AMYLYX

Investor Presentation

June 2023

photo 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 the timing of any regulatory re-examination process 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 surpranuclear palsy and Wolfram syndrome; 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, and the impact that the ongoing COVID-19 pandemic will 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, 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

RELYVRIO® and ALBRIOZA™

RELYVRIO (sodium phenylbutyrate and taurursodiol) and ALBRIOZA (sodium phenylbutyrate and ursodoxicoltaurine) are the first drug to show statistically significant functional benefit and observed survival benefit in ALS

Strong Global IP Position

Composition of matter patents issued; NCE exclusivity received; orphan drug exclusivity received

Approved in the United States and Canada

Pending CHMP re-examination process in Europe following negative CHMP Opinion in June 2023 – supported by robust clinical data published in *The New England Journal of Medicine*

Jun. 2022	Sep. 2022	Fall 2023
		
ALBRIOZA approved for use with conditions	RELYVRIO approved	Final CHMP Opinion post re-examination*

* Amylyx intends to seek re-examination of the negative CHMP opinion as announced on June 23, 2023.

Why ALS

> We need to work on the ALS clock… I lost the privilege of working on the human clock on January 6, 2018. My clock is a lot faster.

Sandy Morris, 51-year-old mother of three, person who lived with ALS

photo in memory of Eric, a husband and father, who was a courageous skydiver and Army veteran

ALS is Relentlessly Progressive and Universally Fatal

- Significant unmet need for new treatment options
- ALS leads to deteriorating muscle function, the inability to move and speak, respiratory paralysis, and death[1,2]

>90%

of people living with ALS have no family history of the disease

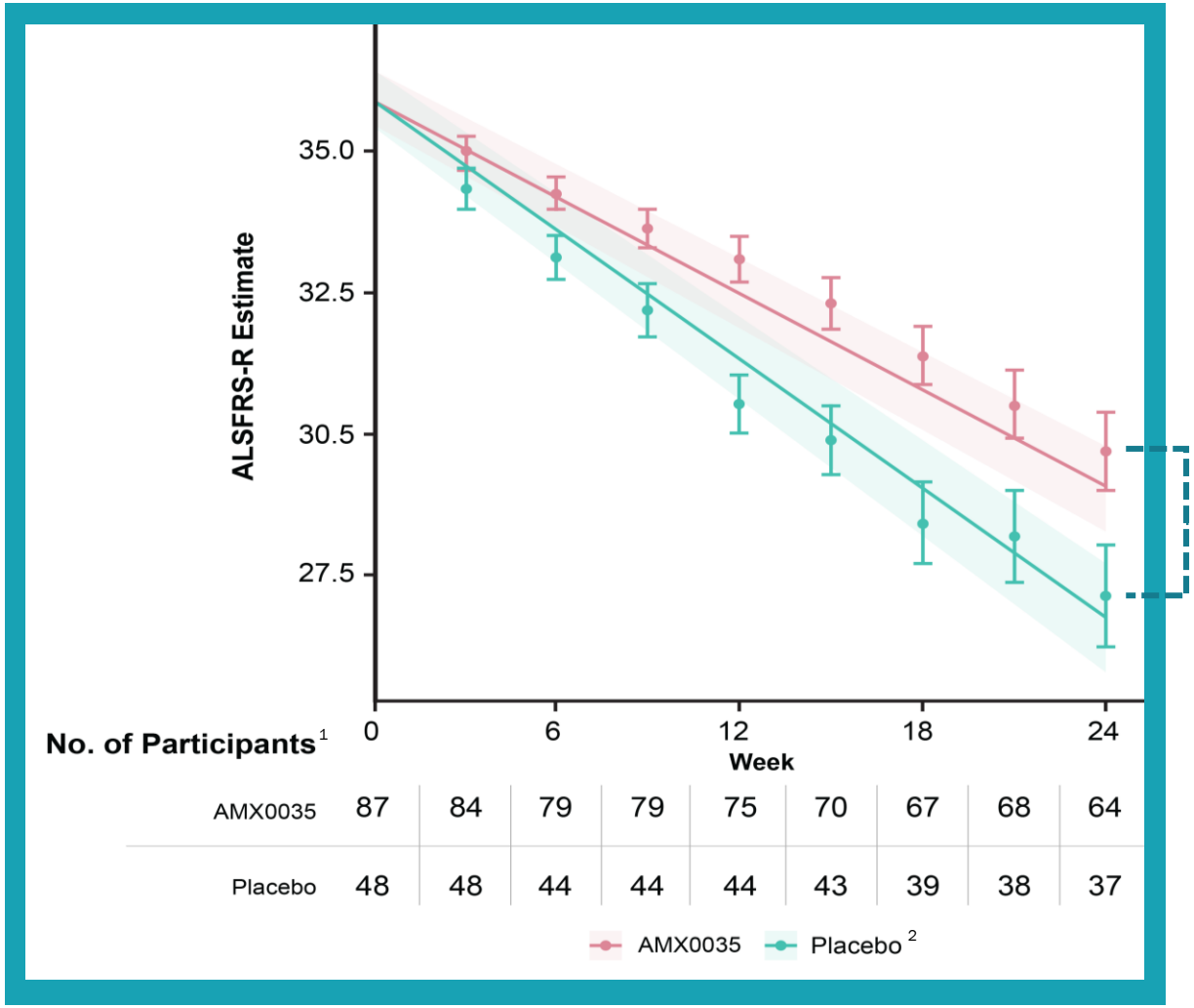
~50%

of people with ALS will pass away in about 2 years from diagnosis[3]

References: 1. Brown RH, 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.** Knibb JA, Keren N, Kulka A, et al. J Neurol Neurosurg Psychiatry. 2016;87(12):1361-1367.

CENTAUR Trial Results

Statistically Significant Functional Benefit as Measured by the ALSFRS-R, the Gold Standard Clinical Scale in ALS



Trial of Sodium Phenylbutyrate–Taurursodiol for Amyotrophic Lateral Sclerosis

Published in The New England Journal of Medicine

Sabrina Paganoni, M.D., Ph.D., Eric A. Macklin, Ph.D., Suzanne Hendrix, Ph.D., James D. Berry, M.D., Michael A. Elliott, M.D., Samuel Maiser, M.D., Chafic Karam, M.D., James B. Caress, M.D., Margaret A. Owegi, D.O., Adam Quick, M.D., James Wymer, M.D., Ph.D., Stephen A. Goutman, M.D., Daragh Heitzman, M.D., Terry Heiman-Patterson, M.D., Carlayne E. Jackson, M.D., Colin Quinn, M.D., Jeffrey D. Rothstein, M.D., Ph.D., Edward J. Kasarskis, M.D., Ph.D., Jonathan Katz, M.D., Liberty Jenkins, M.D., Shafeeq Ladha, M.D., Timothy M. Miller, M.D., Ph.D., Stephen N. Scelsa, M.D., Tuan H. Vu, M.D., Christina N. Fournier, M.D., Jonathan D. Glass, M.D., Kristin M. Johnson, D.O., Andrea Swenson, M.D., Namita A. Goyal, M.D., Gary L. Pattee, M.D., Patricia L. Andres, M.S., D.P.T., Suma Babu, M.B., B.S., M.P.H., Marianne Chase, B.A., Derek Dagostino, B.A., Samuel P. Dickson, Ph.D., Noel Ellison, M.S., Meghan Hall, M.S., Kent Hendrix, B.S., Gale Kittle, R.N., M.P.H., Michelle McGovern, B.S., Joseph Ostrow, B.S., Lindsay Pothier, B.A., Rebecca Randall, M.S., R.D., Jeremy M. Shefner, M.D., Ph.D., Alexander V. Sherman, M.Sc., Eric Tustison, B.A., Prasha Vigneswaran, M.S., Jason Walker, B.S., Hong Yu, M.S., James Chan, M.A., Janet Wittes, Ph.D., Joshua Cohen, B.S.E., Justin Klee, Sc.B., Kent Leslie, M.S., Rudolph E. Tanzi, Ph.D., Walter Gilbert, Ph.D., Patrick D. Yeramian, M.D., David Schoenfeld, Ph.D., and Merit E. Cudkowicz, M.D.

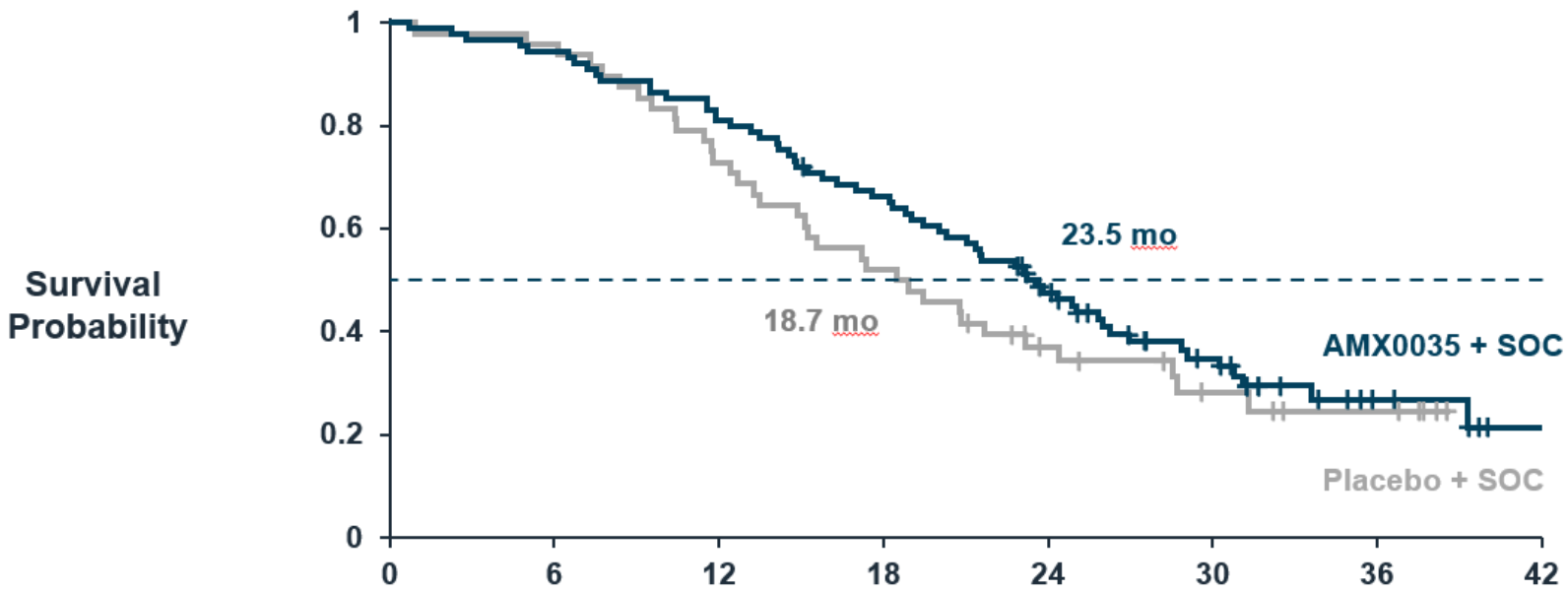
2.32 point difference, p=0.03

"Each category in the ALSFRS-R seems clinically important, and because each domain includes only five levels that span 0 (cannot do) to 4 (normal), prevention of even 1 unit of worsening in a single domain seems meaningful and desirable for individuals with ALS".[3]

References: 1. Two participants did not have follow-up efficacy assessments and were not included in the efficacy population (modified intention to treat n=135). **2.** 77% of participants were on Riluzole or edaravone at or prior to study entry. **3.** FDA Center for Drug Evaluation and Research, Application Number 209176Orig1s000, Office Director Memo, Ellis F. Unger, MD, May 4, 2017.
Paganoni S, et al. New Eng J Med. 2020.

CENTAUR Trial Results

Participants Randomized to RELYVRIO Were Observed to Survive Longer Than Those Randomized to Placebo



In a post hoc exploratory, long-term Intention-to-treat (ITT) survival analysis using data from the last participant last visit in the open-label phase (March 2021), median survival duration was 23.5 months in the group originally randomized to RELYVRIO and 18.7 months in the group originally randomized to placebo (4.8-month difference, HR=0.64, 95% CI=0.416-0.995)*

	Cox Regression Model
HR (95% CI)	**0.64** (0.416, 0.995)
# of events	94

Note: This is an ITT (all 137 patients) analysis
Survival defined as All Cause Mortality (True Overall Survival)

SOC = standard of care; CI = confidence interval; HR = hazard ratio.

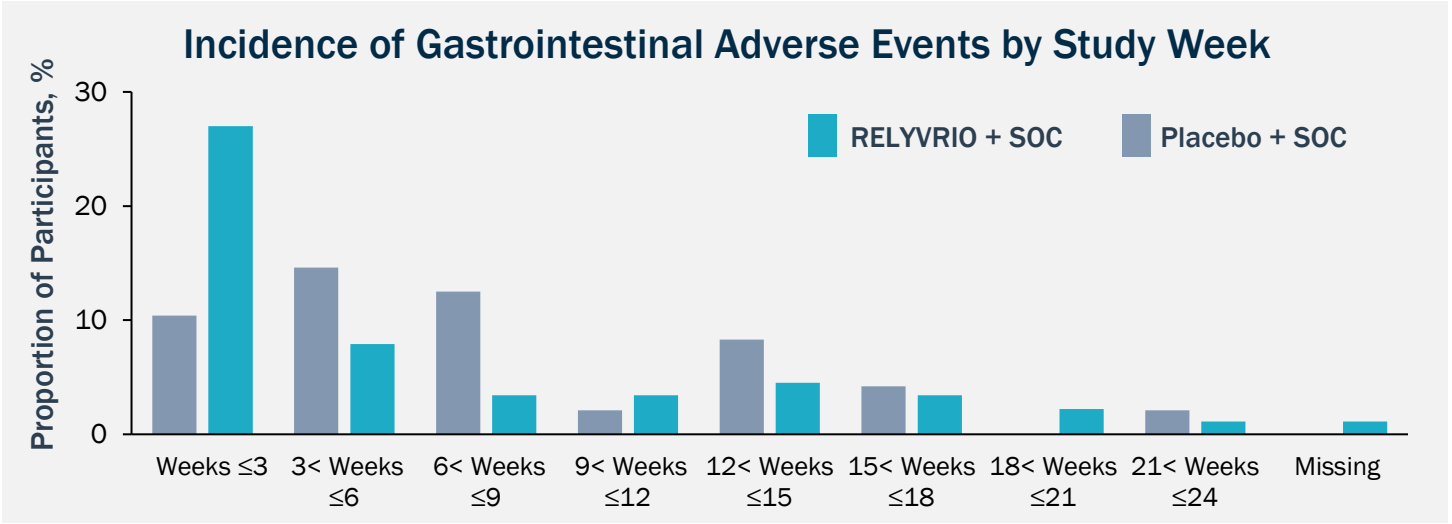
*This exploratory analysis should be interpreted cautiously given the limitations of data collected outside of a controlled study, which may be subject to confounding.

CENTAUR Adverse Events (AEs)

The most common adverse events occurring with RELYVRIO (at least 15% and at least 5% greater than placebo) were diarrhea, abdominal pain, nausea, and upper respiratory tract infection. Gastrointestinal-related adverse reactions occurred throughout the study but were more frequent during the first three weeks of treatment.

Adverse Reactions Reported in More than 5% of RELYVRIO-Treated Patients with ALS and at least 5% Greater than Placebo

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



* Adverse reaction is composed of several similar terms. Paganoni S, et al. N Engl J Med. 2020;383:919-930.

Overview of Prescribing Information

Indication Statement	RELYVRIO is indicated for the treatment of amyotrophic lateral sclerosis (ALS) in adults.
Dosing and Administration	Administered orally or via a feeding tube. The recommended dosage for the first 3 weeks of treatment is 1 packet daily, increasing to 2 packets daily starting at the beginning of week 4.
Most common adverse events occurring with RELYVRIO	• Diarrhea • Abdominal pain • Nausea • Upper respiratory infection

Please see full Prescribing Information at RELYVRIO.com

Significant Unmet Need in the U.S. and Globally

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

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

United States
~29,000 People[1]
living with ALS

Canada
~3,000 People[2]
living with ALS

Europe
>30,000 People[3]
living with ALS
(European Union and United Kingdom)

References: 1. Nelson LM, et al. Neuroepidemiology. 2021 Dec 20. DOI: 10.1159/000521591 **2.** Shoesmith C, et al. CMAJ Nov 2020, 192 (46) E1453-E1468; DOI: 10.1503/cmaj.191721 **3.** Brown CA, et al. Neuroepidemiology. 2021;55(5):342-353.

Helping People with ALS Gain Access to RELYVRIO

Experienced Commercial Team Educating the Market

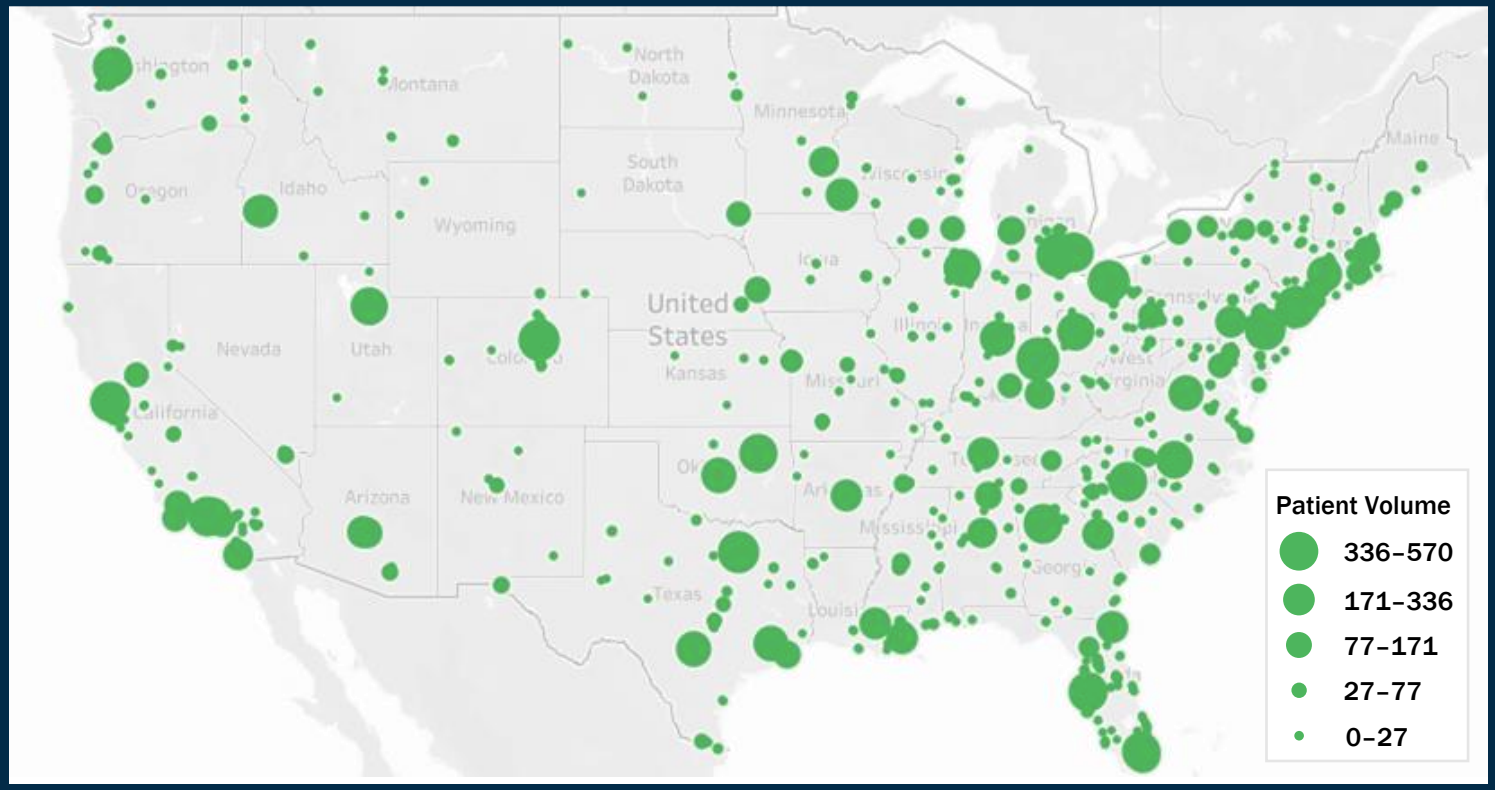
Focused on three key priorities to support a successful launch

1. Driving awareness and education of RELYVRIO
2. Engaging payors on access
3. Ensuring people living with ALS have positive interactions through their treatment journey with RELYVRIO and ALS clinics have positive interactions with Amylyx

Targeted Approach Covering The Vast Majority of the U.S. Market

~2,700 potential ALS prescribers in the U.S.[1]

Physicians Treating ALS by Patient Volume[2]



References: 1. Amylyx Internal Data; Mar. '23 **2.** Amylyx Internal Data; Sep '22.

Amylyx Care Team (ACT) Support Program

Ready to provide personalized support to adults living with ALS that have been prescribed to RELYVRIO and healthcare professionals

Compassionate support from a caring team

You'll get to know the ACT™ team as people who are deeply dedicated to your well-being, providing personalized support throughout your treatment journey.

Team of actual Amylyx employees

ACT Care Support Specialists

- Committed to answering your questions by phone before you are enrolled in ACT
- Help you get enrolled in the program

Your ACT Care Coordinator

- Will be paired with you throughout your treatment journey
- Available by phone or email, once you are enrolled in ACT
- An experienced, full-time Amylyx employee
- Dedicated to providing the highest levels of customer service

ACT Care Educators

- Registered nurses who can provide additional education about ALS and RELYVRIO™ (sodium phenylbutyrate and taurursodiol)*

*Your doctor is always your best source for treatment information.

Your ACT Care Coordinator is your primary source for one-on-one support

For more information about RELYVRIO, please see additional Important Safety Information throughout and the full Prescribing Information and Medication Guide.

A wide range of support

ACT™ Amylyx Care Team

Through your dedicated ACT Care Coordinator, you will be connected with the following support and resources.

Reimbursement & Insurance Support
We can help you understand your insurance coverage and benefits for RELYVRIO.

Financial Assistance, if Eligible
We can provide resources for access support through our $0 Co-Pay Program,* Interim Access Program, and Patient Assistance Program. Talk to your ACT Care Coordinator or visit AmylyxCareTeam.com to learn more.

ALS Education
Our team is here to support you with learning more about ALS and your treatment.

Your doctor is always your best source for treatment information.

Partnership With Specialty Pharmacies
Because RELYVRIO is a specialty medication, it is only available through specialty pharmacies. We'll partner with these facilities to coordinate delivery to your home. To learn more, visit AmylyxCareTeam.com.

Continuous Support
We'll help you get started on RELYVRIO treatment and keep supporting you as you continue on it.

Call ACT Today
866-318-2989
Monday-Friday, 8 AM to 8 PM ET

*Out-of-pocket costs related to medication, appointments, evaluations, testing, or other related services are not covered by the RELYVRIO Co-Pay Program. The RELYVRIO Co-Pay Program is not available for prescriptions purchased under Medicare, Medicaid, TRICARE, or other federal- and state-funded programs. Amylyx reserves the right to amend or terminate the Program at any time without notice. Co-pay amounts after applying co-pay assistance may depend on the individual's insurance plan and may vary. The RELYVRIO Co-Pay Program is intended to help individuals afford RELYVRIO.

IMPORTANT SAFETY INFORMATION (continued)
Before you receive RELYVRIO, tell your doctor about all of your medical conditions, including if you:
- Have high blood pressure
- Have kidney problems

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

Canada

ALBRIOZA™ Commercial Launch Underway in Canada

Pr albrioza™
sodium phenylbutyrate and ursodoxicoltaurine powder for suspension

1st First Regulatory Approval for Amylyx Worldwide

ALBRIOZA commercial launch in Canada underway; moving with urgency to make ALBRIOZA available to Canadians living with ALS. Approximately 1,000 people die from ALS in Canada every year, with a similar number of diagnoses annually.

New Treatment Option Available for Canadians

ALBRIOZA is only the third product candidate to be approved for the treatment of ALS in Canada in the past 30 years. Unmet need remains high, with ~3,000 Canadians living with ALS.

Navigating Complex Reimbursement System

~40% of Canadians are covered by private insurance.

Negotiated agreements with all of the largest private insurers to cover ALBRIOZA, represents ~80% of privately insured population

~60% of Canadians rely on public insurance.

By the end of 2023, Amylyx expects to finalize and sign product listing agreements with the majority of federal, provincial, and territorial public drug plans.

Experienced Team Driving Successful Launch in Canada

Staffed by a team with considerable experience with new therapy launches in Canada

Chris Aiello
Head of Canada and General Manager
sanofi · Bioverativ · Biogen

Julie Girodat
Head of Patient Services & Distribution
AMGEN · Bristol Myers Squibb · Celgene

Tracey Jason, PhD
Head of Medical Affairs
abbvie · Celgene · Pfizer

Jason Lee
Head of Market Access
Bayer · Biogen · Lilly

Blaine MacNeil
Head of Sales, Marketing and Commercial Operations
sanofi

Europe

Path to commercialization

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]

Targeted, Local Commercial Approach

Actively preparing launch in the EU and engaging with key stakeholders in each member state. Expect to launch in Germany first, followed by expansion in additional countries; reimbursement process and timelines differ by country

Working with ALS community and reimbursement bodies to facilitate access to ALBRIOZA®, if approved

Experienced, Established Local Leadership Team

Accomplished cross functional leadership team in place developing commercialization strategy for ALBRIOZA in EMEA and ensuring its implementation, including Regional Head of EMEA, Head of EMEA Market Access, Head of EMEA Regulatory, Head of EMEA Medical, and GMs for major European markets, including Germany

Continuing to build a highly targeted and lean team

References: 1. Chiò /Logroscino /Traynor /Collins / Simeone /Goldstein /Nelson LM, et al. Neuroepidemiology. 2021 Dec 20. doi: 10.1159/000521591. **2.** Source: IQVIA MIDAS data.

Germany

Case Study

High Unmet Need

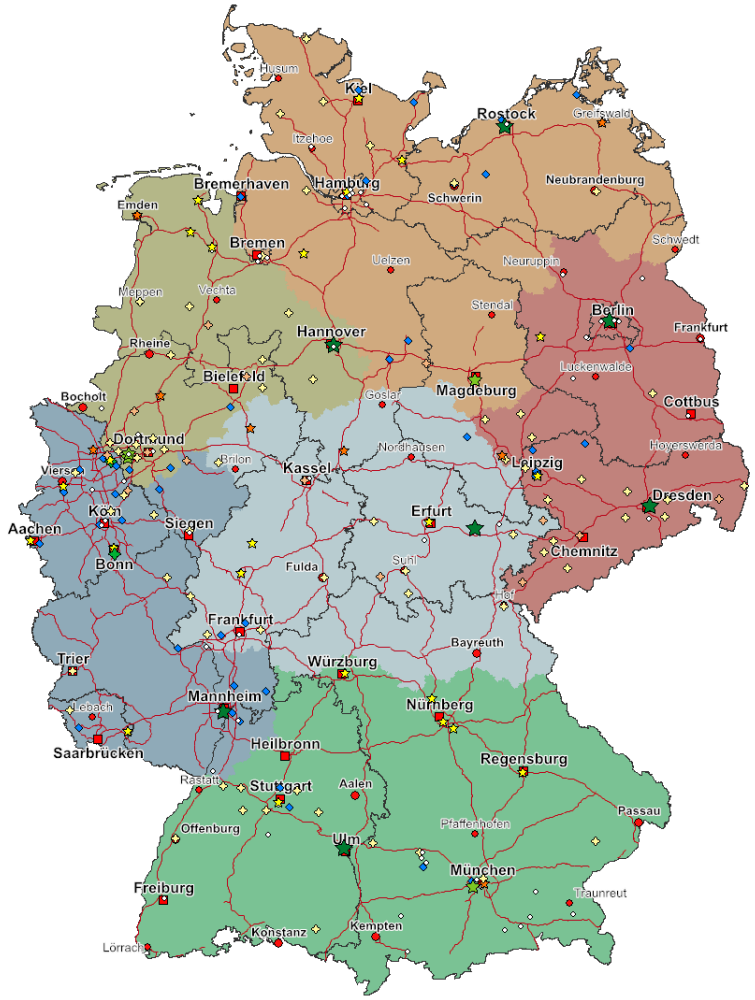
~7,000 people living with ALS in Germany[1],majority of patients diagnosed and initially treated in ~25 ALS centers of expertise

Focused Outreach to Key Physicians

- Engagement with top national KOLs, including KOLs at five participating PHOENIX trial sites
- Dividing country into six territories to target ~25 ALS centers of expertise and ~200 community-based neurologists that are responsible for the majority of Riluzole prescriptions
- Local team hired in Germany

Commercial Launch Followed by Reimbursement Negotiations

Preparing to commercialize in Germany after EU approval; free pricing at launch; reimbursement negotiations then typically take ~12 months following pricing and reimbursement dossier filing



[1] Rosenbohm et al, J Neurol (2017) 264:749–757, Epidemiology of amyotrophic lateral sclerosis in Southern Germany, 'ALS registry Swabia pts diagnosed 10/2008 - 12/2014', N=648 prospective patients were analyzed

EMEA Leadership

Highly Experienced, Local Team to Lead Commercialization in Europe

Stéphanie Hoffmann-Gendebien

Head, General Manager, EMEA

Secoya, clementia, Alexion, genzyme

Chiara Troncatti

Head of Commercial Operations, EMEA

Qral Group, AKCEA Therapeutics, Boehringer Ingelheim, ZS

Leo Stričan

Head of Market Access, EMEA

bluebirdbio, Biogen, Novartis

Bernd-Jan Sanson, M.D.

Head of Medical Affairs, EMEA

CellPoint, AstraZeneca, Sanofi Genzyme, Kiadis pharma

Lugdivine Le Dez

Head of Patient Advocacy and Government Affairs, EMEA

Alcon, Alexion, Celgene

Brid Carberry

Head of Supply Chain, EMEA

Novartis, Pfizer, BioMarin

Thomas Biet

Head of Finance, EMEA

Biogen, Pfizer, agios

Jan van Emous

Head of Regulatory Affairs, Europe

Novartis, Sanofi Genzyme, Bristol Myers Squibb, Schering-Plough

Susanne Digel

General Manager, Germany

oncopeptides, Spark Therapeutics, bluebirdbio, Alexion

Eric Litjens

Head of Marketing & Corporate Communications, EMEA

Horizon, Hansa Biopharma, Orphan Now Consulting

photo in memory of Mick, a husband and father, who was a gifted tattoo artist and musician

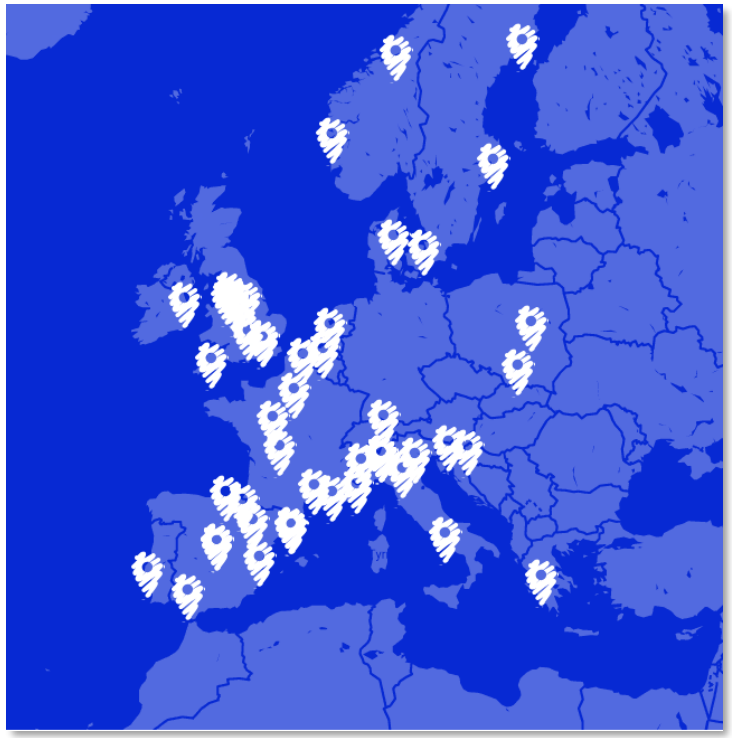
PHOENIX Phase 3 Trial

Designed to provide additional safety and efficacy data on RELYVRIO for the treatment of ALS to further support our global regulatory efforts

Nov 2021	First participants dosed
Feb 2023	Trial completed enrollment with 664 participants
Mid-2024	Topline data anticipated

PHOENIX is a Large, Global Phase 3 Clinical Trial in ALS

Designed to Support Global Regulatory Efforts and Continue to Provide Data on RELYVRIO



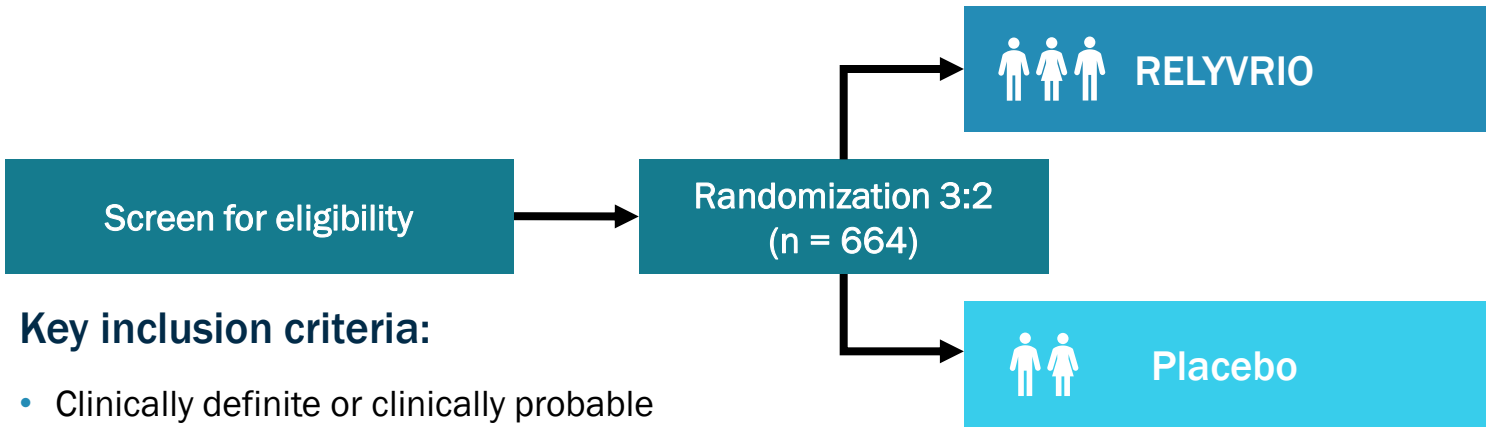
TRICALS
The highway towards a cure

NEALS
Northeast Amyotrophic Lateral Sclerosis Consortium

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

PHOENIX Trial Design for RELYVRIO

- 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[1] 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)

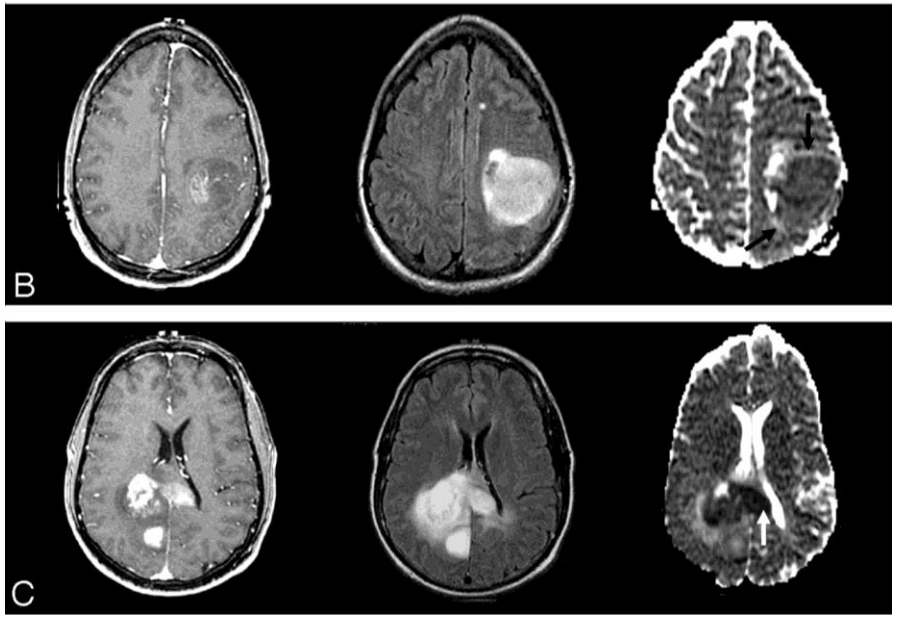
*40 item assessment questionnaire which provides a subjective health measure to specifically assess quality of life for patients with ALS.

AMX0035

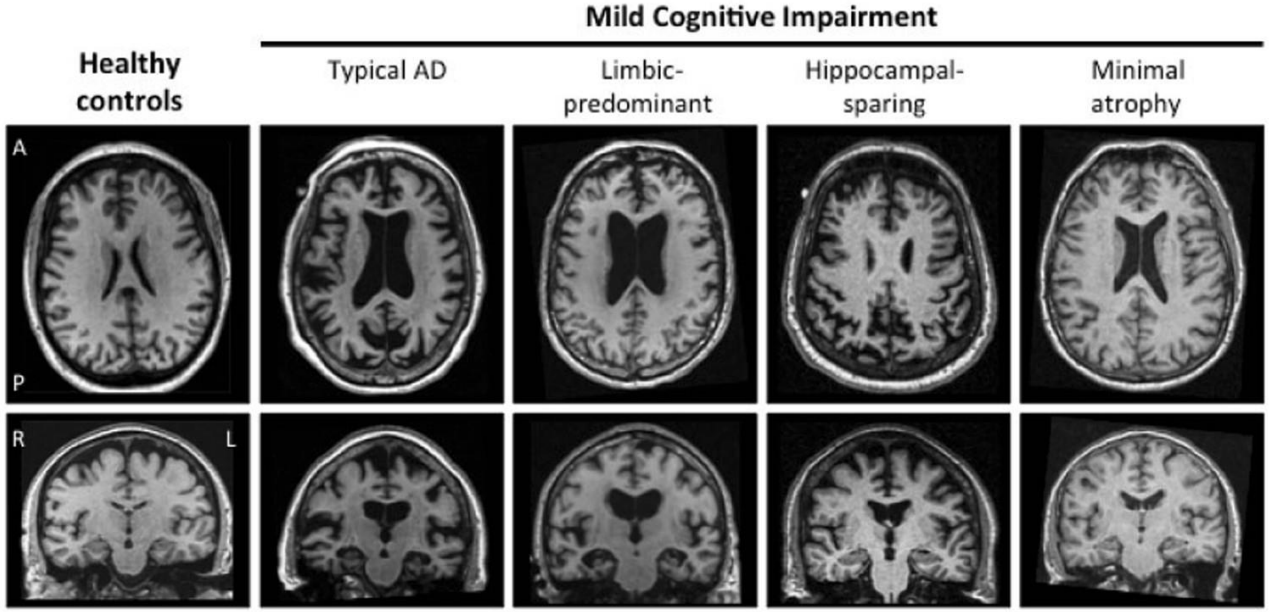
Potential to Treat Several Diseases of Neurodegeneration

Neurodegenerative Diseases are the Biological Opposite of Cancer

Cancer is Characterized by Abnormal Cellular Growth; Neurodegenerative Diseases are Characterized by Abnormal Cellular Death



WHO grade III (top row) and grade IV (bottom row) astrocytomas.



Subtypes of brain atrophy patterns in MCI from visual rating scales

Update on Brain Tumor Imaging: From Anatomy to Physiology S. Cha American Journal of Neuroradiology Mar 2006, 27 (3) 475-487
Ekman, U., Ferreira, D. & Westman, E. The A/T/N biomarker scheme and patterns of brain atrophy assessed in mild cognitive impairment. Sci Rep 8, 8431 (2018). https://doi.org/10.1038/s41598-018-26151-8

The 2002 Nobel Prize in Physiology or Medicine was for Discoveries in the Field of Programmed Cell Death

Cancer is Characterized by Abnormal Cellular Growth; Neurodegenerative Diseases are Characterized by Abnormal Cellular Death

The Nobel Prize in Physiology or Medicine 2002

Sydney Brenner | H. Robert Horvitz | John E. Sulston

The Nobel Prize in Physiology or Medicine 2002 was awarded jointly to Sydney Brenner, H. Robert Horvitz and John E. Sulston "for their discoveries concerning genetic regulation of organ development and programmed cell death'."

Proc. Natl. Acad. Sci. USA
Vol. 95, pp. 4997–5002, April 1998
Cell Biology

Bax directly induces release of cytochrome *c* from isolated mitochondria

JULIANE M. JÜRGENSMEIER, ZHIHUA XIE, QUINN DEVERAUX, LISA ELLERBY, DALE BREDESEN, AND JOHN C. REED*

Program on Apoptosis and Cell Death Research, The Burnham Institute, 10901 North Torrey Pines Road, La Jolla, CA 92037

Edited by Lewis T. Williams, Chiron Technologies, Emeryville, CA, and approved February 23, 1998 (received for review October 10, 1997)

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Review Article | Published: 21 October 2019

Mitochondria as multifaceted regulators of cell death

Florian J. Bock & Stephen W. G. Tait

Nature Reviews Molecular Cell Biology **21**, 85–100 (2020) | Cite this article

21k Accesses | **256** Citations | **131** Altmetric | Metrics

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Endoplasmic reticulum stress: cell life and death decisions

Chunyan Xu, Beatrice Bailly-Maitre, and John C. Reed

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Published: December 2008

Cell death and endoplasmic reticulum stress: disease relevance and therapeutic opportunities

Inki Kim, Wenjie Xu & John C. Reed

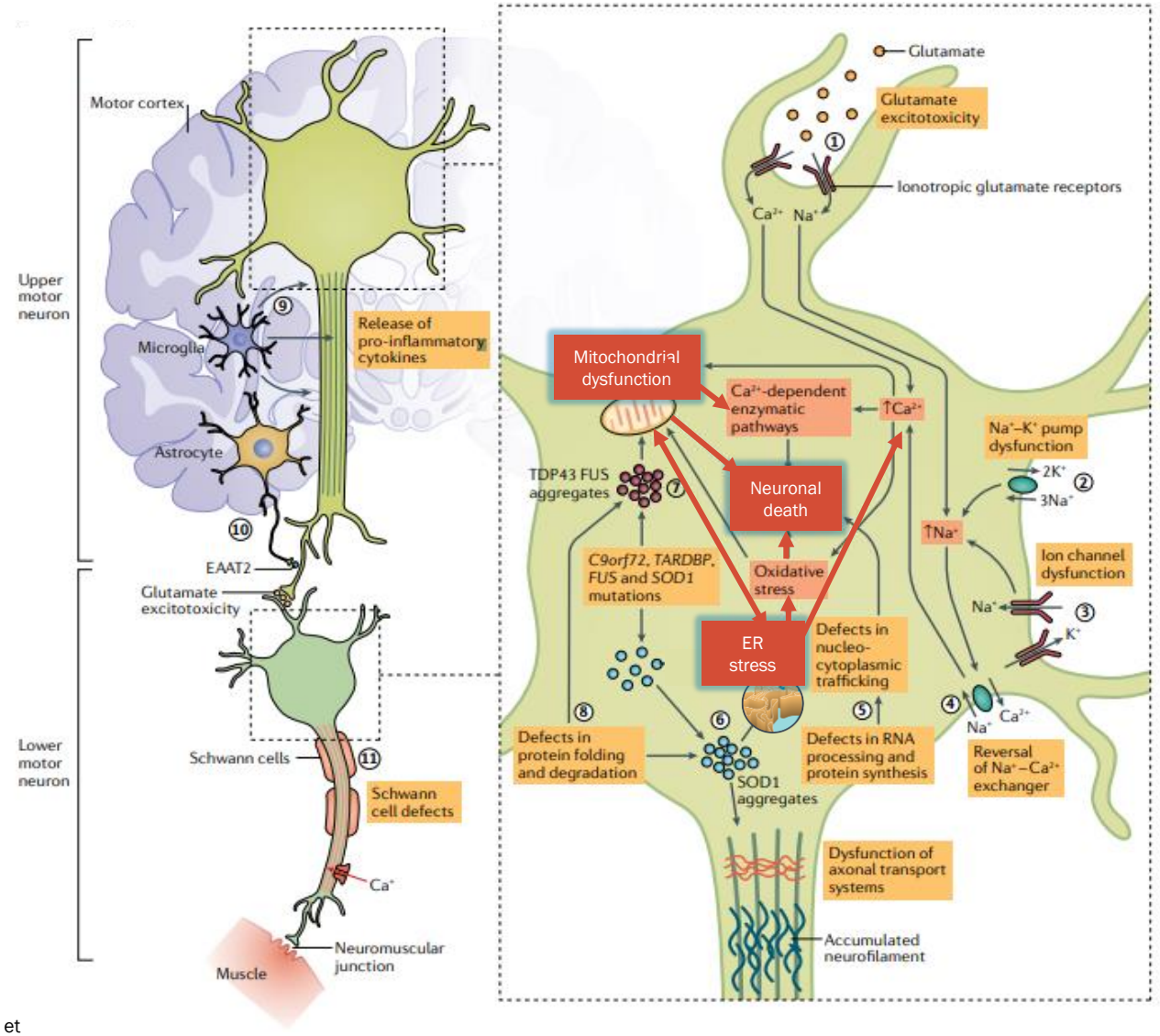
The Nobel Prize in Physiology or Medicine 2002 - NobelPrize.org

In ALS, Multiple Pathways May Converge on ER and Mitochondrial Dysfunction to Cause Neuronal Death

Multiple pathways are implicated in ALS with many thought to cause and exacerbate ER stress and mitochondrial dysfunction, two pathways central to neuronal death

Mitochondrial death proteins, including BAX, are upregulated in post-mortem ALS spinal cord samples, as are unfolded protein response (UPR) related proteins

Genetic causes of ALS, including the most well-known genes *SOD1, C9orf72* and *TDP43*, are mechanistically linked to mitochondrial and ER dysfunction



Adapted from Kiernan, M.C., Vucic, S., Talbot, K. et al. Improving clinical trial outcomes in amyotrophic lateral sclerosis. Nat Reviews Neurology 17, 104–118 (2021). https://doi.org/10.1038/s41582-020-00434-z

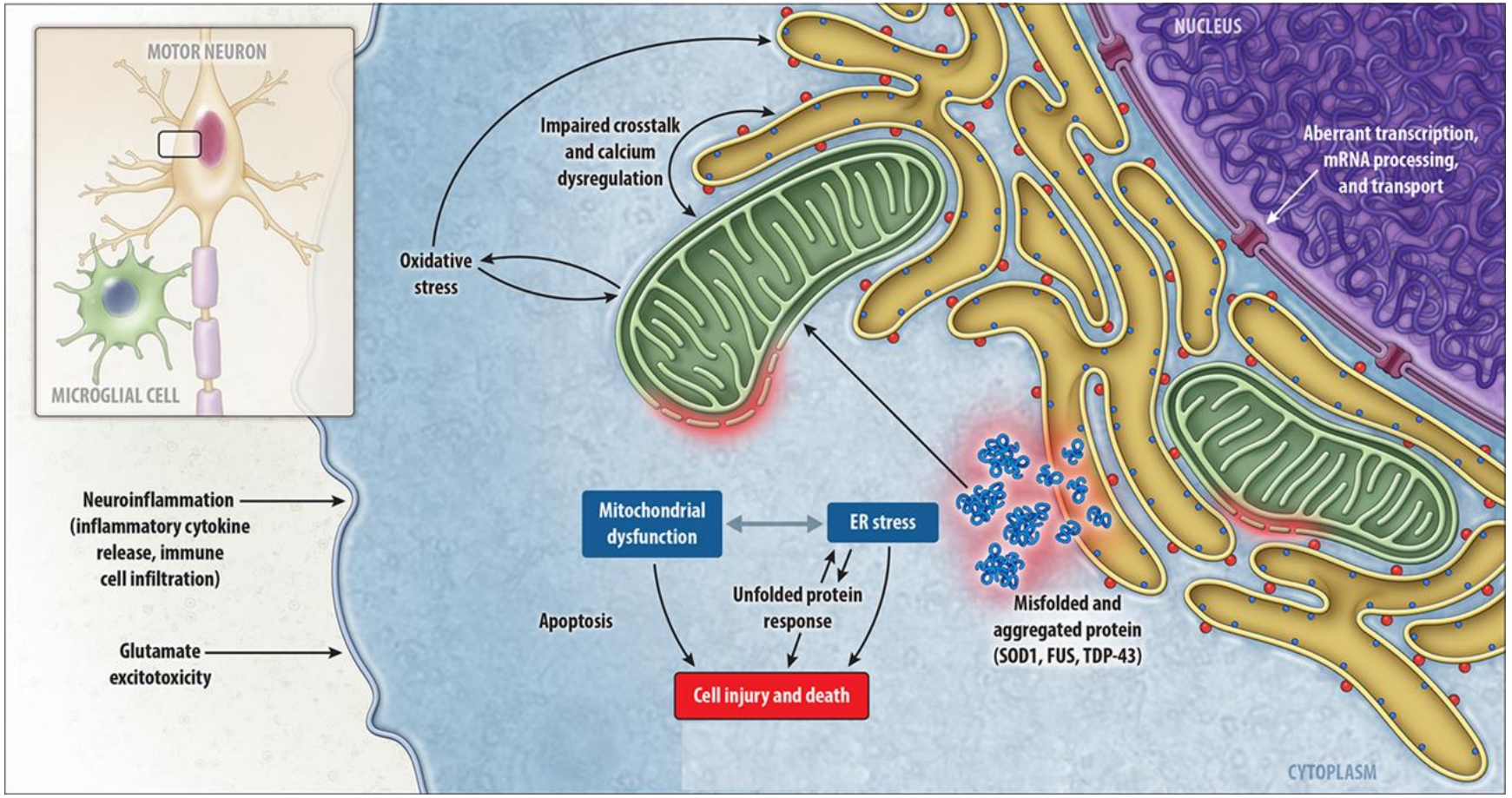
Mu, X Annals of Neurology 1996, Israelson A et al., 2010; Pickles S and Van de Velde C., 2012; Nishitoh H et al., 2008; Kiskinis E et al., 2014; Farg et al., 2012 Archana P et al., 2019; Huang C et al., 2020; Tan W et al., 2014; Choi SY et al., 2019; Mehta AR et al., 2021; Tsai Y-L et al., 2020; Nakaya T et al., 2018, Montibeller, L. Cell Stress Chaperones. 2018; Manfredi G, Kawamata H. Mitochondria and endoplasmic reticulum crosstalk in amyotrophic lateral sclerosis. Neurobiol Dis. 2016;90:35-42. doi:10.1016/j.nbd.2015.08.004; Smith EF, Shaw PJ, De Vos KJ. The role of mitochondria in amyotrophic lateral sclerosis. Neurosci Lett. 2019;710:132933. doi:10.1016/j.neulet.2017.06.052.

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]

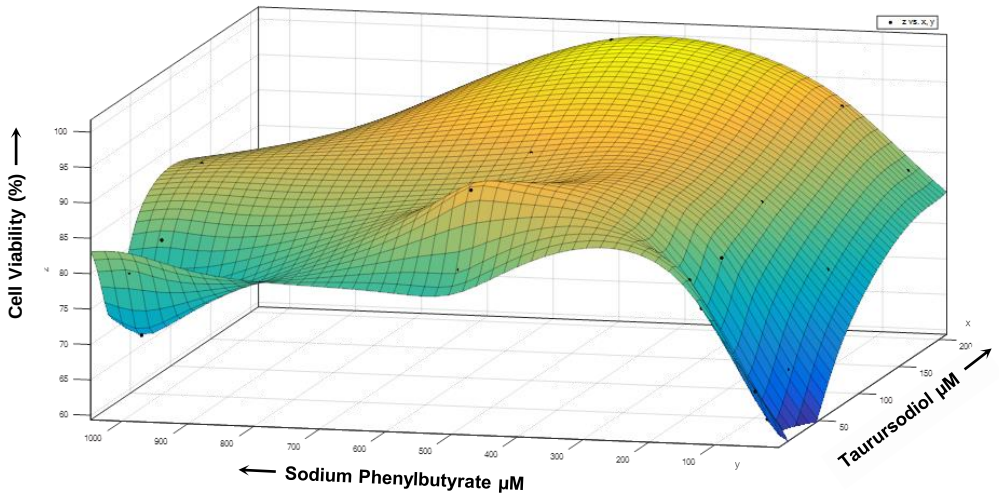


Figure from Cohen J, et al. Clinical trial design for a phase II, randomized, placebo-controlled trial of AMX0035 in amyotrophic lateral sclerosis (CENTAUR). Poster presented at: 28th International Symposium for ALS/MND; December 4–10, 2017; Boston, MA.

MOA of AMX0035 in ALS is unknown

1. Data on File. Amylyx Pharmaceuticals. 1. 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
- ☐ Potential to move directly into a Phase 3 pivotal trial
- ☐ Adjacencies and synergies with ALS
- ☐ Interest and support from KOLs and advocacy groups

Progressive Supranuclear Palsy (PSP) Selected as Next Indication for AMX0035

- **Clear unmet need**
  Typically fatal within just 5 to 8 years; no disease-modifying treatments for PSP
- **Strong scientific rationale**
  PSP leads to rapid & significant neurodegeneration and is characterized by tau protein deposition in affected regions of brain; AMX0035 shown preclinically to protect neurons against degeneration and clinically to lower tau
- **Biomarker evidence**
  AMX0035 demonstrated a statistically significant lowering of phosphotau181 & total tau in the CSF of people with Alzheimer's disease
- **Existing and robust understanding of the natural history of the disease**
  PSP progression is predictable and well understood
- **Potential to move directly into a Phase 3 pivotal trial**
  Preparing for Phase 3 study with ~600 adults in a randomized, placebo-controlled study
- **Adjacencies and synergies with ALS**
  Shares mechanistic characteristics with ALS – unfolded protein response, mitochondrial dysfunction and related cell death
- **Interest and support from KOLs and advocacy groups**
  Collaborated with key global academic leaders, people living with PSP, and advocacy groups

Upcoming Pivotal Phase 3 Study in Progressive Supranuclear Palsy (PSP)

PSP is Associated with Tau Protein

Rare neurological disorder that affects body movements, walking and balance, and eye movement. Pathology characterized by widespread neurodegeneration **associated with tau protein deposition** in subcortical regions of the brain.

Estimated prevalence of **5-7 in 100,000 worldwide**[1]

PSP is typically fatal within **5 to 8 years**[2,3]

AMX0035 Demonstrates Potent Impact on Tau[4, 5]

Data from Phase 2 PEGASUS study in Alzheimer's disease demonstrated that AMX0035 **lowered total tau by 64.9 pg/mL** and **lowered phosphorylated tau by 14.6 pg/mL** at week 24.

Select CSF Biomarkers Linear mixed effect model estimation	Change from Baseline to Week 24		Week 24 LS Mean (95% CI) Difference between AMX0035 and Placebo	p-value (nominal)
	AMX0035	Placebo		
Total Tau (pg/mL)	-64.9	8.8	-73.7 (-106.8, -40.7)	<0.0001
Phosphorylated Tau (pTau181) (pg/mL)	-14.6	-0.3	-14.4 (-21.5, -7.2)	0.0002

1. Shoeibi A., Olfati N., Litvan I. Frontrunner in translation: Progressive supranuclear palsy. Front. Neurol. 2019;10:1125. doi: 10.3389/fneur.2019.01125. Swallow D.M., Zheng C.S., Counsell C.E. Systematic review of prevalence studies of progressive supranuclear palsy and corticobasal syndrome. Mov. Disord. Clin. Pract. 2022;9:604–613. doi: 10.1002/mdc3.13489. 2. Williams DR, Lees AJ. Progressive supranuclear palsy: clinicopathological concepts and diagnostic challenges. Lancet Neurol 2009;8(3):270–279. 3. Guasp M., Molina-Porcel L., Painous C., Caballol N., Camara A., Perez-Soriano A., Sánchez-Gómez A., Garrido A., Muñoz E., Marti M.J. Association of PSP phenotypes with survival: A brain-bank study. Parkinsonism Relat. Disord. 2021;84:77–81. doi: 10.1016/j.parkreldis.2021.01.015. 4. Analysis conducted with biomarker core lab of the Mass General Institute for Neurodegenerative Disease (MIND) on CSF samples. Data from Phase 2 PEGASUS trial of AMX0035 for the treatment of Alzheimer's disease. Arnold et al. CTAD 2022. 5. Marie K. Bondulich, Tong Guo, Christopher Meehan, John Manion, Teresa Rodriguez Martin, Jacqueline C. Mitchell, Tibor Hortobagyi, Natalia Yankova, Virginie Stygelbout, Jean-Pierre Brion, Wendy Noble, Diane P. Hanger, Tauopathy induced by low level expression of a human brain-derived tau fragment in mice is rescued by phenylbutyrate, Brain, Volume 139, Issue 8, August 2016, Pages 2290–2306, https://doi.org/10.1093/brain/aww137

Potential of AMX0035 in Wolfram syndrome

Wolfram syndrome

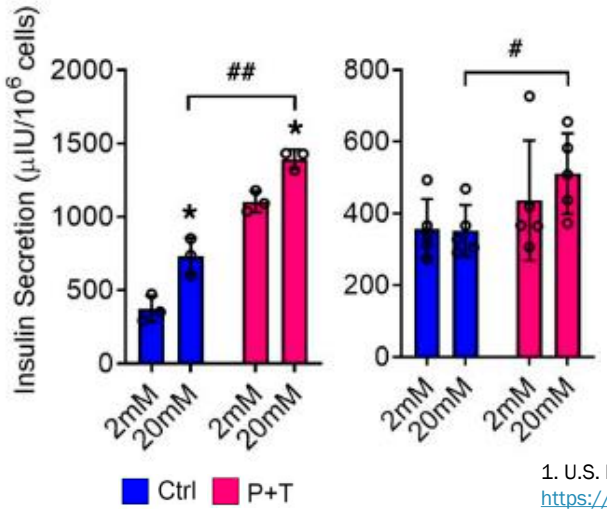
Ultra-rare disease, affecting ~5,000 people in U.S.,[1] with an estimated prevalence of 1 in 500,000 people worldwide.[2] Causes multi-system failure resulting in blindness, deafness, diabetes, ataxia, neurodegeneration, and typically death by early adulthood. Characterized as a prototypical disease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

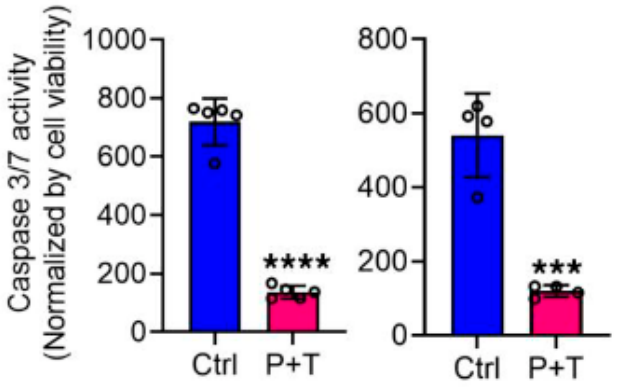
Effect of AMX0035 in Preclinical Studies[3]

JCI insight

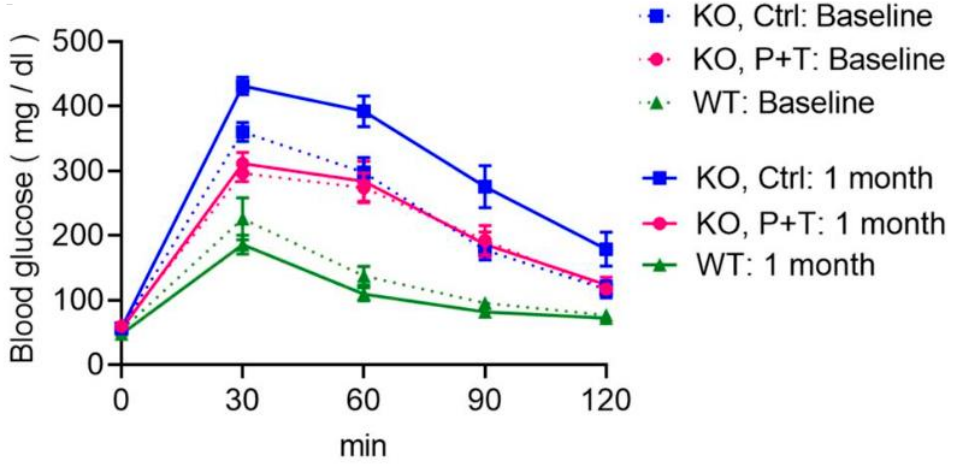
Improved WFS1 protein expression and increased insulin secretion in β cells with the WFS1 variant (Figure)



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

24 weeks

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

Primary Efficacy Outcomes

- C-peptide response
- Safety and tolerability

Secondary Efficacy Outcomes

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

First participant dosed in April 2023

Topline results anticipated in 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

59

issued patents worldwide

47

additional patents pending

+

many additional filings planned

FISH & RICHARDSON

Patents and patent applications cover:

- Composition of matter of the combination of PB and TURSO, including in the U.S. – through 2033*
  - And in some territories, the combination of related compounds
- Method of use of the combination and related combinations for treating neurodegenerative disease
- Formulation of the combination and manufacturing process
- Methods of treating ALS based on clinical trial results – through 2040
- Five orange book listed patents directed to RELYVRIO and/or its method of use

NCE exclusivity and Orphan exclusivity granted; protects against generics (7 years in US, 10 in EU, 8 in Canada)

* Once approved in a jurisdiction, we plan to seek any applicable patent term extensions (PTE). PTE applications have been filed in the 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

Tammy Sarnelli

Global Head of Regulatory Affairs

30+ years in Regulatory, including at Biogen leading approvals of Tysabri and Tecfidera Former Head of Global Regulatory Affairs, Neurology & Immunology at EMD Serono

Keith White

Head of Global Market Access

20+ years in Market Access, including at Genentech, Intermune, and Intercept

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

Debra Canner

Chief HR Officer

Former CHRO at Akamai, Juniper, several others; VP HR at Genzyme

Timothy Lee

Head of US Commercial Development and Global Commercial Training

20+ years of sales, marketing and product commercialization experience, including at Alexion Pharmaceuticals, Novartis, and Pfizer

Jim Frates

Chief Financial Officer

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

Tom Holmes

Global Head of Supply Chain

Former Head of Global External Manufacturing at Biogen

Maryellen Garrett

Head of Global Accounting and Finance Operations

CPA with 20+ years of finance and accounting experience, including at Entasis Therapeutics, Cubist Pharmaceuticals and PWC

Shauna Horvath

Head of Global Marketing

15+ years of marketing experience, including at Cambridge BioMarketing

Margaret Olinger, MBA

Chief Commercial Officer

2nd commercial employee at Alexion; helped oversee launch of Soliris and Strensiq at Alexion. 30+ years in commercial

John Landry

Head of Commercial Operations

25+ years of sales and operations experience, including at Akcea Therapeutics, Alexion Pharmaceuticals and Novartis

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

Patrick Yeramian, MD, MSC, MBA

Chief Medical Officer

Over 25 years as clinical trialist, CMO, and clinical consultant including as CMO of Viragen

Machelle Manuel, PhD

Head of Global Medical Affairs

Former Head of Global Medical Scientific Affairs at Ironwood

20+ years in medical affairs

Financial Overview

Amylyx Select Financial Data

Statement of Operations ($ thousands except per share data)	1Q23	4Q22
Product revenue, net	$ 71,428	$ 21,885
Cost of sales	5,283	2,821
Research and development	24,192	22,813
Selling, general and administrative	44,006	40,844
Total operating expenses	$ 73,481	$ 66,478
Net income (loss)	$ 1,573	$ (42,704)
Net income (loss) per share - diluted	$ 0.02	$ (0.65)

Balance Sheet ($ thousands)	1Q23	4Q22
Cash, cash equivalents and short-term investments	$ 345,674	$ 346,945

Focused Priorities

Helping people gain access to RELYVRIO® in the U.S. and ALBRIOZA™ in Canada, bringing a much-needed new treatment option to people with ALS

ALBRIOZA Commercial Launch in Canada

RELYVRIO Commercial Launch in U.S.

Final CHMP Opinion expected Fall 2023 with decision in late Q4'23 at the earliest*

* Amylyx intends to seek re-examination of the negative CHMP opinion as announced on June 23, 2023.

AMYLYX

Thank you.

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

Every day, we strive for better therapies.