risk of death or tracheostomy/permanent assisted ventilation at any time point over the duration of follow-up



Parameter	AMX0035 (n=87)	Placebo (n=48)
Number of events, n (%)	42 (48.3)	30 (62.5)
Median (IQR) Tracheostomy/PAV-free survival duration, mo	25.8 (14.8 - 33.6)	18.5 (11.7 - NR)
Hazard ratio (95% CI)	0.51 (0.32 - 0.84)	
P value	0.007	

- 44% lower risk of first hospitalization at any time point over the duration of follow-up



Parameter	AMX0035 (n=87)	Placebo (n=48)
Number of events, n (%)	37 (42.5)	26 (54.2)
Median (IQR) hospitalization-free duration, mo	NR (6.9 - NR)	14.1 (4.2 - NR)
Hazard ratio (95% CI)	0.56 (0.34 - 0.95)	
P value	0.03	

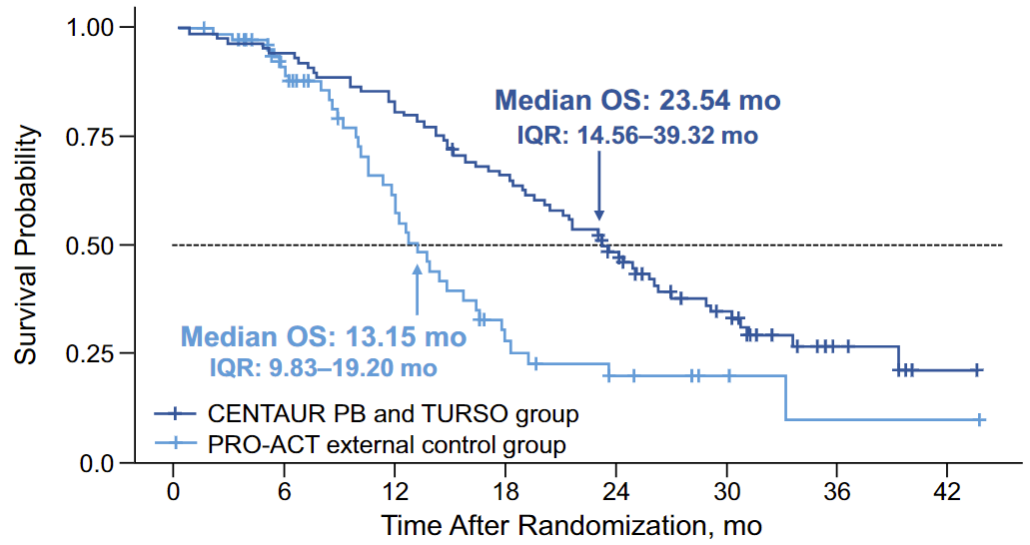
Because ascertainment of key events other than death was limited to the on-trial period, some post-dropout tracheostomy, PAV, or hospitalization events may not have been recorded

Survival Analysis Comparing CENTAUR to Historical Clinical Trial Control

Post-hoc Survival Analysis

ANNALS of Clinical and Translational Neurology Open Access
AMERICAN NEUROLOGICAL ASSOCIATION

- Median overall survival was **10.4 months longer** in the CENTAUR AMX0035 vs. the PRO-ACT external control group



The results demonstrate a longer survival and a 52% lower risk of death over the duration of follow-up in the CENTAUR AMX0035 group versus the PRO-ACT external control group (HR, 0.48; 95% CI, 0.31-0.72; P=.00048)

	Originally Randomized Treatment Group in CENTAUR[1]		PRO-ACT External Control Group (n=85)
	PB and TURSO (n=87)[a]	Placebo (n=48)	
Mean ALSFRS-R progression rate, points/mo	−1.24	−1.66	−1.66

PRO-ACT external control group also demonstrated a very similar mean change in ALSFRS-R total score from baseline through 24 weeks compared to the CENTAUR placebo group (-1.66 points/month), highlighting that the comparison groups were well-matched and the predictability of ALS progression

AMYLYX

[a]Modified intent-to-treat population, which excluded two participants who died soon after randomization.

1. Paganoni S, et al. N Engl J Med. 2020;383:919-930.

RELYVRIO® is Generally Well Tolerated

Phase 2 CENTAUR Trial Results

Adverse Reactions Reported in more than 5% of RELYVRIO-Treated Patients with ALS and at least 5% Greater than Placebo[1]

Adverse Reaction	RELYVRIO (n=89) %	Placebo (n=48) %
Diarrhea*	25	19
Abdominal pain*	21	13
Nausea	18	13
Upper respiratory tract infection*	18	10
Fatigue*	12	6
Salivary hypersecretion	11	2
Dizziness	10	4

Real-World Safety Data from Expanded Access Program (EAP)[2]

- U.S. EAP ran from May to September 2022 and enrolled a broader and relatively more advanced population of people living with ALS compared to CENTAUR (n=194)
- Provides important data on real-world ALS population
- AMX0035 was generally well-tolerated with an acceptable safety profile
- EAP safety data was consistent with the AMX0035 arm from CENTAUR

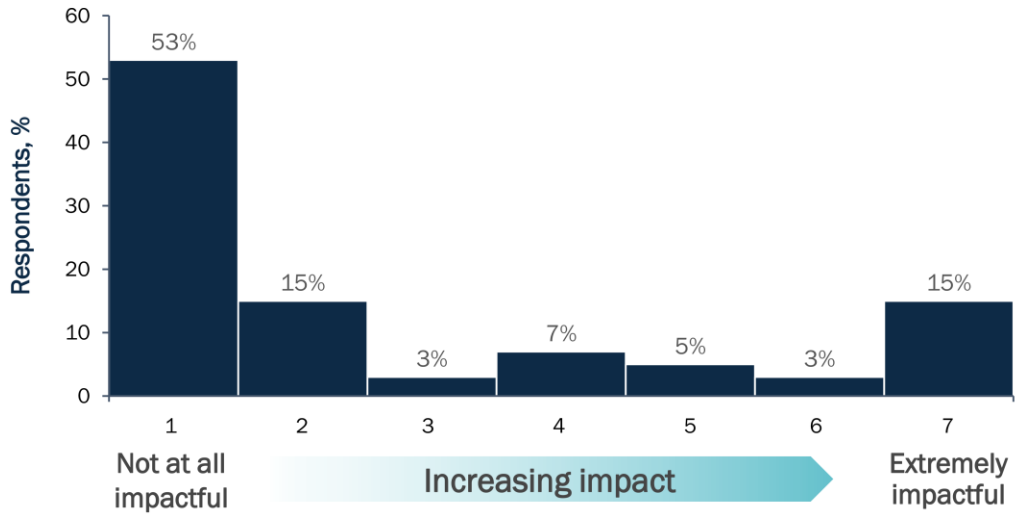
*Adverse reaction is composed of several similar terms.

1. RELYVRIO. Prescribing information. Amylyx Pharmaceuticals, Inc.; 2022. **2.** Poster presented at the 22nd Annual NEALS Meeting; October 4-6, 2023.

New Formulation for RELYVRIO® in Development to Improve Taste

NEALS Northeast Amyotrophic Lateral Sclerosis Consortium®

FIGURE 1. IMPACT OF TASTE OF PB&TURSO ON WILLINGNESS TO TAKE AS PRESCRIBED (N=150)



Real-world data on RELYVRIO taste presented at NEALS 2023[1]

- Overall, taste did not impact willingness to take, adherence to, or planned future use of AMX0035
- Majority of participants found way to improve palatability of AMX0035
- Perceptions of taste improved over time for nearly a third of individuals

New Formulation Development

- New formulation with a less bitter taste is being explored
- Expect to file an IND and conduct Phase 1 testing for formulation in 2024

AMYLYX

1. Poster presented at the 22nd Annual NEALS Meeting; October 4-6, 2023.

Global Opportunity

Evaluating opportunities to expand access to RELYVRIO® globally

ALS is a global disease that affects at least **200,000 people worldwide**

Affects people globally regardless of ethnic, geographic, or racial background

Our strategy to get innovative medicines to people who may benefit:

Research and developing a robust data package demonstrating both efficacy and safety in collaboration with the communities we serve and experts in the field

Continue to plan for the expansion of our global efforts into regions outside North America, Europe and Israel

Interacting with stakeholders in Japan and other places around the world

Move through regulatory and reimbursement processes as quickly and efficiently as possible, following each country's distinct pathways and timelines

Europe

Significant Unmet Need in Europe

30,000+ people are living with ALS in the EU and U.K.[1] There is a crucial need for new, effective treatments for ALS in Europe, which only has one approved therapy (Riluzole), and no new therapies in over 25 years.

Riluzole is prescribed to 75-90% of people living with ALS across Germany, France, Spain, Italy, and the U.K.[2]

Continued Focus on PHOENIX

If PHOENIX is supportive, we plan to seek approval in the EU as quickly as possible.* Topline results are anticipated in Q2 2024.

Experienced, Established Local Leadership Team

Accomplished cross functional leadership team in place to continue to work on educational efforts as well as on operational readiness efforts as we prepare for commercialization throughout Europe

AMYLYX

1. Brown CA, et al. Neuroepidemiology. 2021;55(5):342-353. **2.** Source: IQVIA MIDAS data. *The Committee for Medicinal Products for Human Use, or CHMP, confirmed its June 2023 negative opinion on the MAA for AMX0035 in October 2023. The CHMP opinion will be forwarded to the European Commission, which will adopt the final decision on this application; anticipated by the end of 2023. Amylyx continue to focus on the completion of global PHOENIX Phase 3 clinical trial.

Phase 3 PHOENIX Trial and Additional Data in ALS

Learnings from CENTAUR Applied to PHOENIX

- Designed CENTAUR and PHOENIX with top ALS leaders
- PHOENIX and CENTAUR populations have similar baseline characteristics
  - Within one point of CENTAUR on baseline ALSFRS-R and within one month of CENTAUR on baseline time since onset[1]
  - Within 0.3% percent predicted normal SVC
- PHOENIX enrolled 664 participants as compared to 137 in CENTAUR
- PHOENIX has same primary endpoint, ALSFRS-R progression, as CENTAUR

Table 2. Baseline Characteristics of the Overall PHOENIX and CENTAUR Trial Populations

Characteristic[a]	PHOENIX (N=664)	CENTAUR (N=137)
Sex, n (%)		
Male	411 (62)	93 (68)
Female	253 (38)	44 (32)
Race, n (%)		
White	554 (83)	130 (95)
Asian	9 (1)	3 (2)
Black	6 (1)	3 (2)
American Indian or Alaska Native	1 (<1)	0
Other	5 (1)	0
Unknown	2 (<1)	1 (<1)
Not reported	87 (13)	0
Age, y	59.5 ± 10.81	57.7 ± 9.60
BMI[b], kg/m^2	25.3 ± 4.32	26.7 ± 4.92
SVC[b], percent predicted normal	82.8 ± 17.73	83.1 ± 17.93
Time since ALS symptom onset, mo	14.4 ± 5.30	13.5 ± 3.75
Time since ALS diagnosis, mo	5.6 ± 4.52	6.1 ± 3.28
Bulbar onset, n (%)	148 (22)	36 (26)
Riluzole and/or edaravone use, n (%)	612 (92)	106 (77)
Riluzole	611 (92)	98 (72)
Edaravone	20 (3)	47 (34)
ALSFRS-R total score[b], points	36.7 ± 6.06	36.0 ± 5.52
ALSAQ-40 total score[c], points	51.4 ± 27.11	N/A[d]

[a]Plus-minus values are means ± SD.
[b]At the time of this preliminary analysis, data for these baseline characteristics were available for 662 participants in PHOENIX.
[c]At the time of this preliminary analysis, data for this baseline characteristic were available for 641 participants in PHOENIX.
[d]ALSAQ-40 total score was not assessed in CENTAUR.
ALS, amyotrophic lateral sclerosis; ALSAQ-40, Amyotrophic Lateral Sclerosis Assessment Questionnaire (40 items); ALSFRS-R, Amyotrophic Lateral Sclerosis Functional Rating Scale–Revised; BMI, body mass index; mo, months; N/A, not applicable; SVC, slow vital capacity, y, years.

1. Poster presented at ENCALS 2023; July 12-14, 2023.

PHOENIX Phase 3 Trial

Designed to provide additional safety and efficacy data on RELYVRIO® in ALS to further support global regulatory efforts

NOV 2021 — First participants dosed

FEB 2023 — Trial completed enrollment with 664 participants

Q2-2024 — Topline data anticipated

TRICALS
The highway towards a cure

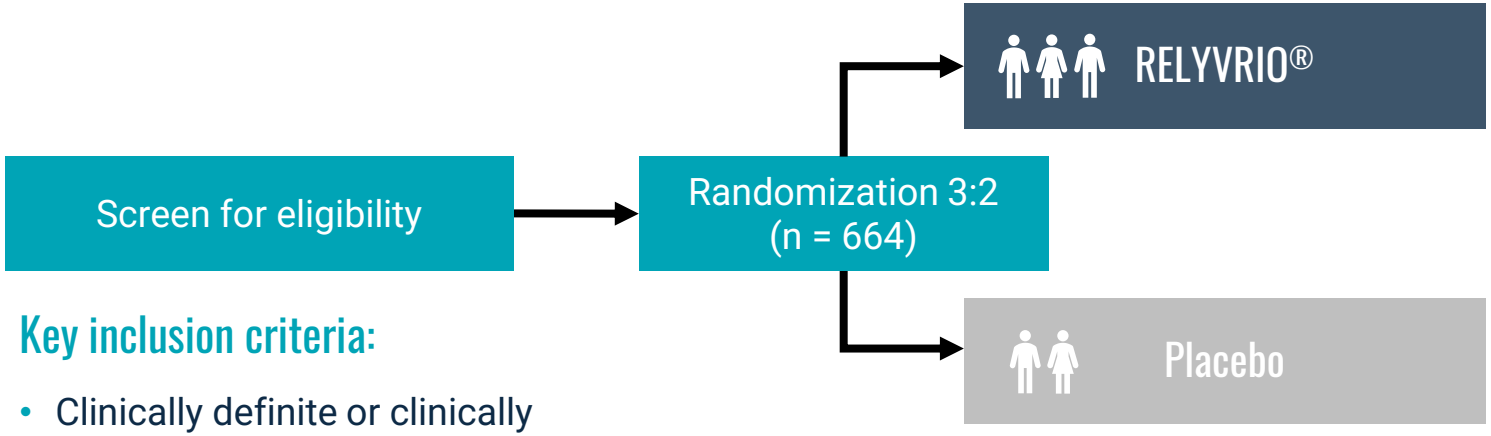
Note: 23 of the 41 PHOENIX sites in the EU are TRICALS member sites.

NEALS Northeast Amyotrophic Lateral Sclerosis Consortium®

Note: 26 of the 28 PHOENIX sites in the U.S. are NEALS member sites.

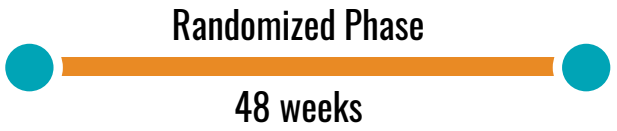
PHOENIX Phase 3 Trial

- Slightly broader inclusion-exclusion criteria than CENTAUR; substantially greater statistical power
- Stratified PHOENIX based on whether people meet CENTAUR inclusion criteria or not
- Plan to analyze subset of participants who meet CENTAUR criteria as well as the broader population



Key inclusion criteria:

- Clinically definite or clinically probable ALS by El Escorial criteria (2-4 body areas with clinical signs consistent with ALS)
- <24 months from symptom onset
- Slow vital capacity (SVC) >55%
- Riluzole/edaravone use permitted



Primary Efficacy Outcomes

- ALSFRS-R
- Safety and tolerability

Secondary Efficacy Outcomes

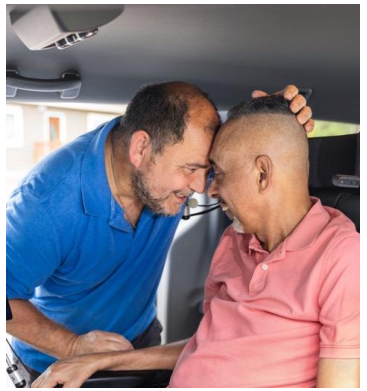
- ALSAQ-40*
- Overall Survival
- Slow vital capacity (SVC)

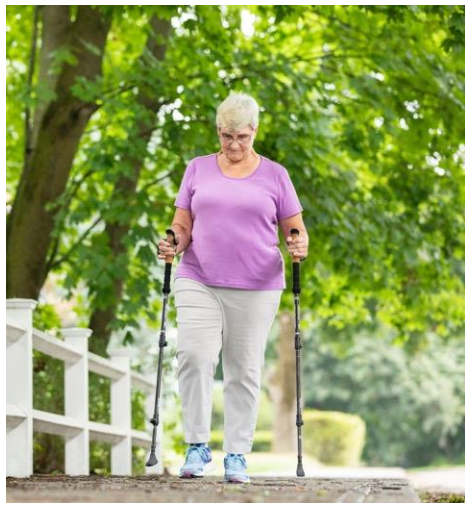
*40 item assessment questionnaire which provides a subjective health measure to specifically assess quality of life for patients with ALS.

Planned Real-World Studies in People Living with ALS

Goal: to further assess the safety and efficacy of AMX0035 in a real-world setting

- Collaborative Real-World Studies Assessing:
  - Single center experience
  - Payer database observational study
- Fulfill post-marketing requirements by:
  - Examining the potential for drug–drug interactions
  - Evaluating AMX0035 pharmacokinetics in specific populations

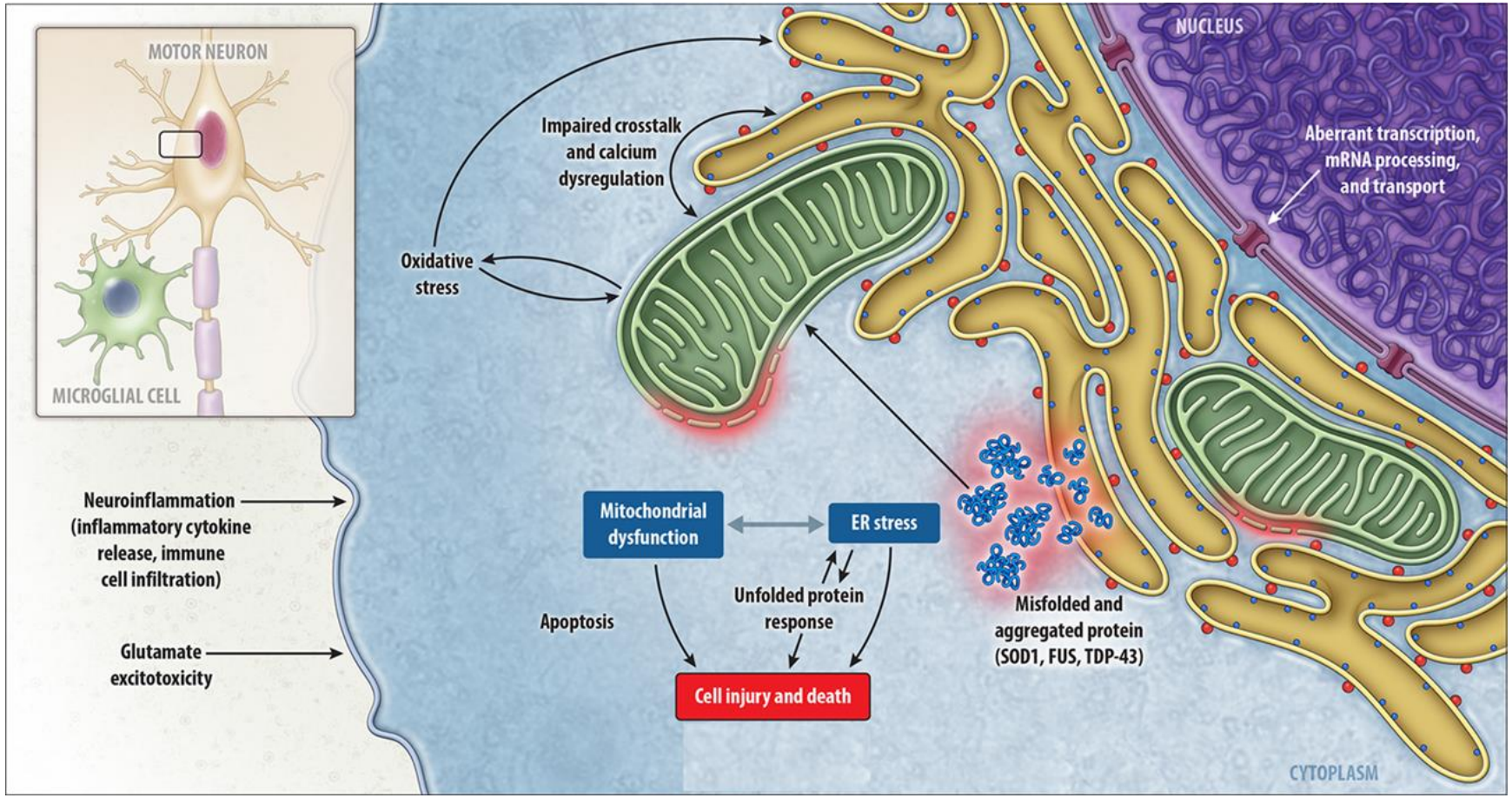




Research Pipeline Focused on Neurodegenerative Diseases

RELYVRIO®/AMX0035 — Designed to Reduce Neuronal Cell Death

- AMX0035: Dual UPR, mitochondrial apoptosis targeting
  - Reduces ER dependent death
  - Reduces Mito dependent death



MOA of AMX0035 in ALS is unknown

Zhou W. J Biol Chem. 2011;286(17):14941-14951.; Rodrigues CM, Steer CJ. Expert Opin Investig Drugs. 2001;10(7):1243-1253.; Rodrigues CM, et al. Biochemistry. 2003;42(10):3070-3080.; Fels JA, et al. Ann Clin Transl Neurol. 2022. doi.org/10.1002/acn3.51648.
The mechanism of action is unknown

AMX0035 Targets Both Pathways Simultaneously to Prevent or Slow Cell Death

AMX0035 Effect in Relevant Preclinical Models

Glutamate excitotoxicity model showing favorable effects on neuronal survival[1]

Models of primary mitochondrial disease showing restoration of mitochondrial functions[1]

Protection against neuronal death in model of primary cortical neuron damage[2]

AMX0035 demonstrates synergistic protection of cortical neurons against peroxide-mediated neuronal death in a range of ratios[2]

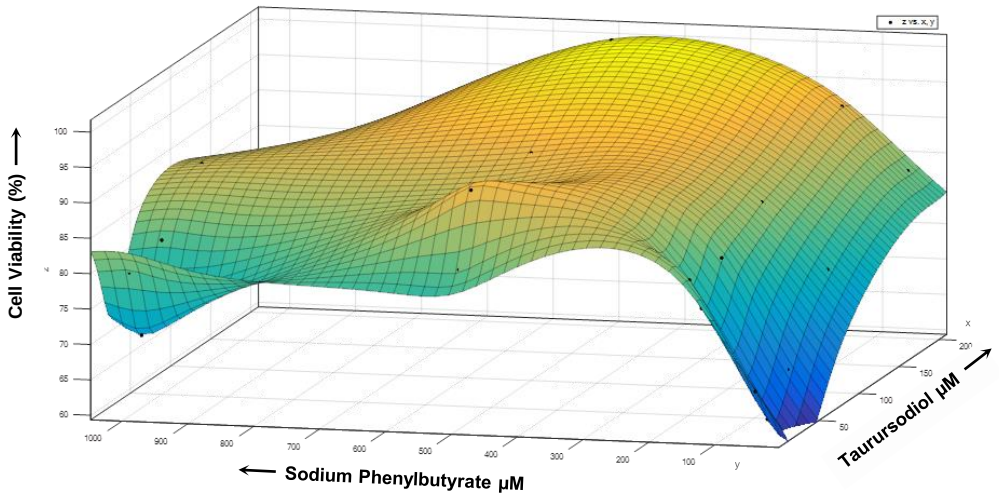


Figure from Cohen J, et al. Clinical trial design for a phase II, randomized, placebo-controlled trial of AMX0035 in amyotrophic lateral sclerosis (CENTAUR). Poster presented at: 28th International Symposium for ALS/MND; December 4–10, 2017; Boston, MA.

MOA of AMX0035 in ALS is unknown

1. Data on File. Amylyx Pharmaceuticals. **2.** 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.

Framework to Select Future Indications

Rigorous process in place to determine next indication for AMX0035

- Clear unmet need
- Strong scientific rationale
- Biomarker evidence
- Existing and robust understanding of the natural history of the disease
- Adjacencies and synergies with ALS
- Interest and support from KOLs and advocacy groups

Progressive Supranuclear Palsy (PSP)

PSP is a Rare, Progressive and Fatal Tauopathy

- Rare neurological disorder affecting body movements, walking and balance, and eye movement.
- No disease modifying therapies creates significant unmet need.
- PSP is a tauopathy associated with tau dysfunction, tau aggregation and widespread neurodegeneration.

ESTIMATED PREVALENCE:

7 in 100,000 worldwide[1,2]

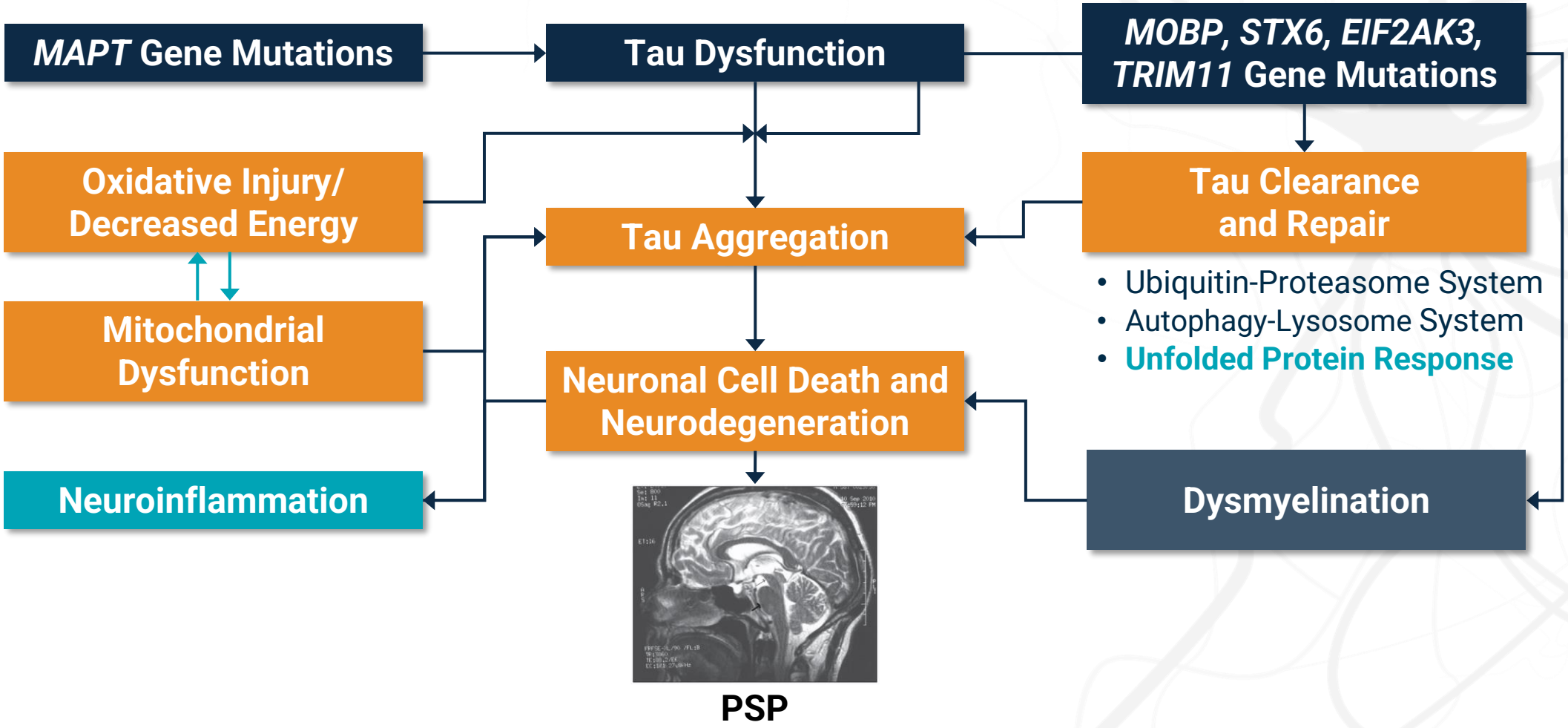
ESTIMATED INCIDENCE:

0.81 in 100,000 worldwide[2]

PSP is typically fatal within 6-8 years from symptom onset[3-6]

AMYLYX **1.** Swallow DMA, et al. Mov Disord Clin Pract. 2022 Jun 28;9(5):604-613. doi: 10.1002/mdc3.13489. **2.** Lyons S, et al. J Neurol.2023; June 8. epub ahead of print. **3.** Stamelou M, et al. Nat Rev Neurol. 2021;17(10):601-620. **4.** Viscidi E, et al. Front Neurol. 2021;12:571800. **5.** Golbe and Ohman-Strickland. Brain. 2007;130(6):1552-65. **6.** Swallow and Counsell. J Neurol. 2023;270(7):3464-3474

AMX0035 May Influence PSP Tau Pathology through Multiple Mechanisms[1-9]

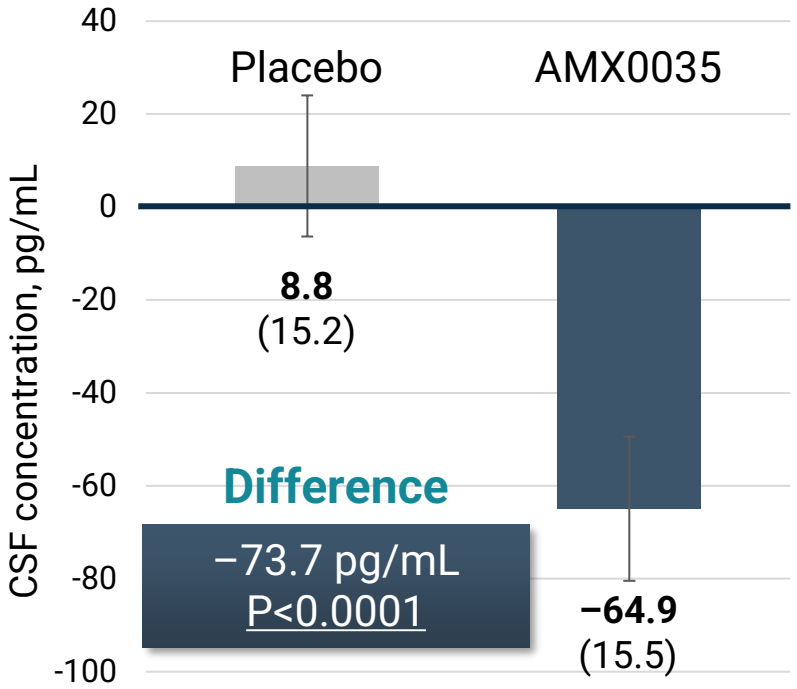


1. Park HK, et al. J Mov Disord. 2021; 14(2):103-113. **2.** Cohen J, et al. Poster presented at: 28th International Symposium for ALS/MND; December 4-10, 2017; Boston, MA. **3.** Zhou W. J Biol Chem. 2011;286(17):14941-14951. **4.** Rodrigues CM, Steer CJ. Expert Opin Investig Drugs. 2001;10(7):1243-1253. **5.** Rodrigues CM, et al. Biochemistry. 2003;42(10):3070-3080. **6.** Ricobaraza A, et al. Neuropsychopharmacology. 2009;34(7):1721-1732. **7.** Bondulich MK, et al. Brain. 2016;139(8):2290-2306. **8.** van der Harg JM, et al. Cell Death Dis. 2014;5(8):e1393. **9.** Arnold SE, et al. Poster presented at: 15th Clinical Trials on Alzheimer's Disease; November 29-December 2, 2022; San Francisco, CA.

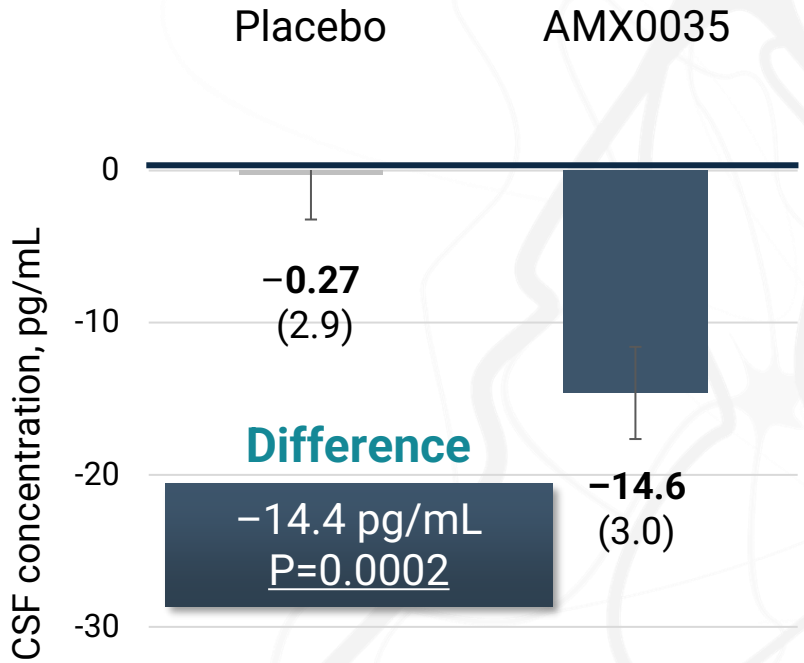
AMX0035 Significantly Lowered CSF Tau and p-Tau in Randomized Placebo Controlled Trial in People with Alzheimer's Disease

PEGASUS

Week 24 Mean (SE) CSF t-tau Change From Baseline



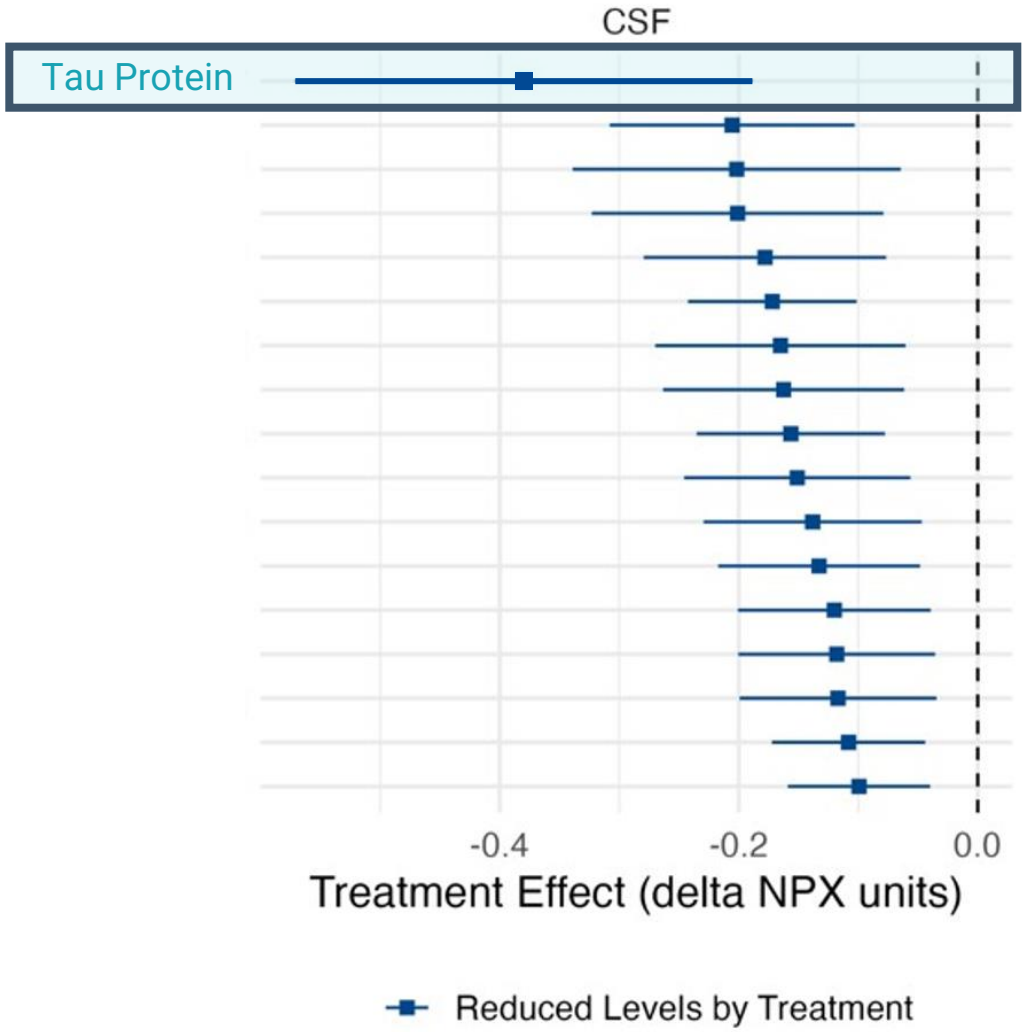
Week 24 Mean (SE) CSF p-tau181 Change From Baseline



Arnold SE, et al. Cerebrospinal Fluid Biomarker Effects From a Fixed-Dose Combination of Sodium Phenylbutyrate and Taurursodiol in Alzheimer's Disease:Results From the PEGASUS Trial. Poster presented at: 15th Clinical Trials on Alzheimer's Disease CTAD, November 29-Dec2; California.

AMX0035 a met the primary endpoint of safety and tolerability in the PEGASUS trial of AMX0035 for the treatment of Alzheimer's disease. The 6-month trial was not powered to evaluate differences between groups in efficacy outcomes and no differences were seen in the primary efficacy outcome, a newly developed composite outcome of cognitive, functional, and imaging measures, or secondary efficacy outcomes of cognition, function, and imaging.

AMX0035 Shown to Reduce Tau Protein in Proteomic Analysis



288

Of 288 proteins measured in CSF and plasma, Tau protein was the most significantly changed protein by AMX0035[1]

1. Poster presented at 16th Annual CTAD Meeting; October 24-27, 2023.
The Proteomic analysis was a pre-specified, exploratory analysis in the PEGASUS trial of AMX0035 for the treatment of Alzheimer's disease.

AMX0035 Slowed Disease Progression and Prolonged Survival in ALS[1,2]

ALS and PSP Share Several Phenotypic Features and Shared Disease Mechanisms[3-5] Suggests that a Drug Effective for ALS May be Effective for PSP[3]

Shared Disease Mechanisms[3]	Shared Phenotypic Features[4,5]
Unfolded protein response	Swallowing difficulty
Mitochondrial dysfunction	Respiratory dysfunction
Neuroinflammation	Speech disturbance
Protein misfolding and aggregation	Impaired cognition

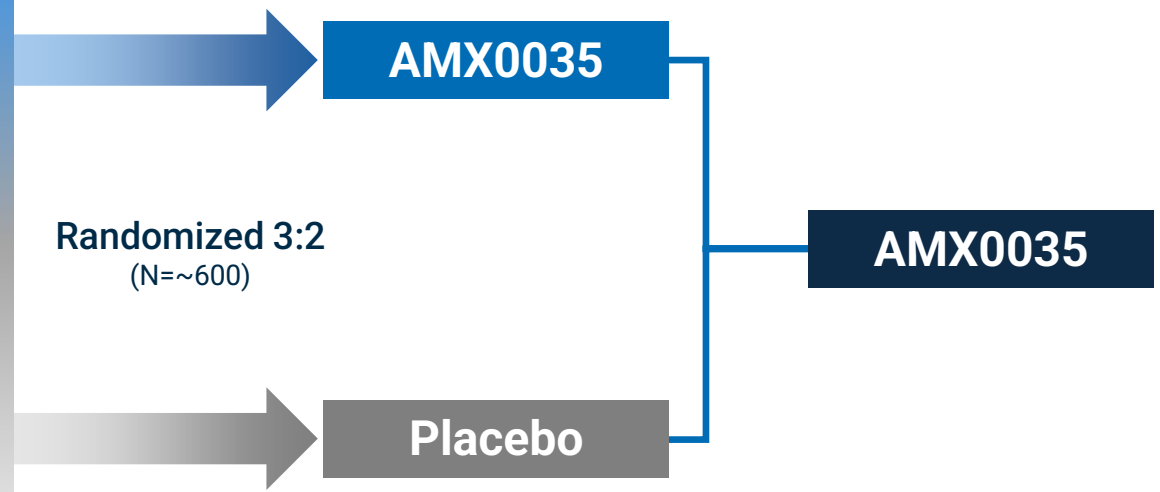
1. Paganoni S, et al. N Engl J Med. 2020;383(10):919-930. **2.** RELYVRIO. Prescribing information. Amylyx Pharmaceuticals, Inc.; 2022. **3.** Wilson DM 3rd, et al. Cell. 2023 Feb 16;186(4):693-714. **4.** Viscidi E, et al. Front Neurol. 2021;12:571800. **5.** Brown RH, Al-Chalabi A. N Engl J Med. 2017;377(2):162-172.

ORION: Phase 3 Clinical Trial of AMX0035 in PSP

Primary Objective: To assess the impact of AMX0035 compared to placebo on disease progression rate as measured by PSPRS

Key Eligibility Criteria

- Adults 40-80 years old
- Possible or Probable PSP (Steele-Richardson-Olszewski Syndrome) according to MDS 2017 criteria[1,2]
- Presence of PSP symptoms < 5 years
- Able to walk independently or with minimal assistance[3]
- PSPRS total score < 40
- MMSE score ≥ 24
- Study partner required
- No feeding tube use



Screening	Double-Blind Treatment	Open Label Extension
≤ 6 weeks	52 weeks	52 weeks

Primary Endpoint

- Total PSPRS score (28-item)

Secondary Endpoints

- Modified 10-item PSPRS score
- MDS-UPDRS Part II score

Additional Endpoints

- Brain volume (MRI)
- Participant QoL and caregiver burden
- CSF and plasma biomarkers of neuronal injury and neuro-inflammation
- Overall survival

Plan to initiate trial by year-end 2023

Plan to enroll sites in U.S., Canada, Europe, and Japan

MDS, Movement Disorders Society; MMSE, mini-mental status exam; PSPRS, Progressive Supranuclear Palsy Rating Scale; MRI, magnetic resonance imaging; QoL, quality of life; CSF, cerebrospinal fluid

1. Gradually progressive disorder, with age at disease onset ≥ 40 years **2.** Either or both of the following two items are met: i. Vertical supranuclear gaze palsy OR slow velocity of vertical saccades AND postural instability with repeated unprovoked falls within 3 years OR tendency to fall on the pull-test within 3 years ii. Slow velocity of vertical saccades AND postural instability with more than two steps backward on the pull-test within 3 years. 1,2. Höglinger et al. Movement Disorders 2017. **3.** Ability to walk 5 steps with minimal assistance (stabilization of one arm).

Wolfram Syndrome

Potential of AMX0035 in Wolfram syndrome

Wolfram syndrome

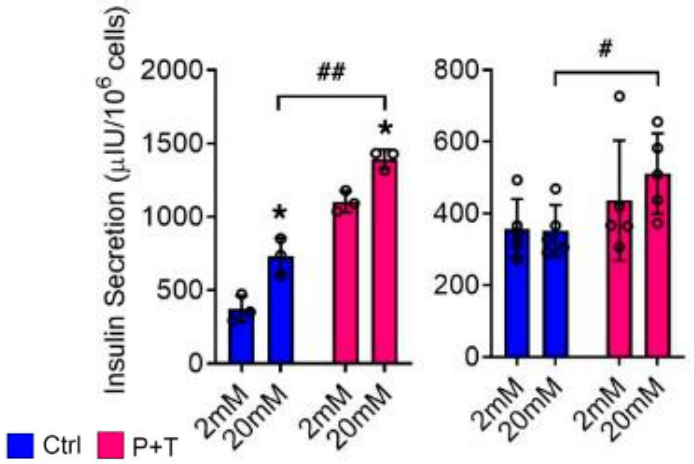
Ultra-rare disease, affecting ~5,000 people in U.S.,[1] with an estimated prevalence of 1 in 500,000 people worldwide.[2] Causes multi-system failure resulting in blindness, deafness, diabetes, ataxia, neurodegeneration, and typically death by early adulthood. Characterized as a prototypical disease of ER stress.

Dysfunction of the WFS1 gene causes the accumulation of unfolded/misfolded proteins in the ER (referred to as ER stress); terminal ER stress and cell death in pancreatic β-cells and neuronal cells thought to be the mechanism of Wolfram syndrome development.[3]

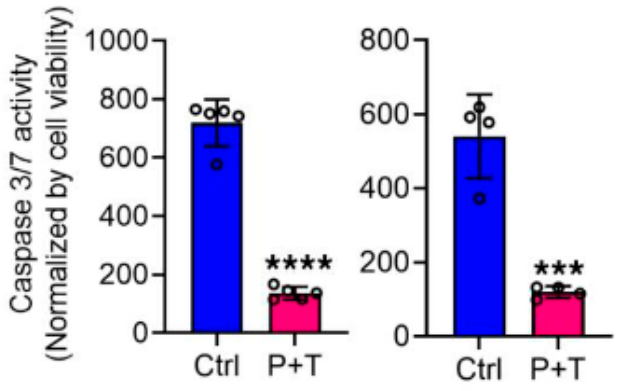
Effect of AMX0035 in Preclinical Studies[3]

JCI insight

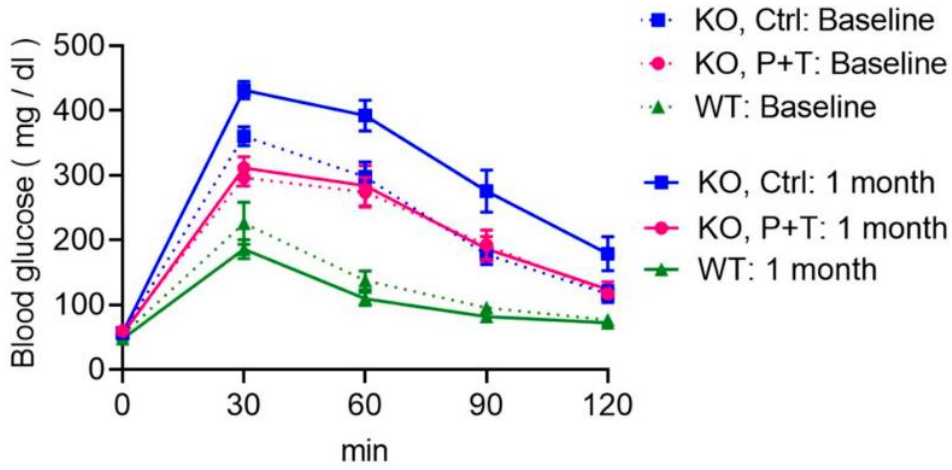
Improved WFS1 protein expression and increased insulin secretion in β cells with the WFS1 variant (Figure)



Inhibited cell death in β cells with the WFS1 variant (Figure), ameliorated organelle dysfunction, mitophagy, ER stress



Delayed onset of the diabetic phenotype in Wolfram syndrome mouse model



1. U.S. Department of Health and Human Services. (n.d.). *Wolfram syndrome*. Genetic and Rare Diseases Information Center. Retrieved April 28, 2023, from https://rarediseases.info.nih.gov/diseases/7898/wolfram-syndrome. **2.** U.S. National Library of Medicine. (n.d.). *Wolfram syndrome*. MedlinePlus. Retrieved April 28, 2023, from https://medlineplus.gov/genetics/condition/wolfram-syndrome/. **3.** Morikawa et al. Front. Endocrinol., 25 March 2022, Sec. Diabetes: Molecular Mechanisms, Volume 13 – 2022, https://doi.org/10.3389/fendo.2022.849204 **4.** Kitamura RA, et al. JCI Insight. 2022;7(18):e156549.

HELIOS: Phase 2 Study of AMX0035 in Wolfram syndrome

12 adult participants

Open-label study at the Washington University School of Medicine in St. Louis

Primary Efficacy Outcomes

- C-peptide response at Week 24 and Week 48
- Safety and tolerability

Secondary Efficacy Outcomes*

- Visual acuity
- Exogenous insulin dose
- Glucose range
- HbA1c levels

*change from baseline to Week 24 and Week 48

First participant dosed in April 2023

Topline results on track for 2024

Orphan drug designation granted to AMX0035 for the treatment of Wolfram syndrome by U.S. FDA

Strong Global IP Position

Portfolio Provides Robust Protection of RELYVRIO® and Related Combinations

>60
issued patents worldwide

>45
additional patents pending

+
potential for additional filings

FISH & RICHARDSON

Portfolio includes:

- Five U.S. Orange Book listed patents directed to RELYVRIO expiring between 2033 - 2040
- Coverage of PB & TURSO composition of matter and its use in treating neurodegenerative diseases, as well as related formulations, combinations and manufacturing processes
- Potential for additional patent term through applicable patent term extensions (PTE); applications are pending in U.S.
- Granted regulatory exclusivities, including NCE through 2027 and ODE though 2029 in U.S.

Team

Deeply Experienced Executive Team to Oversee Global Growth, Clinical Development, Approvals, and Commercial Execution

Joshua Cohen, BSE
Co-CEO and Director

Co-invented AMX0035, dedicated to ALS/neurodegenerative research since 2013, co-designed CENTAUR study, co-led development of AMX0035 as 3-person company for 6 years, then built Amylyx team

Justin Klee, ScB
Co-CEO and Director

Co-invented AMX0035, dedicated to ALS/neurodegenerative research since 2013, co-designed CENTAUR study, co-led development of AMX0035 as 3-person company for 6 years, then built Amylyx team

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

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

Financial Overview

Amylyx Select Financial Data

Statement of Operations ($ thousands except per share data)	3Q23	2Q23
Product revenue, net	**$ 102,693**	**$ 98,216**
Cost of sales	5,218	5,580
Research and development	30,037	29,044
Selling, general and administrative	48,718	43,391
Total operating expenses	**$ 83,973**	**$ 78,015**
Net income (loss)	**$ 20,893**	**$ 22,074**
Net income (loss) per share – diluted	**$ 0.30**	**$ 0.31**

Balance Sheet ($ thousands)	3Q23	2Q23
Cash, cash equivalents and short-term investments	**$ 355,045**	**$ 357,276**

Focused Priorities

Executing on commercial launch of RELYVRIO® in U.S. and ALBRIOZA™ in Canada, evaluating global expansion opportunities in ALS, and advancing research pipeline in neurodegenerative diseases

ALBRIOZA Commercial Launch in Canada

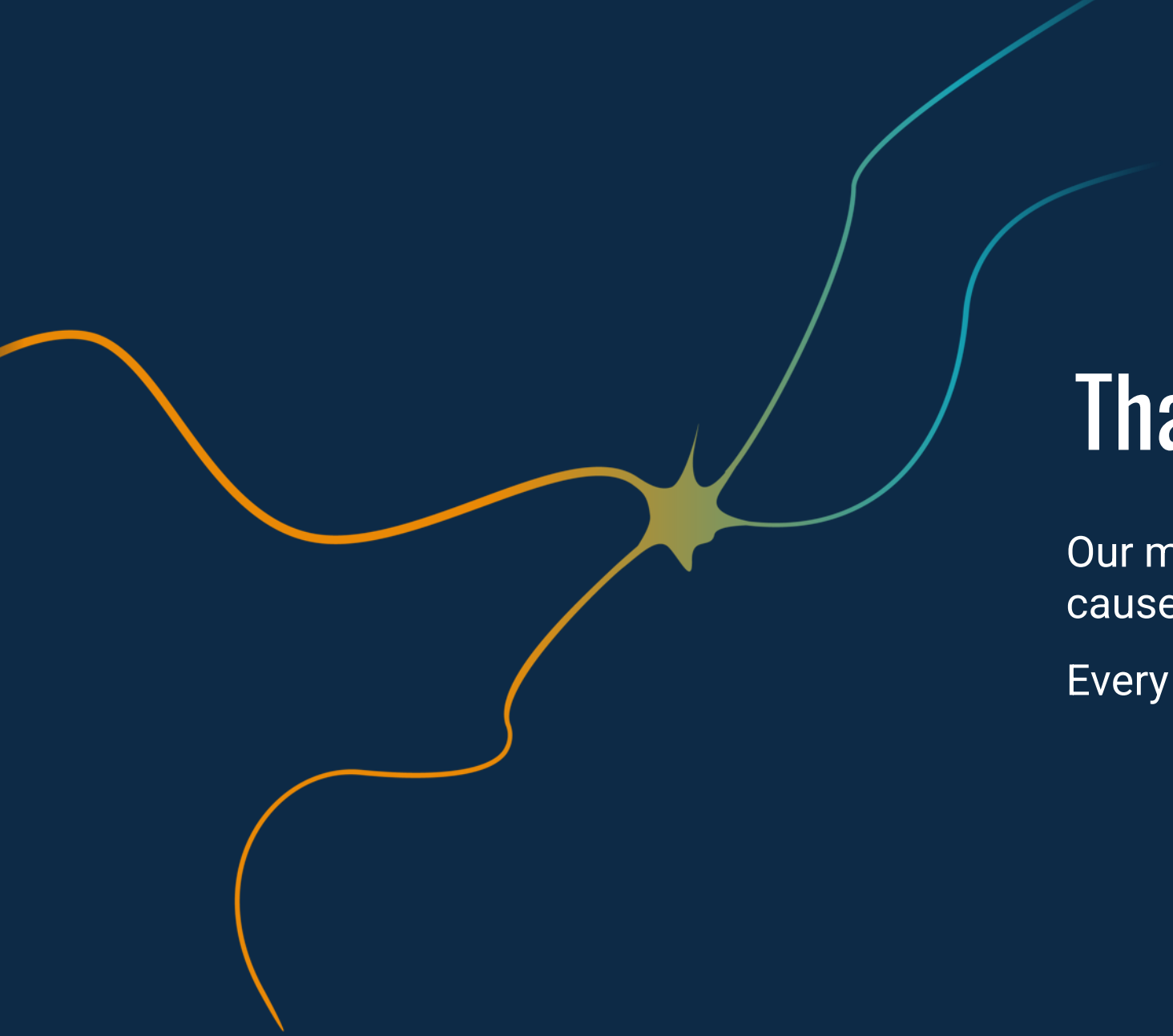
RELYVRIO Commercial Launch in U.S.

Completion of Global PHOENIX Phase 3 Clinical Trial

Seeking Approval in EU if PHOENIX is supportive

Research Priorities

Evaluating AMX0035 in new indications, including Wolfram Syndrome and Progressive Supranuclear Palsy, and building a neurodegenerative pipeline



Thank you.

Our mission is to one day end the suffering caused by neurodegenerative diseases.

Every day, we strive for better therapies.

AMYLYX®