



Company Overview

Our mission is to end the suffering caused by neurodegenerative diseases. Every day, we strive to bring new treatments to people who deserve better.

NASDAQ: AMLX
June 2022

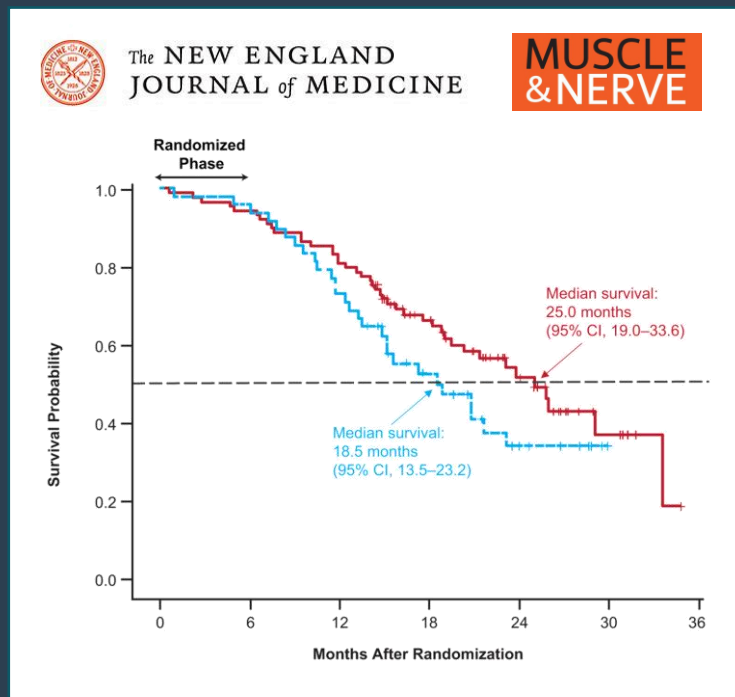
Disclaimer

These materials include express and implied “forward-looking statements,” including forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward looking statements include all statements that are not historical facts, and in some cases, can be identified by terms such as “may,” “might,” “will,” “could,” “would,” “should,” “expect,” “intend,” “plan,” “objective,” “anticipate,” “believe,” “estimate,” “predict,” “potential,” “continue,” “ongoing,” or the negative of these terms, or other comparable terminology intended to identify statements about the future. Forward-looking statements contained in these materials include, but are not limited to, statements regarding our product candidates (including AMX0035 ongoing and future clinical trials), timing of the receipt of regulatory approvals, future results of operations or financial condition, business strategy and plans and objectives of management for future operations. By their nature, these statements are subject to numerous risks and uncertainties, including the impact that the ongoing COVID-19 pandemic will have on our development activities and operations, as well as those risks and uncertainties set forth in our US Securities and Exchange Commission filings that could cause actual results, performance or achievement to differ materially and adversely from those anticipated or implied in the statements. You should not rely upon forward looking statements as predictions of future events. Although our management believes that the expectations reflected in our statements are reasonable, we cannot guarantee that the future results, performance or events and circumstances described in the forward-looking statements will be achieved or occur. Recipients are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date such statements are made and should not be construed as statements of fact. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, any future presentations or otherwise, except as required by applicable law. Certain information contained in these materials and any statements made orally during any presentation of these materials that relate to the materials or are based on studies, publications, surveys and other data obtained from third-party sources and our own internal estimates and research. While we believe these third-party studies, publications, surveys and other data to be reliable as of the date of these materials, it has not independently verified, and we make no representations as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, no independent source has evaluated the reasonableness or accuracy of our internal estimates or research and no reliance should be made on any information or statements made in these materials relating to or based on such internal estimates and research.

Amylyx Highlights

1st

AMX0035 is the first drug candidate to show benefit on function and survival in ALS



Approved in Canada with conditions as ALBRIOZA™

Pending regulatory decisions in U.S. and Europe –filings supported by robust Phase 2 clinical data published in NEJM

DEC
2021



NDA accepted;
PDUFA 9/29/22

FEB
2022



MAA
validated

June
2022



ALBRIOZA™
approved for use



Strong global IP position

Composition of matter patents issued; orphan and NCE exclusivity expected



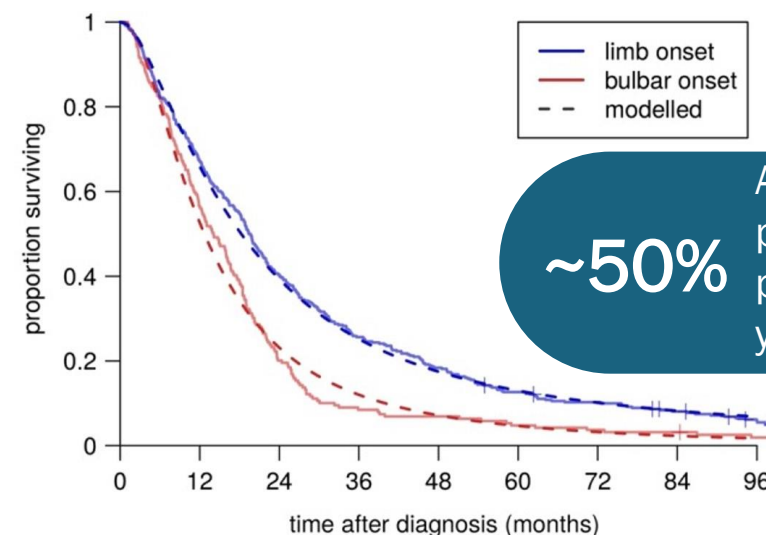
Why ALS

“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 living with ALS, and co-founder of I AM ALS

ALS is Relentlessly Progressive, Debilitating, and Universally Fatal

- ◆ ALS leads to deteriorating muscle function, the inability to move and speak, respiratory paralysis, and death^{1,2}
- ◆ Diagnosis between ages 40 and 75
- ◆ >90% of people with ALS have no family history of the disease



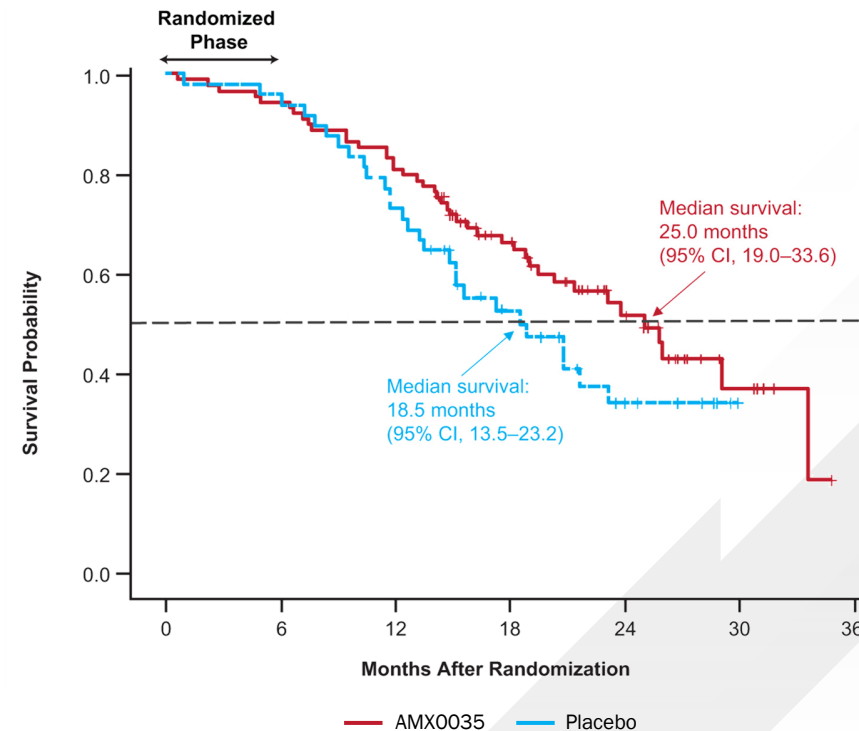
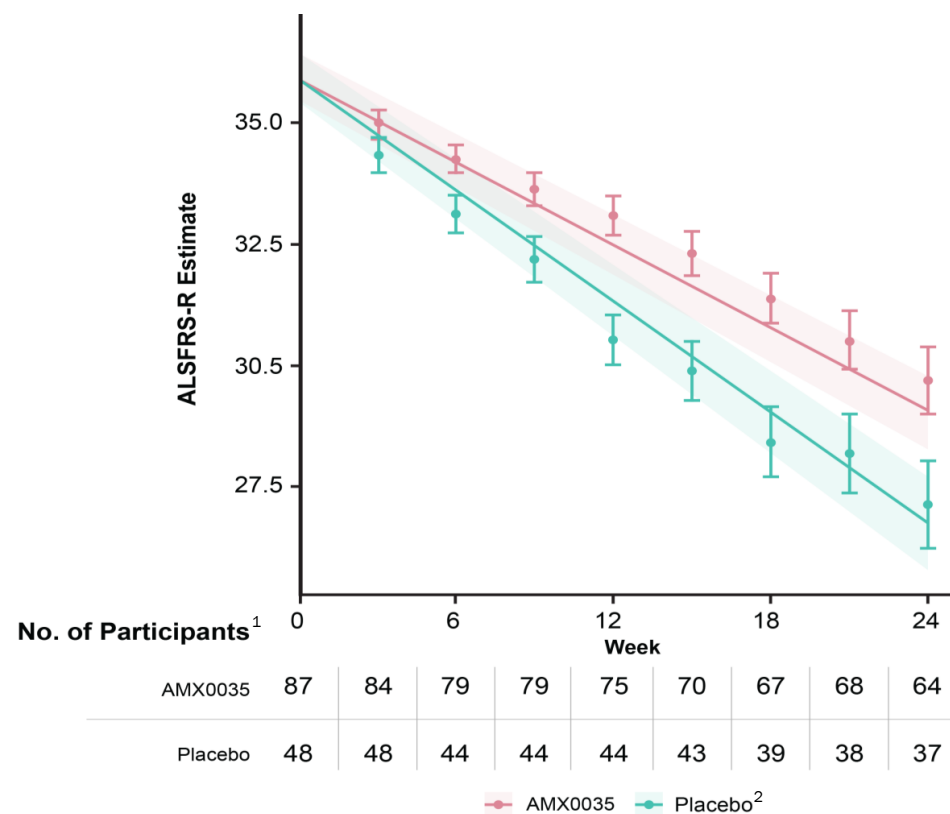
¹- Brown RH, Al-Chalabi A. *N Engl J Med*. 2017;377(2):162-172. ²- Al-Chalabi A, et al. *Lancet Neurol*. 2016;15(11):1182-1194 ³- Knibb JA, Keren N, Kulka A, et al. *J Neurol Neurosurg Psychiatry*. 2016;87(12):1361-1367.

Phase 2 CENTAUR Trial Results

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



The NEW ENGLAND
JOURNAL of MEDICINE



¹Two 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.

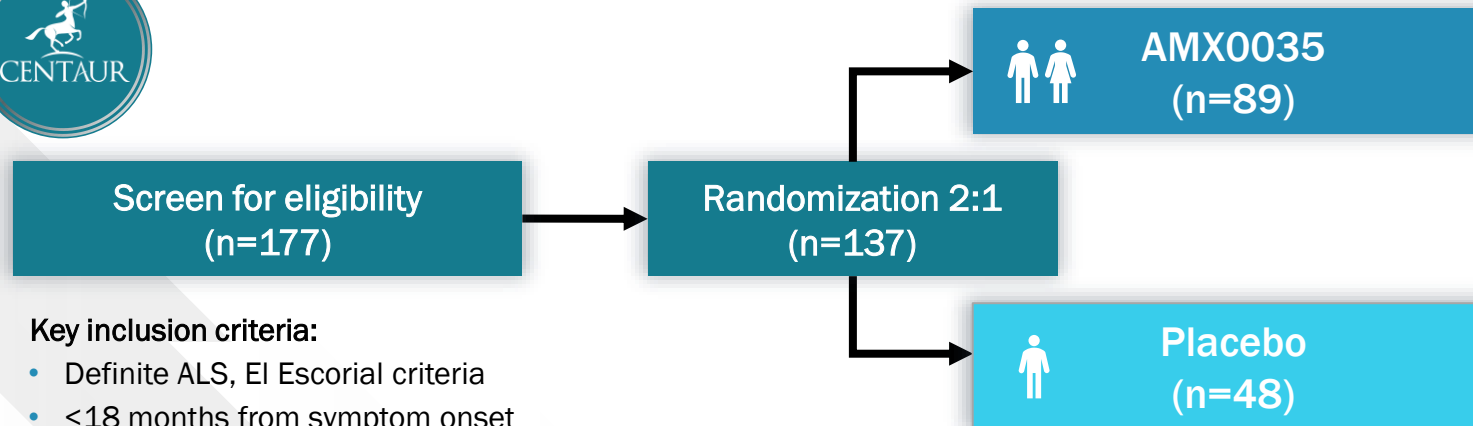
Phase 2 CENTAUR Trial Design for AMX0035

Primary Objectives:

- To determine the **safety** and **tolerability** of AMX0035 taken orally or via feeding tube twice daily
- To measure the **impact** of AMX0035 on ALSFRS-R slope



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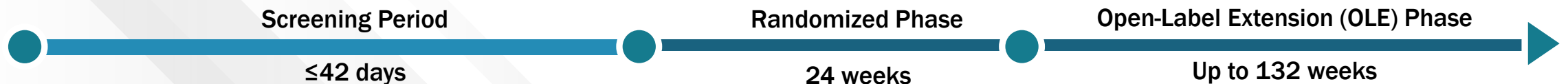


Primary Efficacy Outcomes

- Safety and tolerability
- Rate of decline in ALSFRS-R

Key inclusion criteria:

- Definite ALS, El Escorial criteria
- <18 months from symptom onset
- Slow vital capacity (SVC) >60%
- Riluzole/edaravone use permitted



Baseline Characteristics – CENTAUR



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Characteristic	AMX0035 (n=87)	Placebo (n=48)
Age (y), mean (SD)	57.6 (10.4)	57.3 (7.6)
BMI (kg/m ²), mean (SD)	26.9 (4.4)	26.4 (5.8)
Pre-baseline ALSFRS-R slope (points/mo), mean (SD)	0.95 (0.4)	0.93 (0.6)
Months since ALS diagnosis, mean (SD)	5.9 (3.3)	6.3 (3.2)
Months since ALS symptom onset, mean (SD)	13.5 (3.8)	13.6 (3.6)
Edaravone or riluzole use at or prior to study entry, n (%)	62 (71)	42 (88)
Edaravone use	22 (25)	24 (50)
Riluzole use	59 (68)	37 (77)
Use of both	19 (22)	19 (40)
Bulbar onset, n (%)	26 (30)	10 (21)
SVC (% predicted), mean (SD)	83.6 (18.2)	83.9 (15.9)
Mean ALSFRS-R total score, mean (SD)	35.7 (5.8)	36.7 (5.1)
ATLIS total score (% predicted), mean (SD)	56.8 (20.1)	53.9 (20.9)
ATLIS upper extremity score (% predicted), mean (SD)	54.8 (24.4)	51.4 (25.2)
ATLIS lower extremity score (% predicted), mean (SD)	57.6 (24.9)	57.1 (25.8)

Average age

58

Time from symptom onset

13.5 months

Time from diagnosis

6 months

Bulbar onset

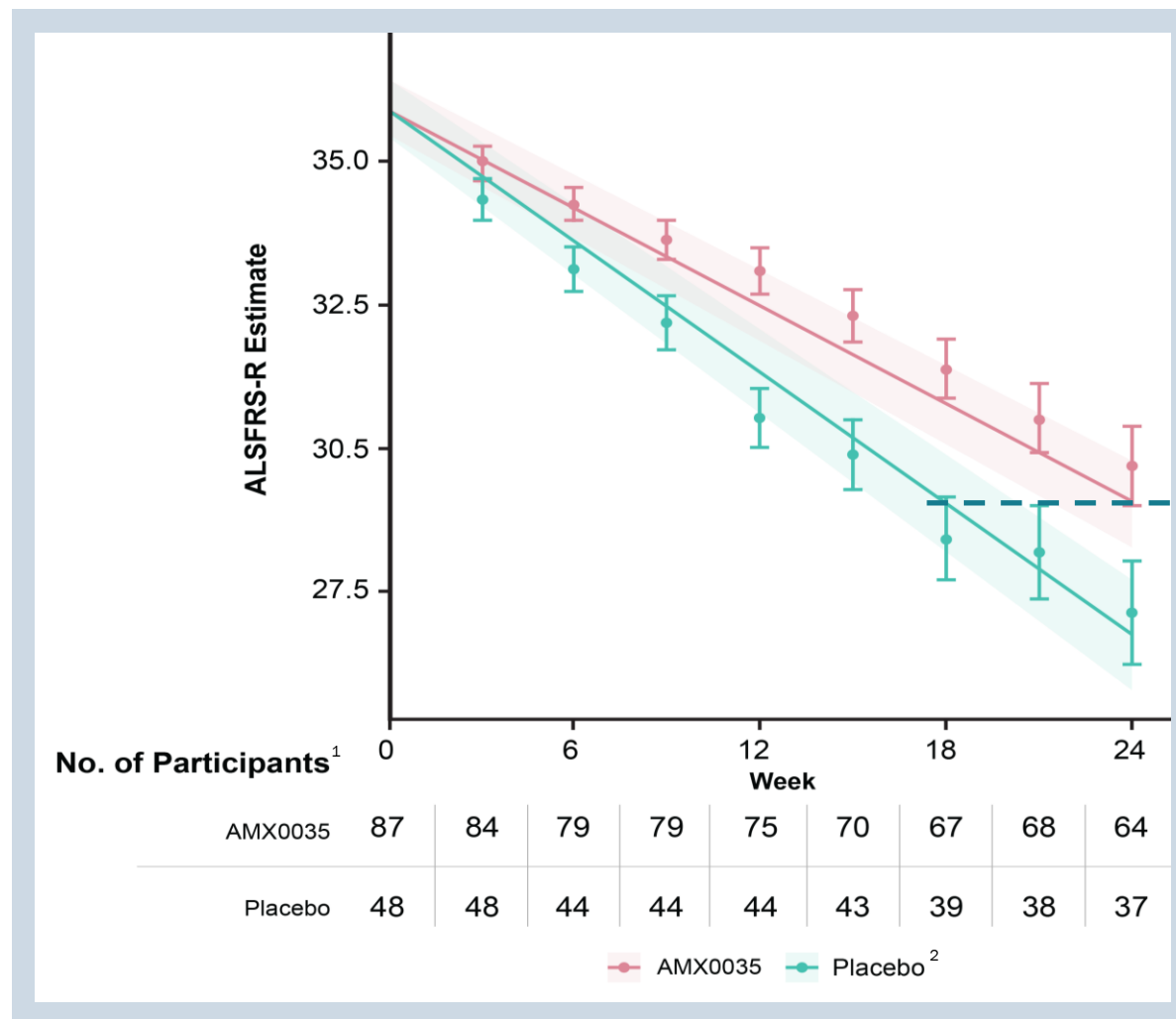
26%

On riluzole or edaravone
at or prior to study entry

77%

CENTAUR Trial Results

Statistically Significant Benefit on the ALSFRS-R, the Gold Standard Clinical Scale in ALS



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Trial of Sodium Phenylbutyrate–Taurursodiol for Amyotrophic Lateral Sclerosis

S. Paganoni, E.A. Macklin, S. Hendrix, J.D. Berry, M.A. Elliott, S. Maiser, C. Karam, J.B. Caress, M.A. Owegi, A. Quick, J. Wymer, S.A. Goutman, D. Heitzman, T. Heiman-Patterson, C.E. Jackson, C. Quinn, J.D. Rothstein, E.J. Kasarskis, J. Katz, L. Jenkins, S. Ladha, T.M. Miller, S.N. Scelsa, T.H. Vu, C.N. Fournier, J.D. Glass, K.M. Johnson, A. Swenson, N.A. Goyal, G.L. Pattee, P.L. Andres, S. Babu, M. Chase, D. Dagostino, S.P. Dickson, N. Ellison, M. Hall, K. Hendrix, G. Kittle, M. McGovern, J. Ostrow, L. Pothier, R. Randall, J.M. Shefner, A.V. Sherman, E. Tustison, P. Vigneswaran, J. Walker, H. Yu, J. Chan, J. Wittes, J. Cohen, J. Klee, K. Leslie, R.E. Tanzi, W. Gilbert, P.D. Yeramian, D. Schoenfeld, and M.E. Cudkowicz

2.32 point difference, $p=0.03$

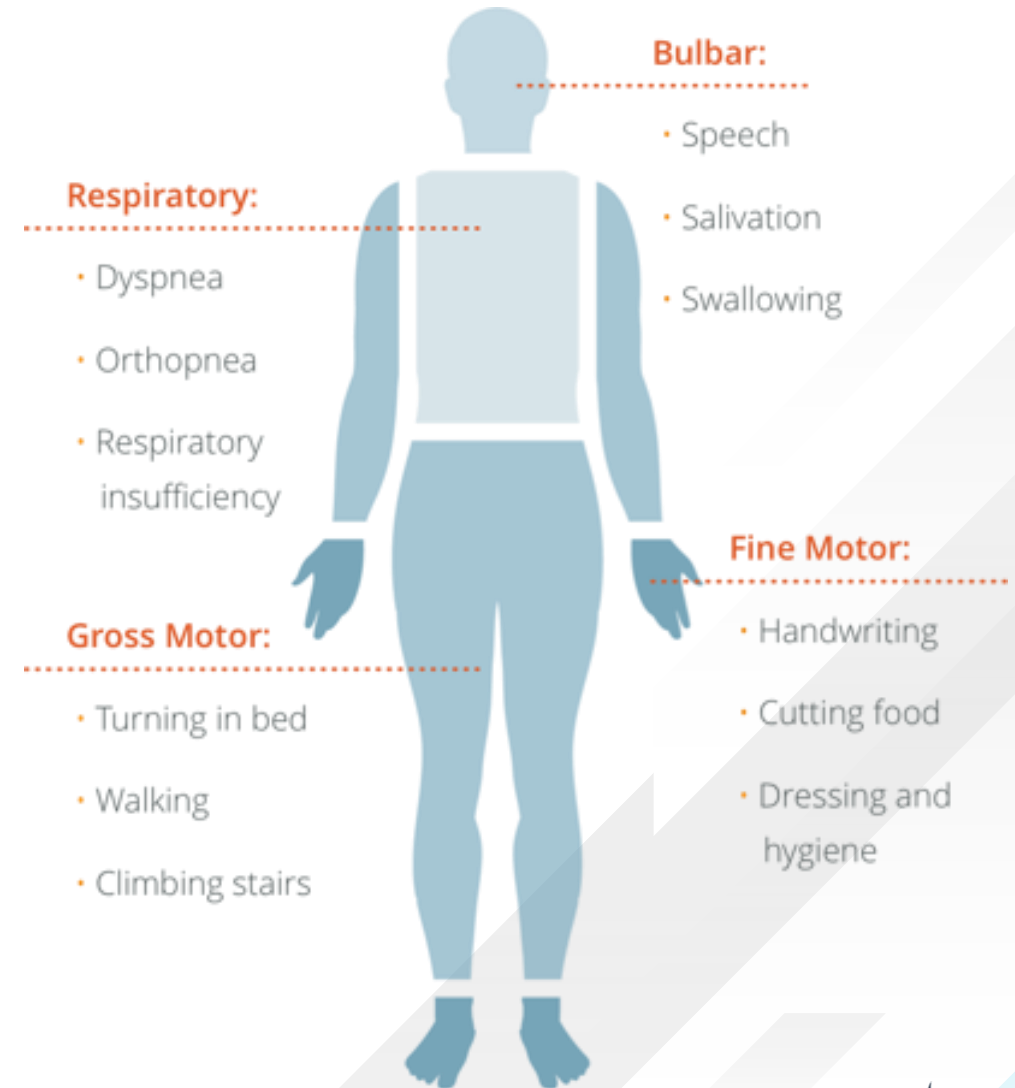
“Each category in the ALSFRS-R seems clinically important, and because each domain includes only five levels that span 0 (cannot do) to 4 (normal), prevention of even 1 unit of worsening in a single domain seems meaningful and desirable for individuals with ALS”.³

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.

The CENTAUR ALS Trial

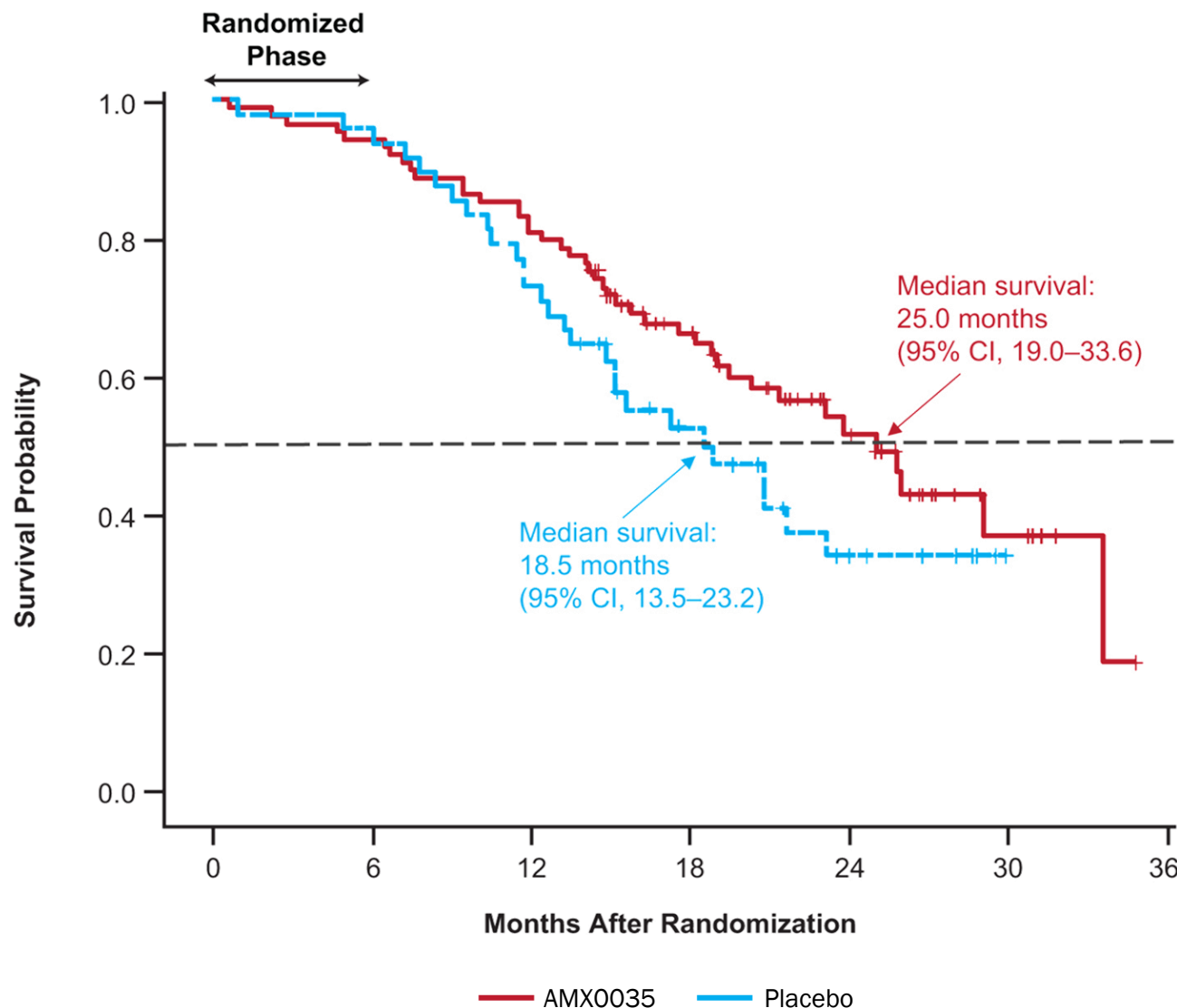
ALSFRS-R – The Most Widely Used ALS Endpoint

- ◆ A small change of just 1-2 points in the ALSFRS-R score can indicate a significant reduction in function
- ◆ The heterogeneity of disease spread and the rate of progression mean that the ALSFRS-R score remains individual in nature. Two people with similar overall scores can still exhibit very different symptoms



CENTAUR Trial Results

AMX0035 Resulted in Longer Lifespan for People with ALS



Treatment with AMX0035 starting at baseline (~6 months earlier) resulted in a 6.5 month difference in survival (HR = 0.56, p=0.02)

*Note: This is an ITT (all 137 patients) analysis

Survival defined as All Cause Mortality (True Overall Survival)

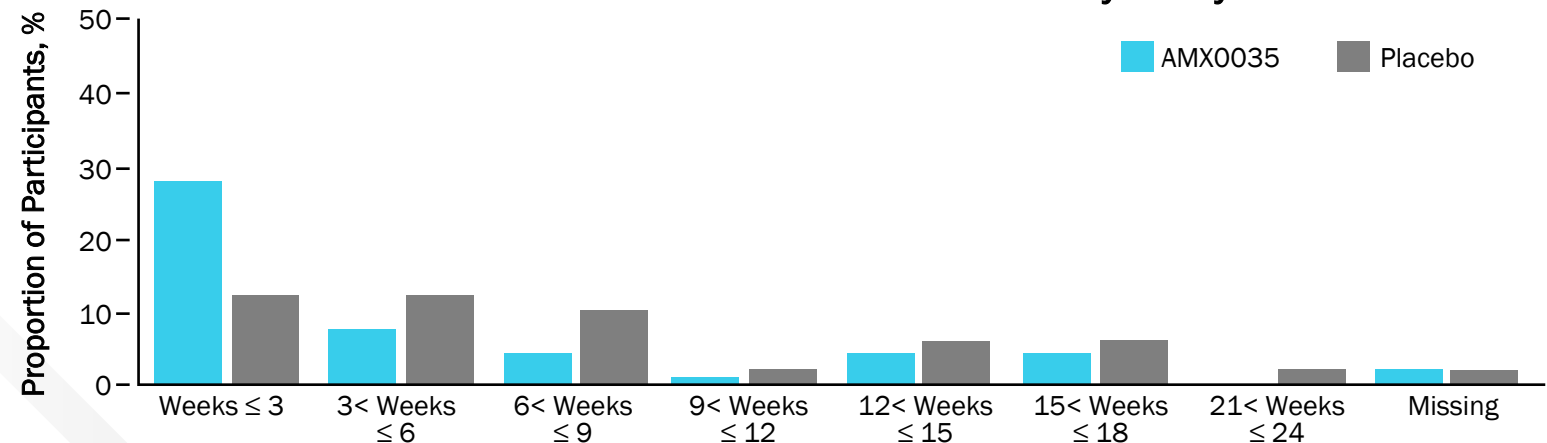
Note: CI = Confidence Interval; HR = Hazard Ratio

Adverse Events (AEs) – CENTAUR

- Nearly all participants (AMX0035, 97%; placebo, 96%) reported one or more AEs during the trial
 - Most did not lead to modification or interruption of study drug dosing and were not considered related to treatment
- Events that occurred with greater ($\geq 2\%$) frequency in the AMX0035 group were primarily GI
 - GI events in the AMX0035 group were reported most frequently in the first three weeks

	AMX0035 (n=89)	Placebo (n=48)	Overall (n=137)
Participants with at least 1 AE – n (%)	86 (97)	46 (96)	132 (96)
Number of distinct events	618	328	946
Drug interrupted due to AE – n (%)	13 (15)	6 (12)	19 (14)
Dose reduced due to AE – n (%)	4 (4)	0	4 (3)
Drug withdrawn due to AE – n (%)	17 (19)	4 (8)	21 (15)
Due to AE considered related	13 (15)	1 (2)	14 (10)
Due to AE considered unrelated	4 (4)	3 (6)	7 (5)

Incidence of Gastrointestinal Adverse Events by Study Week





American Academy of Neurology (AAN) 2021

Long-Term Survival of Participants in the CENTAUR Trial of AMX0035 for ALS

Received Merit of Distinction Award

Distinction is awarded to the abstract deemed to be the top in its topic category in quality of study and interest to the neurologic community

Plenary Session Presentation

Session highlights issues most critical to practicing neurologists, including abstracts related to new therapeutic developments. Amylyx presentation focused on long-term survival benefit of AMX0035

Top Science Press Conference

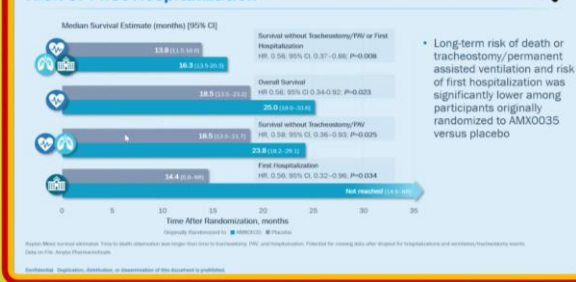
Selected by the Chair of AAN's Science Committee to be featured at the Top Science Press Conference held prior to the meeting

13,000+ virtual attendees from the United States, Canada, Europe, Asia, South America and more



Data Presented:
Significantly lower long-term risk of death or tracheostomy/permanent assisted ventilation and first hospitalization with AMX0035

Long-Term Risk of Death, Tracheostomy/PAV and Risk of First Hospitalization



Sabrina Paganoni, MD, PhD

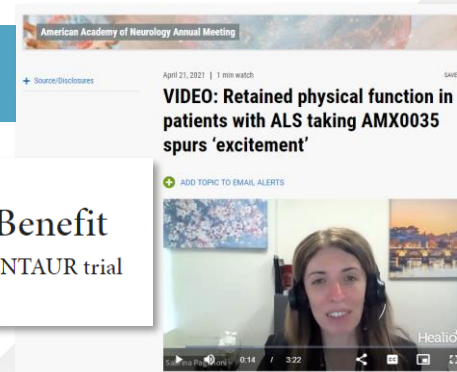
Top Science Press Conference generated additional coverage

Meeting Coverage > AAN

Novel ALS Drug Continues to Show Survival Benefit

— Median time to first hospitalization not yet reached with AMX0035 in CENTAUR trial

by Ed Susman, Contributing Writer, MedPage Today April 19, 2021



Path to Patients

“The CENTAUR study was designed and run through NEALS, was supported by a partnership between The ALS Association and ALS Finding a Cure, and is a phenomenal example of what can happen when a community works closely together.”

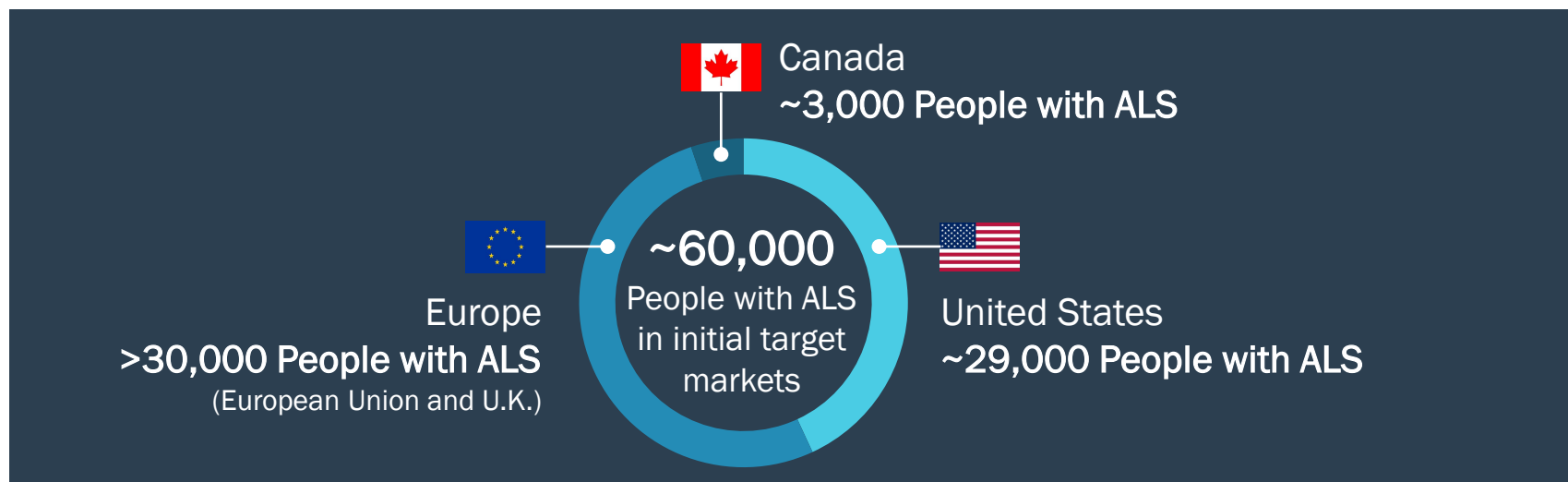
Dr. Merit Cudkowicz, M.D., Chief Medical Officer of ALS Finding a Cure®, Director of the Sean M. Healey & AMG Center for ALS, Chief of Neurology at Mass General, and the Julianne Dorn Professor of Neurology at Harvard Medical School.

Note: NEALS is the Northeast ALS Consortium



The ALS Market

A Large, Global Orphan Disease Market with Significant Unmet Needs



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



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

Regulatory Update

Approved in Canada as ALBRIOZA™
NDA under review for approval by FDA; MAA under review by EMA



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JOURNAL of MEDICINE



Now approved in
Canada; potential for
approval in the U.S.
in Q3'22

Accepted for
Priority Review

December 2021



FDA Advisory
Committee: 3/30/22

PDUFA:
9/29/22

MAA
validated

February 2022



Approved as
ALBRIOZA

June 2022



Expect ALBRIOZA
to be
commercially
available by the
end of July

Canada | Path to Commercialization

1st

First Regulatory Approval for Amylyx Worldwide

Moving with urgency to bring ALBRIOZA™ to Canadians living with ALS as quickly as possible. 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 approximately 3,000 Canadians living with ALS.



Navigating Complex Reimbursement System

Reimbursement pathway is determined by Health Technology Assessment recommendations from CADTH and INESS. Reimbursement process, which is central to a full product launch, can take 6-12 months or longer to complete, depending on payer. Amylyx Care Team (ACT) is ready to assist with eligibility and enrollment support.



17

Well Prepared and Ready to Launch

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

Chris Aiello

Head of Canada and
General Manager



Julie Girodat

Head of Patient Services
& Distribution



Tracey Jason, PhD

Head of Medical Affairs



Jason Lee

Head of Market Access



Blaine MacNeil

Head of Sales, Marketing
and Commercial Operations



Team

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

Joshua Cohen BSE

Co-CEO, Co-Founder, and Director

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

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, Co-Founder, 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 Account Management and 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 Accounting and Finance Operations

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

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

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 Planning and Operations

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

Shauna Horvath

Head of Global Marketing

15+ years of marketing experience, including at Cambridge BioMarketing

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

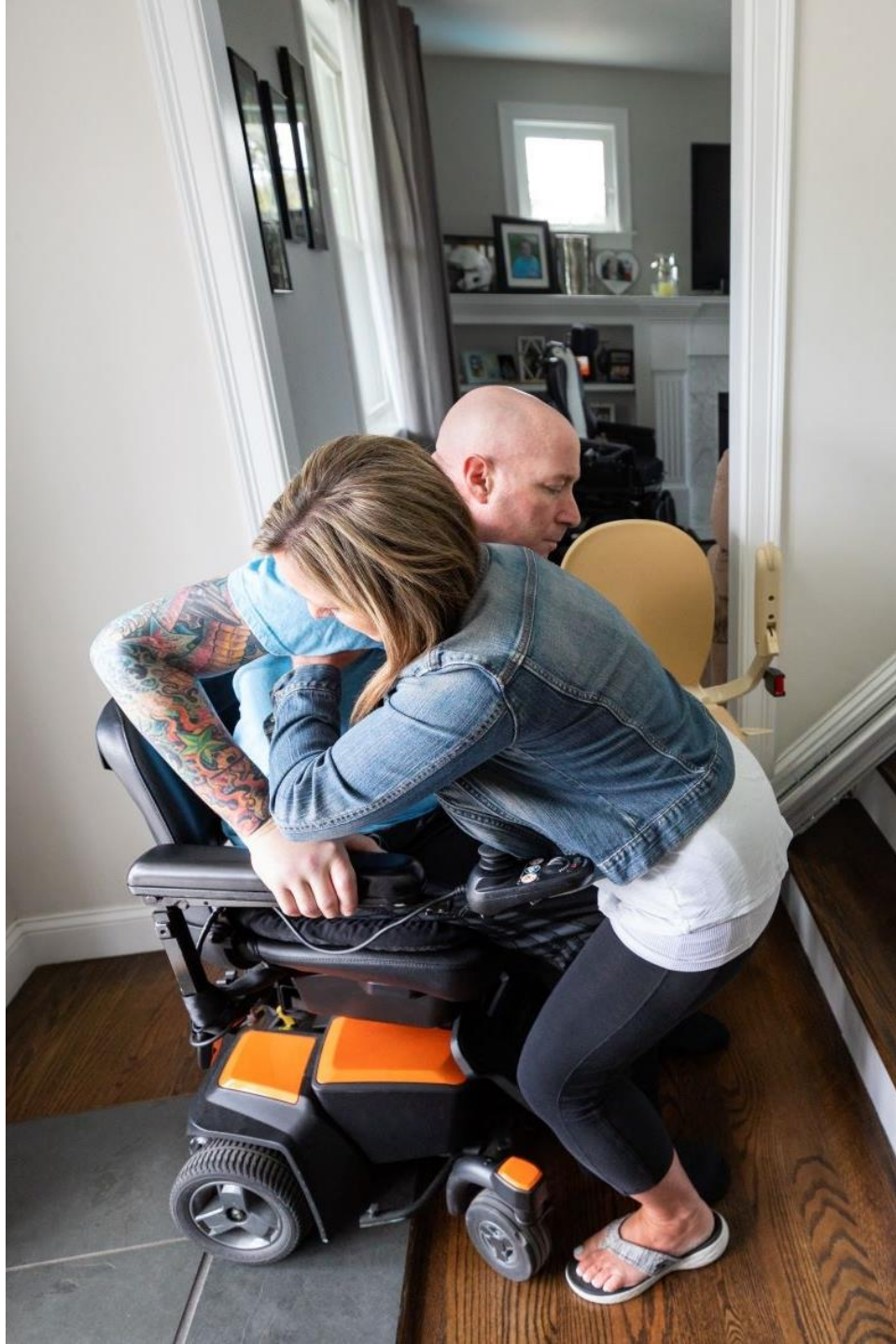
Dave MacLeod

Head of Patient Services and Commercial Distribution

20+ years of biotech and pharma experience, including at Intercept Pharmaceuticals, inVentiv Health, EMD Serono, Express Scripts and Genzyme

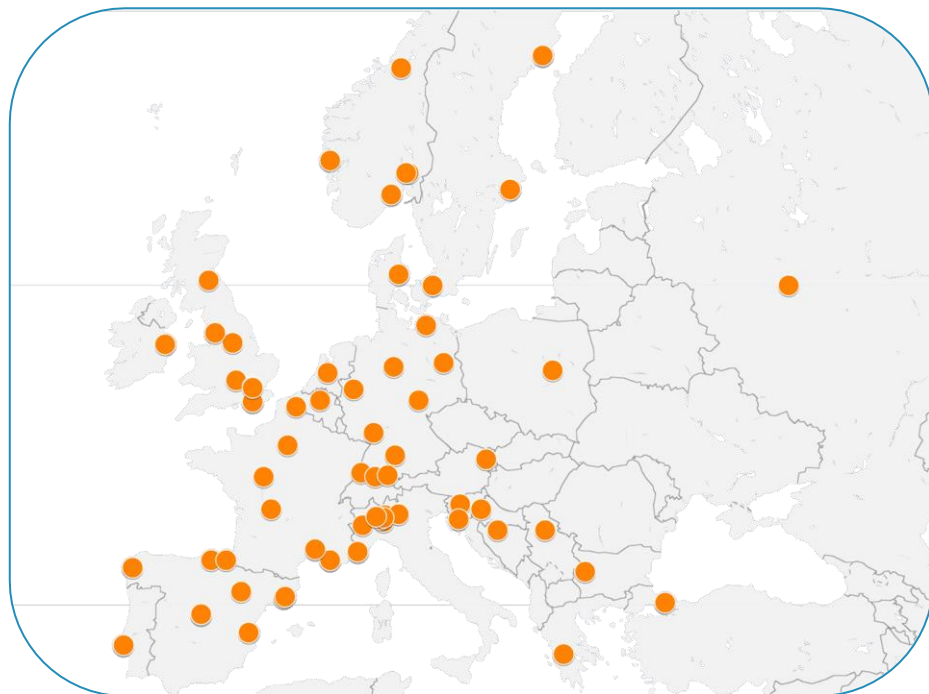
PHOENIX Phase 3 Trial

Designed to provide additional safety and efficacy data on AMX0035 for the treatment of ALS to further support our global regulatory efforts



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

Designed to Support Global Regulatory Efforts and Continue to Provide Data on AMX0035



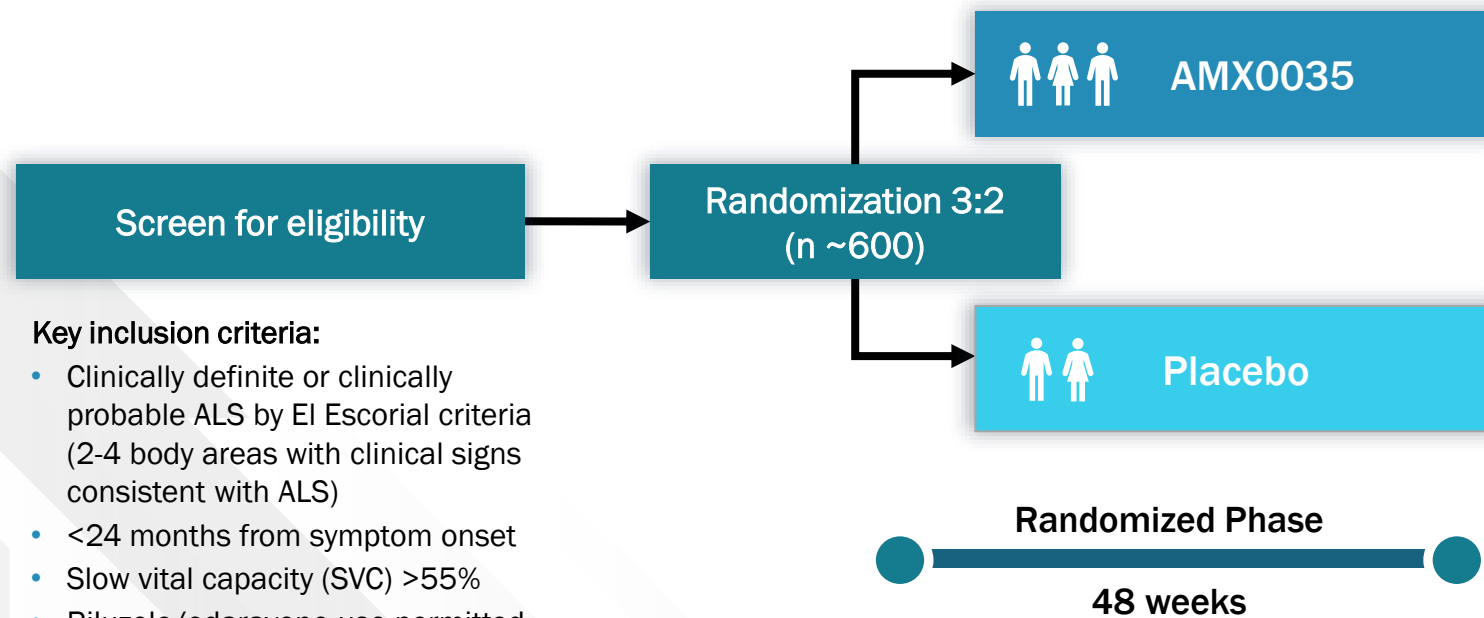
ENCALS



NEALS
Northeast Amyotrophic Lateral Sclerosis Consortium

PHOENIX Trial Design for AMX0035

Similar inclusion-exclusion criteria as CENTAUR; substantially greater statistical power



Primary Efficacy Outcomes

- Joint assessment of function and survival
- Safety and tolerability

Key Secondary Efficacy Outcomes

- Assessment of Function (ALSFRS-R)
- Survival
- Slow vital capacity (SVC)
- ALSAQ-40*
- EQ5D-5L (QOL)**
- Decline in King's and MiToS Stages

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

**Standard quality of life measure

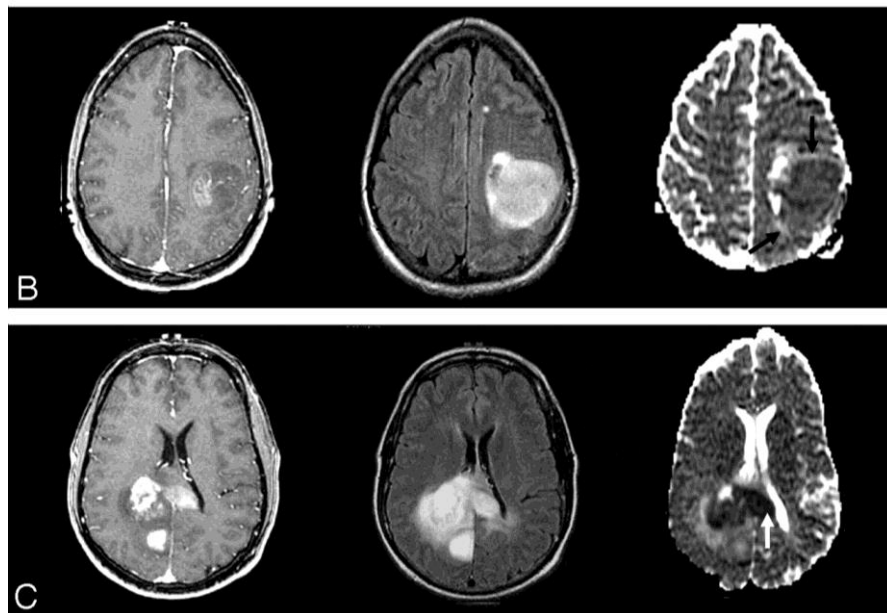
AMX0035

A Broad Therapy to Treat
Diseases of Neurodegeneration

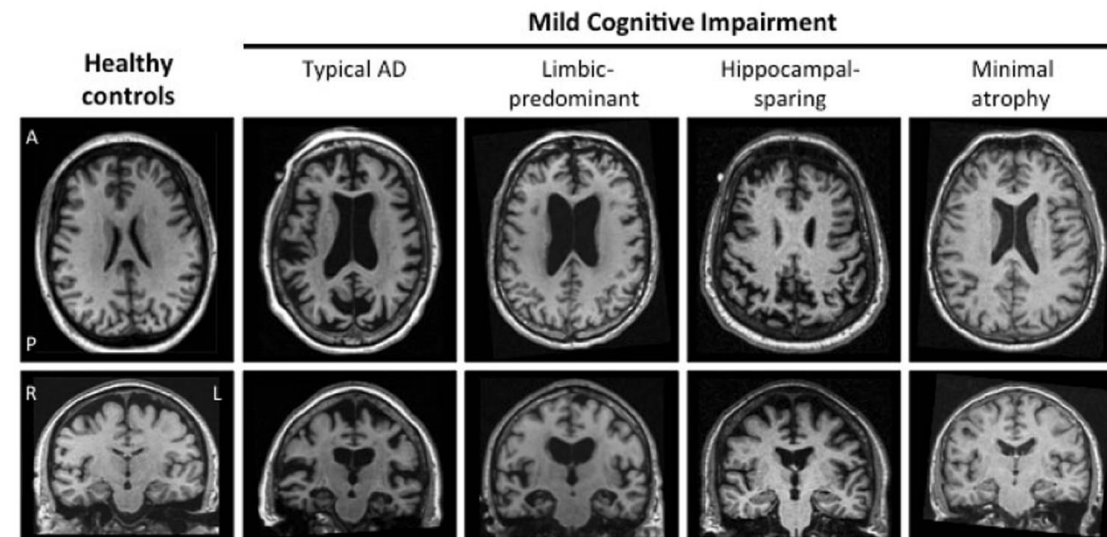


Neurodegenerative Diseases are the Biological Opposite of Cancer

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

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

Since this seminal work, the endoplasmic reticulum unfolded protein response (UPR) and the mitochondrial Bax pathway have been identified as key mediators of cell death

The Nobel Prize in Physiology or Medicine 2002



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)

nature reviews molecular cell biology

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Review Article | [Published: 21 October 2019](#)

Mitochondria as multifaceted regulators of cell death

[Florian J. Beck](#) & [Stephen W. G. Tait](#)

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

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Endoplasmic reticulum stress: cell life and death decisions

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

nature reviews drug discovery

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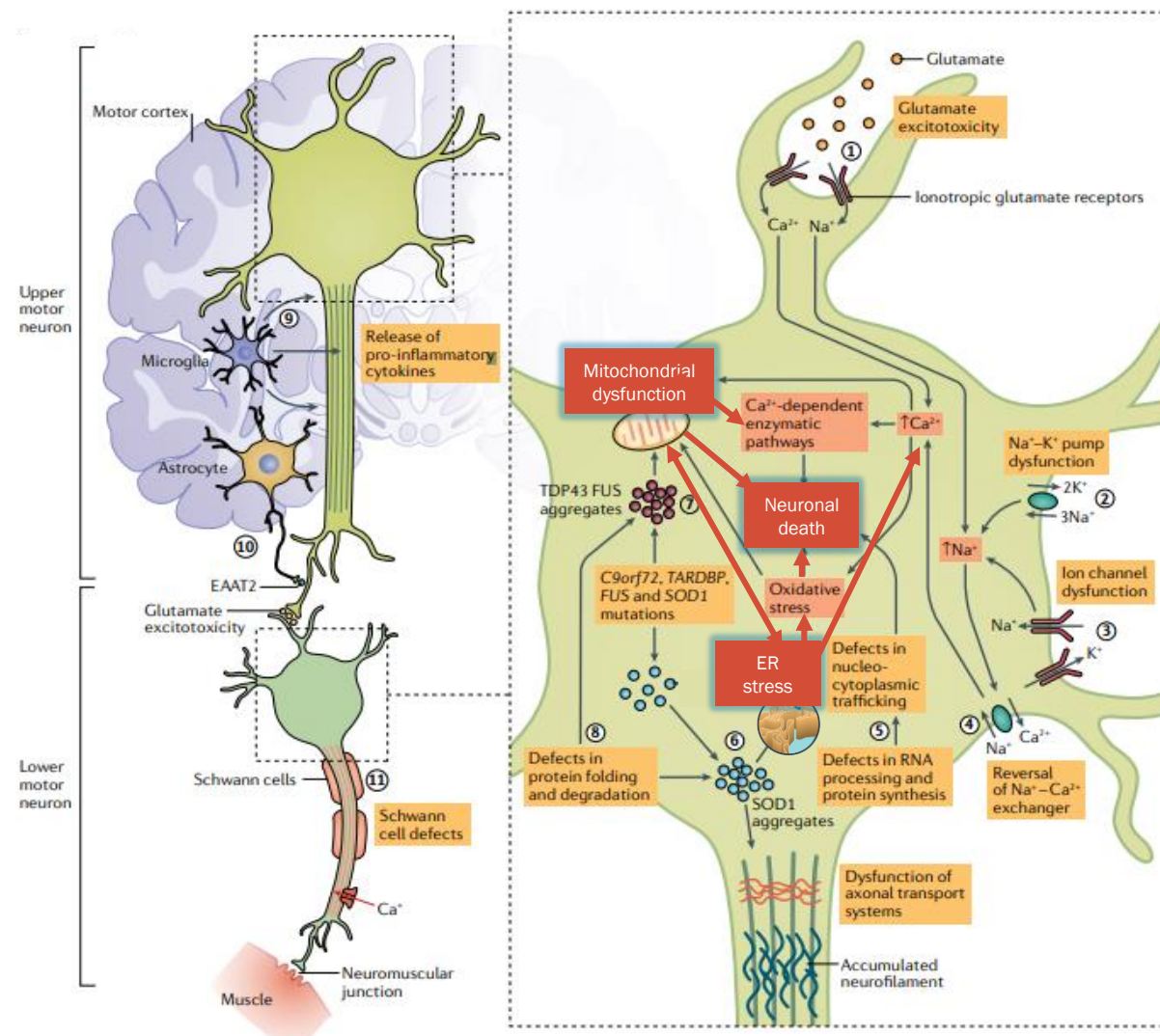
[Published: December 2008](#)

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

[Inki Kim](#), [Wenjie Xu](#) & [John C. Reed](#)

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

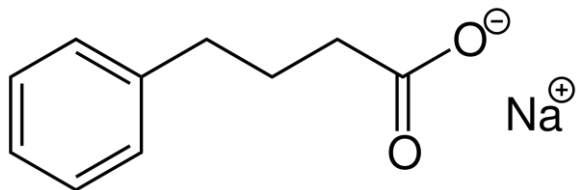
- ◆ Kiernan et al., Nature Reviews Neurology (2021) highlights ER and mitochondrial dysfunction as key convergence points in the neuron death that drives ALS
- ◆ Mitochondrial death proteins, including BAX, are upregulated in post-mortem ALS spinal cord samples, as are UPR related proteins
- ◆ Genetic causes of familial ALS – including the most well-known genes *SOD1*, *C9orf72* and *TDP43* – are mechanistically linked to mitochondria and ER dysfunction



AMX0035 — Targets Key Pathways of Cellular Death

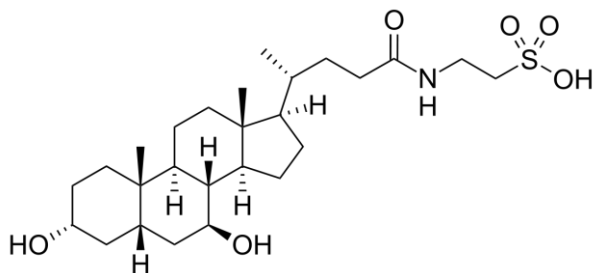
AMX0035: Dual UPR, Bax/Mitochondrial Apoptosis Inhibitor

AMX0035 is a combination of PB and TURSO



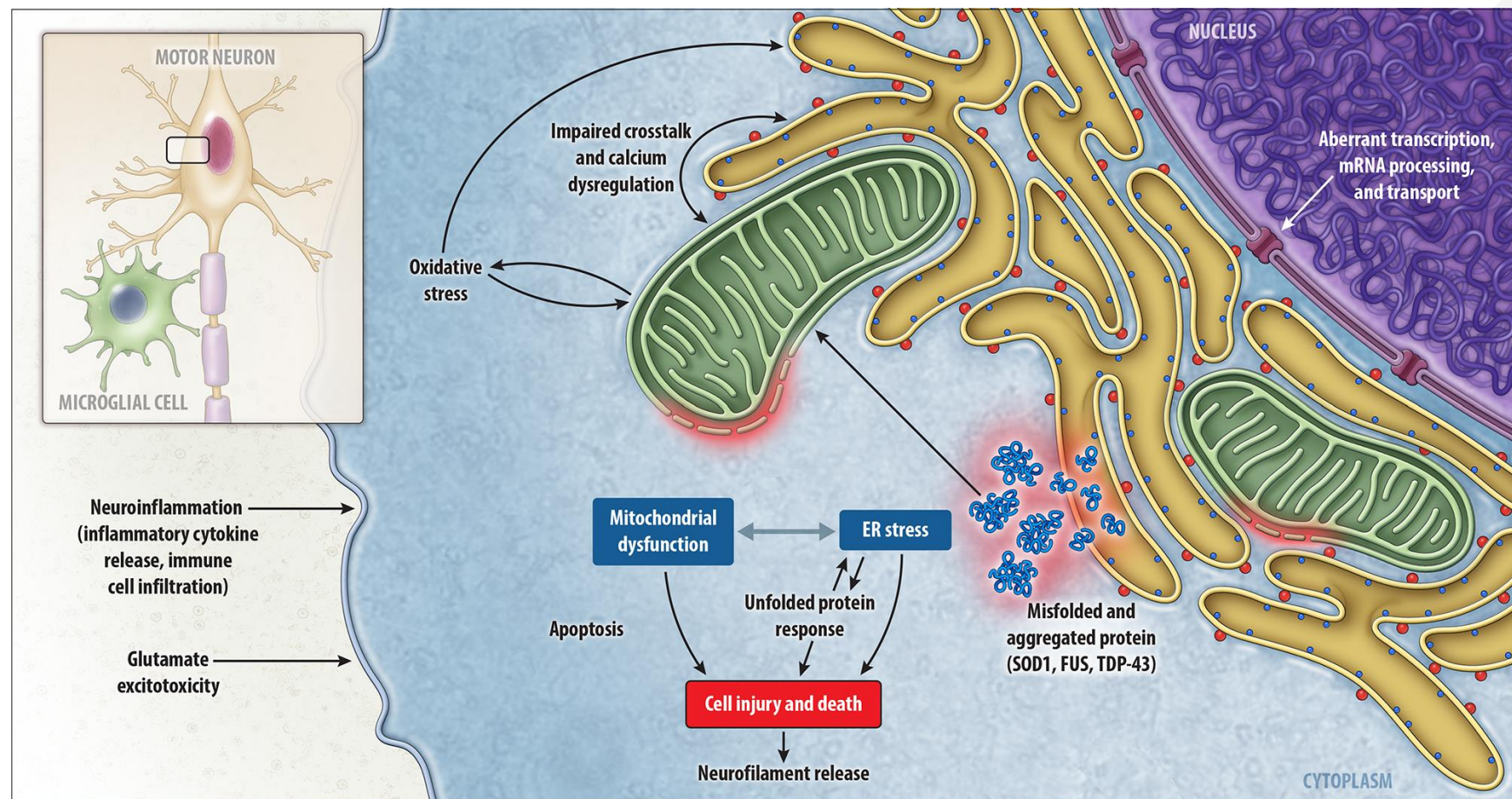
PB: Small Molecular Chaperone

Resolves UPR, reduces ER dependent death



TURSO: Bax Inhibitor

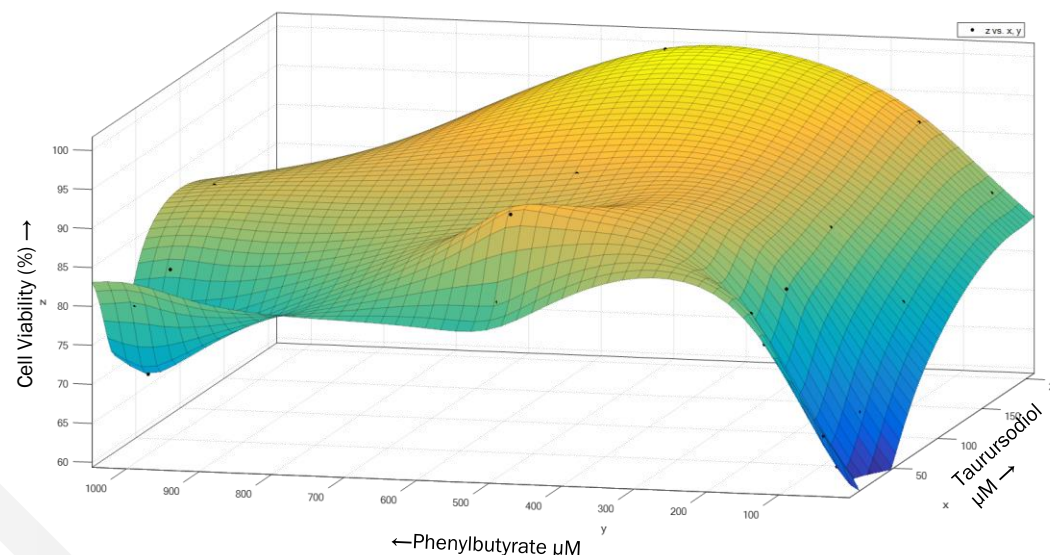
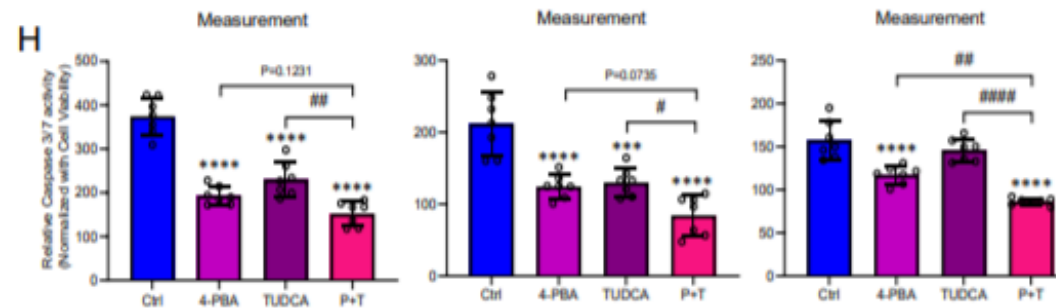
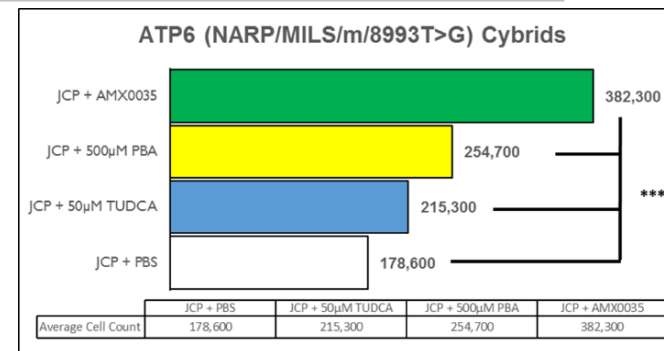
Reduces Mito Dependent Death



AMX0035 Targets Both Pathways Simultaneously to Prevent or Slow Cell Death

Across Many Insult Models

- ◆ AMX0035 has demonstrated synergistic benefit in mitochondrial cybrid model of mitochondria induced cellular death
- ◆ AMX0035 has demonstrated synergistic benefit in models of Wolfram syndrome considered a model of ER stress related cell death
- ◆ AMX0035 observed to prevent nearly 100% neuron death in oxidation induced neuronal death in preclinical studies
- ◆ Combination also demonstrated efficacy in additional models of cell death



Strong Global IP Position

Portfolio Provides Robust Protection of AMX0035 and Related Combinations

- 51 issued patents worldwide
- 28 additional patents pending
- Many additional filings planned



Patents protect:

- *Composition of matter* of the combination of PB and TURSO, including in the US – 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
- NCE/NAS AND Orphan Exclusivity Protect Against Generics (7 years in US, 10 in EU, 8 in Canada)

2022 Milestones



Regulatory
Decisions



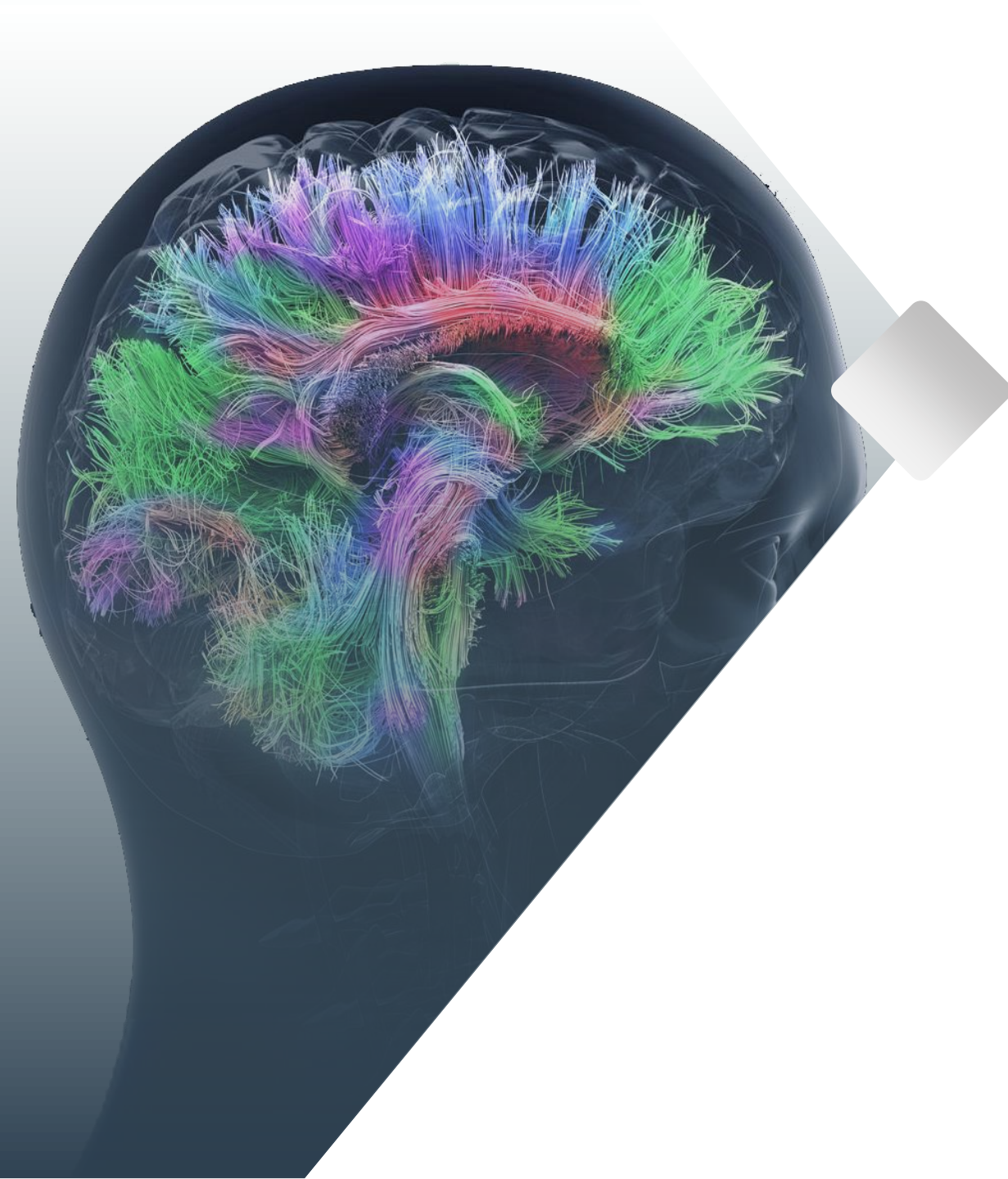
ALBRIOZA™
Commercial
Launch in
Canada

AMX0035
Commercial
Launch in U.S.
(if approved)



IND Submission
for Wolfram
Syndrome and
one additional
indication for
AMX0035

Focus in 2022 will also be placed on developing or in-licensing additional drugs focused on neuronal death and degeneration in ALS, and additional neurodegenerative diseases



Financial Overview

Amylyx Financial Data

Cash, cash equivalents, and short-term investments at 3/31/22: \$255.2M

1Q22 Expenses: \$47.5M



Thank you

Our mission is to end the suffering caused by neurodegenerative diseases. Every day, we strive to bring new treatments to people who deserve better.

NASDAQ: AMLX
June 2022