ASX: PAA

EGM Presentation

February 2024

Dr Michael Thurn

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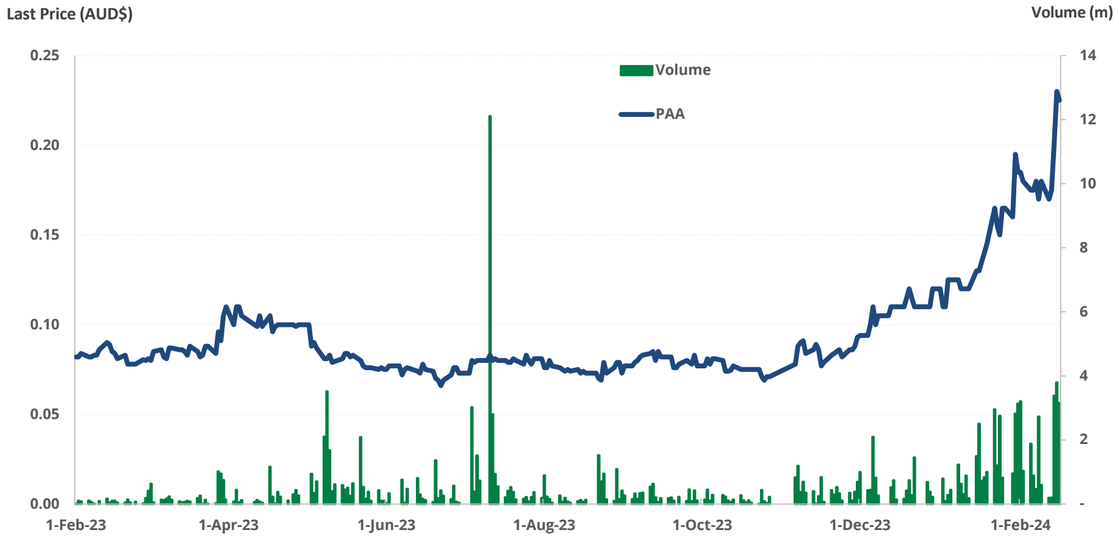
Corporate Overview

Mid-stage biotechnology company targeting human neurodegenerative diseases

Share Price Performance



Capital Structure (AUD$)

	16 Feb 2024
Current Share Price (PAA/PAAOA)	$0.23 / $0.13
52 Week Low / High (PAA)	$0.06/ $0.26
No. of Shares (PAA)	384,965,597
Listed Options (PAAOA)	121,949,093
Market Capitalisation	**$69.2m**
Monthly Turnover	**$4.9m**
Cash (as at 31-Dec-23)	$5.5 m
Debt (as at 31-Dec-23)	Nil
Net Cash	**$5.5m**
Enterprise Value	**$22.4m**
Unlisted Options (10c/15c/17.5c)	11.4 m
Enterprise Value (fully diluted)	**$63.7m**

Board & Management

Dr Roger Aston	Non-Exec Chairman
Dr Michael Thurn	Chief Executive Officer
Mr Neville Bassett AM	Non-Exec Director
Mr Robert Bishop	Non-Exec Director
Dr Thomas Duthy	Non-Exec Director
Mr Sam Wright	Non-Exec Director & Company Secretary

Top Shareholders*

Hybrid Holdings Pty Ltd <Darcy Family Super Fund A/C>	5.78%
Mr Gerald James Van Blommestein & Mrs Gillian Van Blommestein <Van Blommestein S/F A/C>	4.75%
Dr Roger Aston	3.91%
Board & Management	7.84%

* As at 16 Feb 2024

Product candidates for both human and animal health applications

Human and Animal Health
Mid stage biotechnology company focused on large and growing markets in human and animal health

Strong IP Position
Strong intellectual property with patent protection beyond 2030

Repurposing Monepantel
Repurposing an approved veterinary product – monepantel – anthelmintic for sheep

Pipeline Synergies
Pipeline synergies to leverage commercial infrastructure across human and animal health applications

Motor Neurone Disease
Lead clinical program for the treatment of motor neurone disease (MND/ALS)

Experienced Management
Experienced management team with demonstrated execution capabilities

Canine B-Cell Lymphoma
Phase 2 Veterinary program for the treatment of dogs with B-Cell Lymphoma

Broad Investor Base
Healthy mix of loyal institutional and retail investors

Meet Our Team – Chairman and Management

Dr Roger Aston
Non-Executive Chairman

Roger brings more than 30 years experience in the pharmaceutical and healthcare industries in senior roles in the UK, Asia Pacific and Australia. He has had extensive experience including FDA and EU product registration, clinical trials, global licensing agreements, fundraising through private placements, and a network of contacts within the pharmaceutical, banking and stock broking sectors

Dr Michael Thurn
Chief Executive Officer

Michael has over 25 years experience in technical, regulatory, commercial and management roles in research organisations and industry, including early stage, fast growing, private and publicly listed biotechnology companies. Michael has led a variety of US IND applications across a range of therapeutic areas and evaluated drugs and vaccines for registration during his engagement at the TGA.

John Clark
Chief Operating Officer

John has over 20 years of pharmaceutical industry experience in phase I – IV clinical trials across numerous therapeutic areas and multiple geographical regions. John has a thorough knowledge of ICH-GCP and regulatory requirements and held clinical operations leadership roles responsible for implementing global clinical programs.

Dr Carol Worth
CMC Operations Manager

Carol brings over 30 years of industry experience and a passion for focusing on quality control and quality assurance. She recently served as Quality Manager at Epichem Pty Ltd as Chief Technical Officer at Suda Pharmaceuticals and Solbec Pharmaceuticals. Carol has also led product development programs at Thermalife International Pty Ltd/ Pharmasolv Laboratories Pty Ltd

Pipeline

Multiple synergistic product opportunities in human and animal health by repurposing monepantel

Human Health

Indication	Preclinical	Phase 1	Phase 2	Phase 3	Approved / Marketed	Next Major Catalysts
Motor Neurone Disease (Amyotrophic Lateral Sclerosis)					Accelerated approval possible based on Phase 2 data	• Phase 1 Top-line Results Q1 2024 • Orphan Drug Designation • Open IND
Cancers						• Under review • Seek partnership opportunities

Animal Health

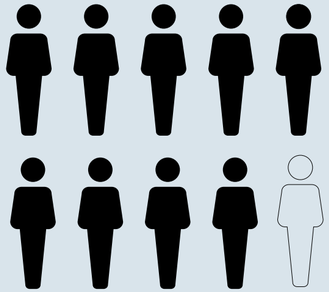
Indication	Preclinical	Phase 1	Phase 2	Field Study / TASS	Approved / Marketed	Next Major Catalysts
Canine B-Cell Lymphoma					Conditional approval possible	• MUMS Waiver • Open INAD • Begin Field Study
Cancers						• Under review • Seek partnership opportunities

IND – Investigational New Drug
MUMS – Minor Use Minor Species
INAD – Investigational New Animal Drug
TASS – Target Animal Safety Trial

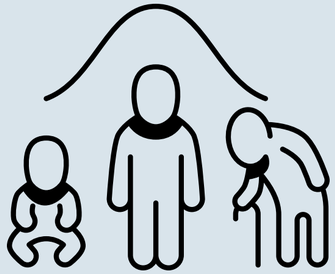
MND /ALS Statistics & Treatments

There is no cure and MND/ALS is always fatal

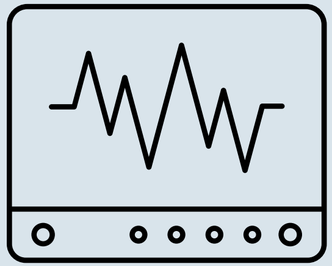
Every **90 minutes** someone is **diagnosed and dies** with MND/ALS



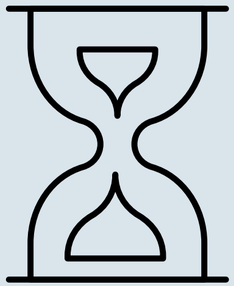
90% of cases occur **without a family history**



Onset is usually between the ages of **40 & 70 years**



Life expectancy on average is just over **2 years**



By **2040 the incidence** of MND/ALS is expected to **increase by 70%**

Current Treatments

Qalsody (tofersen)
Developed to treat ALS associated with a mutation in the superoxide dismutase 1 (*SOD1*) gene. The FDA approved Qalsody to treat *SOD1*-ALS in 2023.

Rilutek (riluzole)
This was the first FDA-approved drug available to treat ALS — in 1995. It inhibits glutamate release and prolongs life ~3 months.

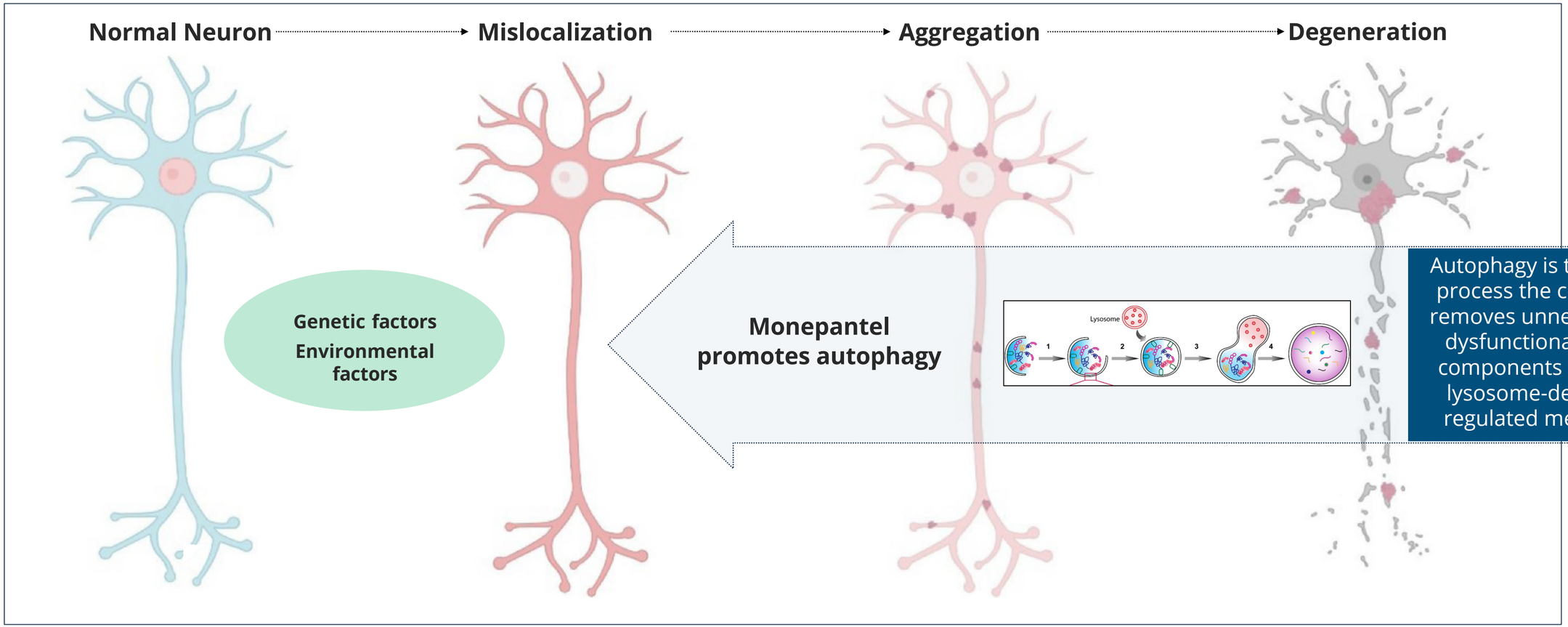
Radicava™ (edaravone)
The FDA approved Radicava™ in 2017, making it the first new treatment specifically for ALS in 22 years. Prolongs life ~6 months.

Relyvrio (AMX0035)
RELYVRIO is a combination of two drugs, sodium phenylbutyrate and taurursodiol. The FDA approved RELYVRIO for use to treat ALS in 2022. Prolongs life ~ 9 months.

These drugs provide limited relief and slow disease progression by only months

MND /ALS Pathology & Disease Progression

Characterised by progressive degeneration of nerve cells in the spinal cord and brain, MND/ALS affects the voluntary control of the arms and legs, eventually leading to trouble with breathing and death



Protein aggregation[1] is an important feature of MND/ALS pathology. Amyloid deposits from different proteins such as TDP-43, C9ORF72 dipeptide repeats, phosphorylated high molecular weight neurofilament protein, rho guanine nucleotide exchange factor, and FUS have been detected in MND/ALS motor neurons. These aberrant protein deposits become toxic to the cells, leading to neurodegeneration and are targets for therapeutic interventions.

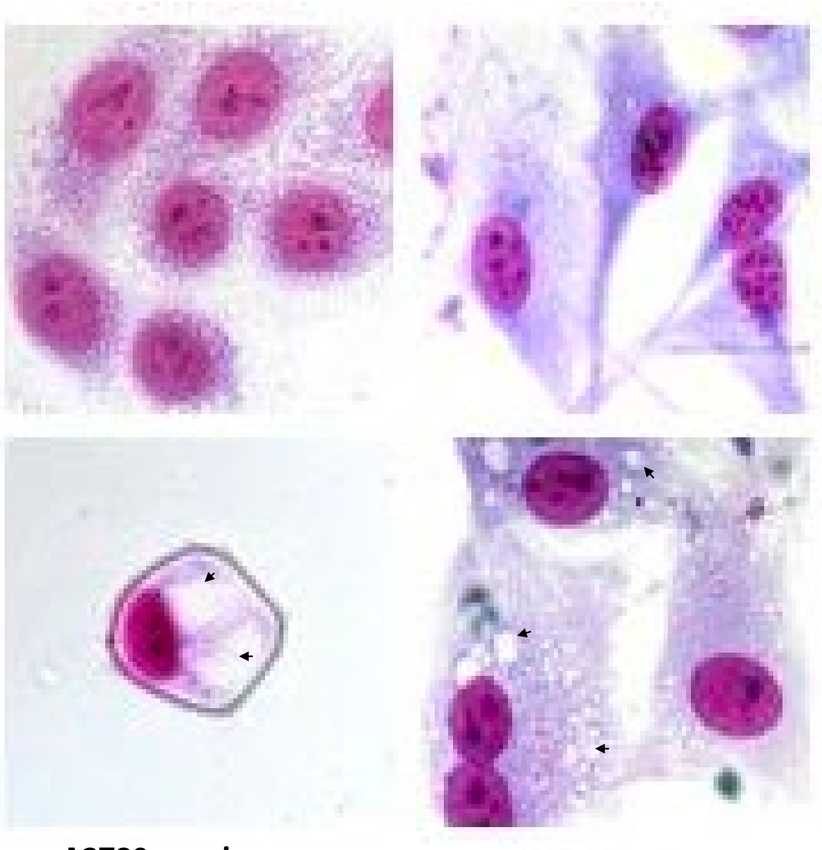
[1]Suk, T.R., Rousseaux, M.W.C. The role of TDP-43 mislocalization in amyotrophic lateral sclerosis. *Mol Neurodegeneration* **15**, 45 (2020). https://doi.org/10.1186/s13024-020-00397-1

Monepantel Induces Autophagy

Accumulating evidence suggests that impaired autophagy contributes to the accumulation of intracellular inclusion bodies consisting of misfolded proteins, which is a hallmark of most neurodegenerative diseases

Control

Monepantel (25 μM)



A2780 ovarian cancer cells

U87-MG glioma cells

International Journal of *Molecular Sciences*

MDPI

Review

Autophagy in Neurodegenerative Diseases: A Hunter for Aggregates

Hyungsun Park [1,2], Ju-Hee Kang [2,3] and Seongju Lee [1,2,*]

ELSEVIER

Contents lists available at ScienceDirect

Ageing Research Reviews

journal homepage: www.elsevier.com/locate/arr

Review

Autophagy in Alzheimer's disease pathogenesis: Therapeutic potential and future perspectives

Zhigang Zhang [a,b], Xifei Yang [d], You-Qiang Song [b,c,*], Jie Tu [a,**]

frontiers | Frontiers in Aging Neuroscience

Targeting the autophagy-lysosomal pathway Huntington disease: a pharmacological perspective

TYPE Mini Review
PUBLISHED 25 May 2023
DOI 10.3389/fnagi.2023.1175598

Junsheng Yang* and Chaoyue Zhang

Clinical and Experimental Immunology, 2022, **209**, 140–150
https://doi.org/10.1093/cei/uxac017
Advance access publication 16 February 2022
Review

Clinical & Experimental IMMUNOLOGY

OXFORD

Review

Autophagy modulation in multiple sclerosis and experimental autoimmune encephalomyelitis

Donghui Shen[1], Kang Liu[2], Hongyan Wang[1] and Haifeng Wang[1,*]

REVIEW Open Access

Therapeutic potential of autophagy-enhancing agents in Parkinson's disease

Tim E. Moors[1*], Jeroen J. M. Hoozemans[2], Angela Ingrassia[1], Tommaso Beccari[3], Lucilla Parnetti[4], Marie-Christine Chartier-Harlin[5,6] and Wilma D. J. van de Berg[1]

REVIEW Open Access

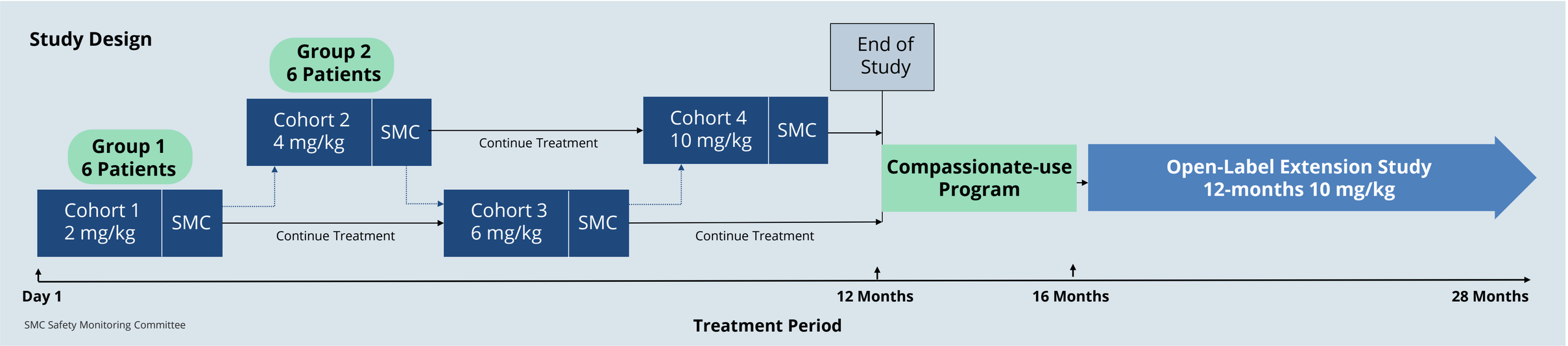
Is amyotrophic lateral sclerosis/ frontotemporal dementia an autophagy disease?

Zhiqiang Deng[1,2,3], Patricia Sheehan[3], Shi Chen[1,2*] and Zhenyu Yue[3*]

Arrows depict autophagolyosomes (small lysosomal sacs or vacuoles that breaks down the cellular junk in our cells during the process of autophagy)

Phase 1
MND/ALS Study

The Phase 1 MEND Study is an open label, multicentre study involving 12 patients with MND/ALS with the goal of determining the recommended Phase 2 dose based on safety and preliminary efficacy



Study Update

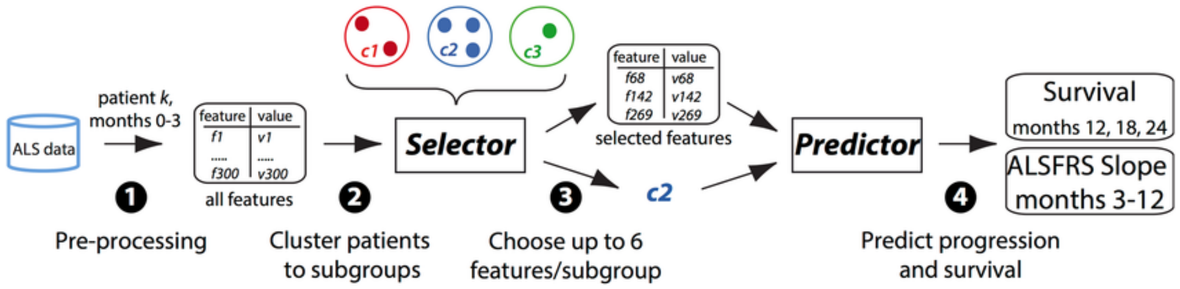
- Analysis near completion to support release of top-line data by end of Q1 CY24
- All patients willing and able to roll-over into 12-month Open-Label Extension Study
- Patients have continued treatment with monepantel under a compassionate-use program
- Treatment continues to be very well-tolerated
- First Group of 6 patients entering their 16 month of continuous treatment with monepantel
- Data will be used to support the Orphan Drug Designation application and to open an IND with the US FDA to commence an adaptive Phase 2/3 Study in H1 CY24

Phase 1
MND/ALS Study

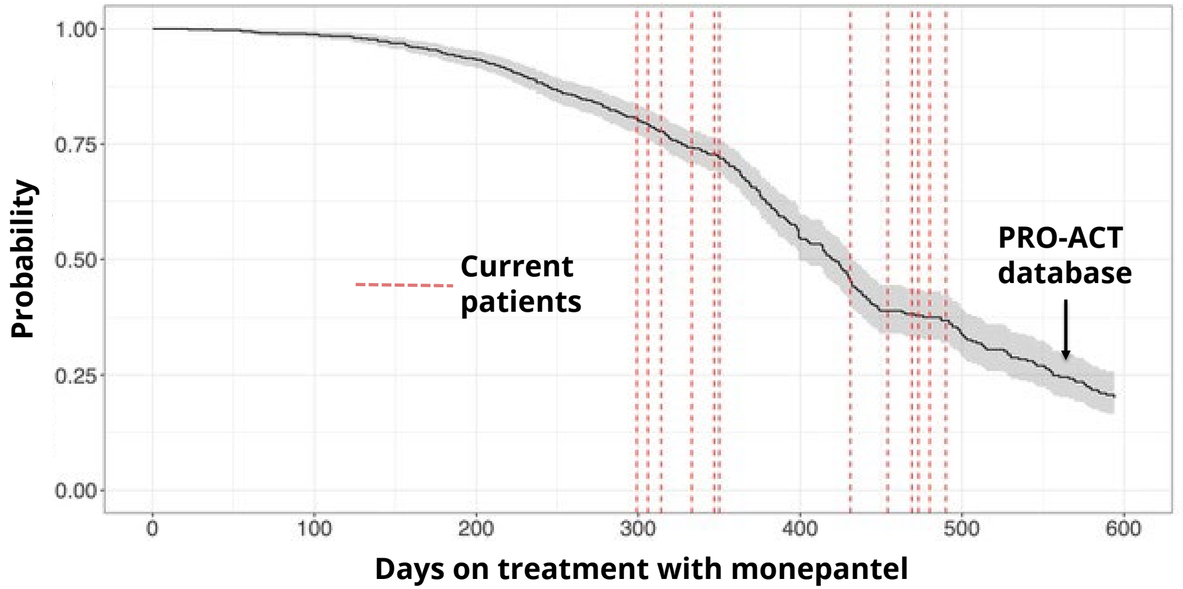
Statistical survival estimations based on comparisons to the PRO-ACT[1] historical ALS database, points to the probability that all 12 patients treated with monepantel being alive today being less than 1 in 1,000

Berry Consultants Statistical Analysis

- Berry's analysis involved **comparing patients in the PRO-ACT database** with **similar characteristics** to those in PharmAust's **Phase 1 MEND Study** adjusting for differing diagnosis durations
- **One-year study survival** rate estimate of **67.7%** with a 95% Confidence Interval
- Considering differential diagnosis durations, the **probability estimates** of **all 12 Phase 1 MEND patients surviving today** without treatment are **less than 0.1%** (less than 1 in 1,000)



Overall Survival Probability



The PRO-ACT database is the largest publicly available repository of merged ALS clinical study data. Data were pooled from 16 completed Phase 2/3 ALS clinical studies and one observational study. Over 8 million de-identified longitudinally collected data points from more than 8,600 persons with ALS, including demographics, family histories, and longitudinal clinical and laboratory data.

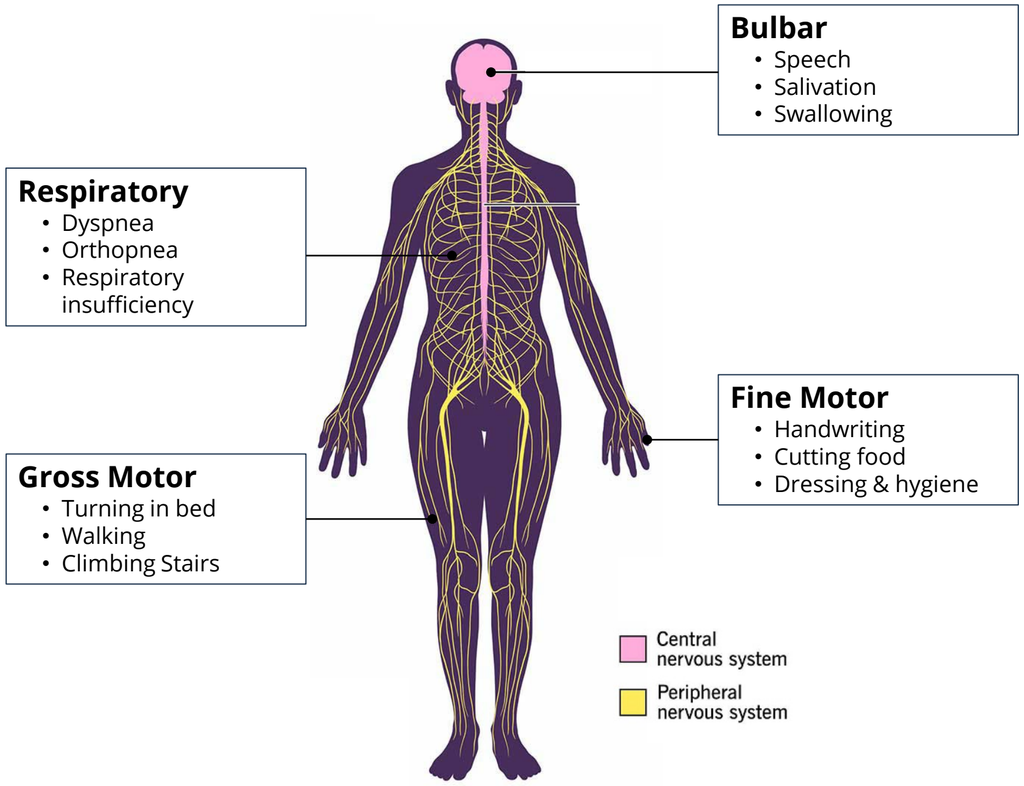
[1]Atassi N, Berry J, Shui A, Zach N, Sherman A, Sinani E, Walker J, Katsovskiy I, Schoenfeld D, Cudkowicz M, Leitner M. The PRO-ACT database: design, initial analyses, and predictive features. Neurology. 2014 Nov 4;83(19):1719-25. doi: 10.1212/WNL.0000000000000951.Epub 2014 Oct 8. PMID: 25298304; PMCID: PMC4239834.

Phase 1

Amyotrophic Lateral Sclerosis Function Rating Score – Revised (ALSFRS-R)

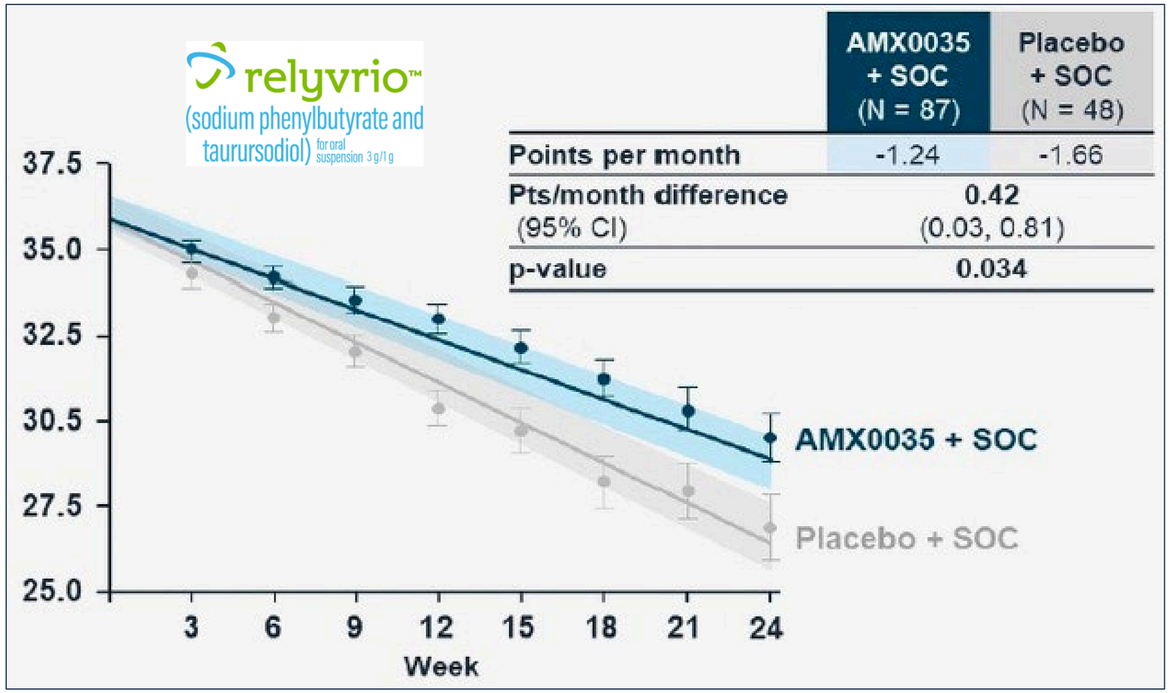
ALSFRS-R is a predictor of survival time in ALS patients.[1] The speed at which ALS progresses, measured by the rate of decline in a patient's ALSFRS-R score over time, can be used to confidently predict disease prognosis.

ALSFRS-R Domains Assessed



Each task is rated on a five-point scale from 0 = can't do, to 4 = normal ability. Individual item scores are summed to produce a reported score of between 0=worst and 48=best.

AMX0035 – 25% Slower Decline in ALSFRS-R



Slowing the decline in ALSFRS-R by 16.5% = 4-5 months median survival[2]

[1]Beghi E, Mennini T, Bendotti C, et al. The heterogeneity of amyotrophic lateral sclerosis: a possible explanation of treatment failure. *Curr Med Chem*. 2007;14(30):3185-3200
[2]Leigh PN, Swash M, Iwasaki Y, et al. Amyotrophic lateral sclerosis: a consensus viewpoint on designing and implementing a clinical trial. Amyotroph Lateral Scler Other Motor Neuron Disord. 2004;5(2):84-98

MND/ALS Progression Statistics

About 50% of patients with ALS live at least 3 years or more after diagnosis; 20% live 5 years or more; and up to 10% survive for more than 10 years[1]

MND / ALS Progression – Typically 2-3 years[2,3]

Survival

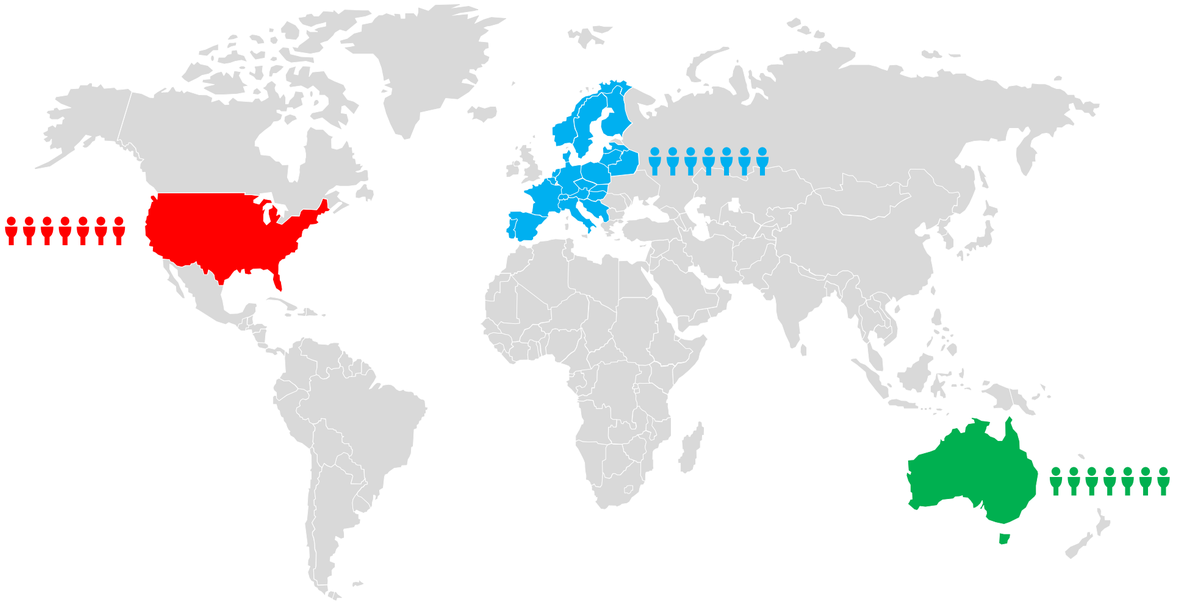
- Median survival ~2 years from diagnosis[4]
- Time to diagnosis on average is 12 months in the US[2]
- Population-based prospective registries report 1 year mortality rates after diagnosis ranging from 22% to 34%[5]
- Shortest time since diagnosis ~16 months compared to the longest ~49 months for the completed Phase 1 MEND Study

[1]Cruz MP. Edaravone (Radicava): A Novel Neuroprotective Agent for the Treatment of Amyotrophic Lateral Sclerosis. P T. 2018 Jan;43(1):25-28. PMID: 29290672; PMCID: PMC5737249.
[2]Paganoni S, Cudkowicz M, Berry JD. Outcome measures in amyotrophic lateral sclerosis clinical trials. Clin Investig (Lond). 2014;4(7):605-618. doi: 10.4155/cli.14.52. PMID: 28203356; PMCID: PMC5305182.
[3]Chiò A, Logroscino G, Hardiman O, Swingler R, Mitchell D, Beghi E, Traynor BG; Eurals Consortium. Prognostic factors in ALS: A critical review. Amyotroph Lateral Scler. 2009 Oct-Dec;10(5-6):310-23. doi: 10.3109/17482960802566824. PMID: 19922118; PMCID: PMC3515205.
[4]Karanevich, A.G., Statland, J.M., Gajewski, B.J. et al. Using an onset-anchored Bayesian hierarchical model to improve predictions for amyotrophic lateral sclerosis disease progression. BMC Med Res Methodol 18, 19 (2018).
[5]Wolf, J., Safer, A., Wöhrle, J.C. et al. Factors predicting one-year mortality in amyotrophic lateral sclerosis patients - data from a population-based registry. BMC Neurol 14, 197 (2014). https://doi.org/10.1186/s12883-014-0197-9

Pre-IND Meeting Response

Successfully completed a Pre-IND meeting with the FDA to confirm the details of the ongoing development program, including the requirements for non-clinical and clinical pharmacology, clinical, chemistry, and manufacturing controls

Global Phase 2/3 Clinical Study



Specific FDA Feedback and Guidance

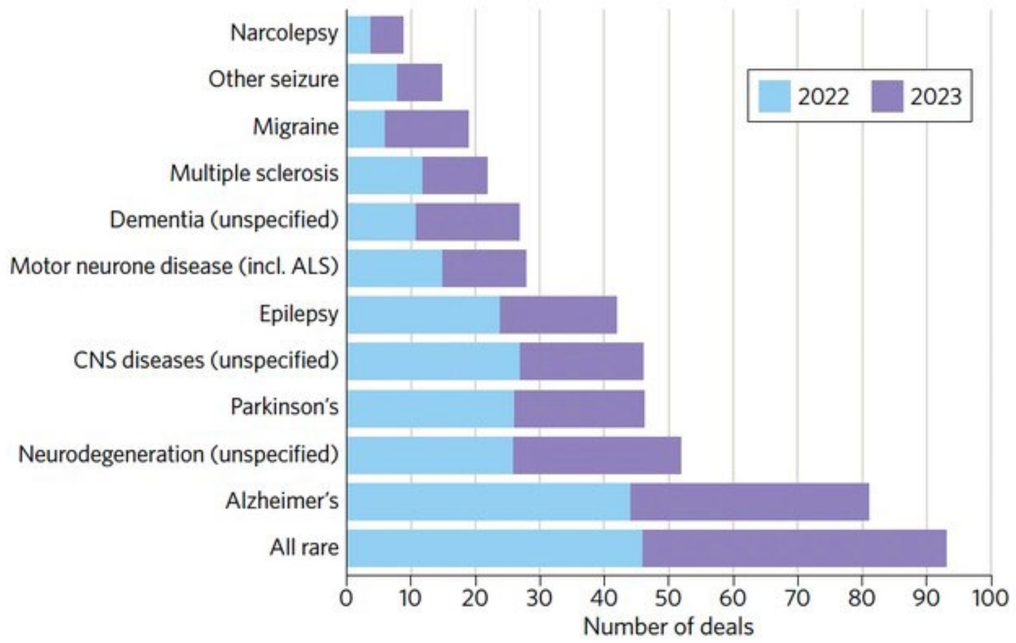
- FDA provided **positive feedback** and outlined the **path required** to potentially receive **accelerated and full approval** of monepantel for the treatment of ALS
- PharmAust will **initiate requirements** requested by the FDA in the **preparation to open an IND application** for the adaptive Phase 2/3 clinical study
- PharmAust will now prepare to **launch clinical sites in Europe and Australia** where data can also be used to **support the FDA drug approval** process
- **Registration in Europe and Australia** now possible with this **global approach**

Single clinical study sufficient
subject to demonstrating substantial evidence of effectiveness and an adequate database supporting safety

Rare Central Nervous System disease market

The global CNS rare disease treatment market is expected to reach US$13.8 billion by 2027 (CAGR > 8.5%)[1]

Neurological disease deals by therapy type in 2022 and 2023 (October)[2]



Selected partnering deals in the CNS field in 2023[2]

Date	Stage	Companies	Deal Value	Target
Jul 2023	Phase 3	Biogen / Reata Pharmaceuticals	US$7.3 Billion Acquisition • Reata just launched Skyclarys (omaveloxolone) in US, under regulatory review in Europe to treat Friedreich's ataxia	Omaveloxolone • Possesses antioxidative and anti-inflammatory activities
Mar 2023	Phase 1	Biohaven / Hangzhou Highlightll	US$970 Million License • US$20 million in cash and equity upfront , development and commercial milestones. tiered royalties	BHV-8000 • Dual Tyrosine Kinase 2 (TYK2)/Janus Kinase 1 (JAK1) inhibitor
Sep 2023	Preclinical	Takeda / Acurastem	US$580 Million License • Combined upfront payment and milestones could reach US$580 million in total, alongside royalties	AS-202 • PIKFYVE-targeted antisense oligonucleotide

Over 49 deals were announced 2023 involving rare CNS diseases, with disclosed deal values totalling more than US$13.2 billion

[1]The Insight Partner March 2020
[2]Mark Zipkin, Neurodegeneration and rare diseases drive CNS therapy deals. Biopharma Dealmakers News Feature. 1 December 2023. doi: https://doi.org/10.1038/d43747-023-00128-7

MND R&D timeline

Timeline

Q4 CY2023

- MEND Study Patient Completes
- ODD Submission
- Management Hires
- Compassionate-use Program
- FightMND Grant Invitation

Q1 CY2024

- Pre-IND Meeting Request
- Berry Consultants Partnership
- OLE Study HREC Approval
- MEND Study Top-line Results
- SAB Appointments

Q2 CY2024

- ODD Response
- Open IND Phase 2 MND Study
- Phase 2/3 Study HREC Approval
- First Patient Dosed MND Study

IND – Investigational New Drug; ODD – Orphan Drug Designation; OLE – Open Label Extension; SAB – Scientific Advisory Board

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