PharmAust Presentation

21 June 2024 – Melbourne Australia: PharmAust Limited (ASX: PAA & PAAOA) ("PharmAust" or "the Company"), a clinical-stage biotechnology company, is pleased to release the appended PharmAust capital raising presentation.

To access a video of CEO Dr Michael Thurn presenting the corporate presentation, please utilise the PharmAust Investor Hub by https://investorhub.pharmaust.com/

This release was authorised on behalf of the PharmAust Board by Dr Michael Thurn.

For further information, please contact:

Dr Michael Thurn
Managing Director
investorenquiries@pharmaust.com

P +61 (3) 9692 7222
W www.pharmaust.com

Media:
Catherine Strong
Morrow Sodali
c.strong@morrowsodali.com
0406 759 268

About PharmAust Limited:

PharmAust Limited is listed on the Australian Securities Exchange (ASX Code: PAA). PAA is a clinical-stage biotechnology company developing therapeutics for neurodegenerative diseases. The company is focused on repurposing monepantel (MPL) for amyotrophic lateral sclerosis (ALS). ALS is the most common form of motor neurone disease (MND) and affects both upper and lower motor neurons.

MPL is a potent and safe inhibitor of the mTOR pathway. This pathway plays a central role in the growth and proliferation of cancer cells and degenerating neurons. The mTOR pathway regulates the cellular "cleaning process", where toxic proteins are broken down into macromolecules to be reused. This autophagic process is disrupted in most neurodegenerative diseases, including ALS.

The company recently announced positive top-line results for its Phase 1 MEND study in participants with ALS. PAA is in the planning stages for a registration adaptive Phase 2/3 STRIKE clinical study and anticipates commencing enrolment in H2 CY 2024. This single pivotal study could potentially lead to accelerated approval with the US Food and Drug Administration for monepantel for the treatment of ALS in 2026.

In 2024, the Neurodegenerative Disease Market size is estimated to be worth USD 55.12 billion, with a forecast growth (CAGR) of 7.14% the market size is expected to reach USD 77.82 billion by 2029.[1]

[1] https://www.mordorintelligence.com/industry-reports/neurodegenerative-disease-market

PharmAust Investor Hub:

We encourage you to utilise our Investor Hub for any enquiries regarding this announcement or other aspects concerning PharmAust. This platform offers an opportunity to submit questions, share comments, and view video summaries of key announcements.

Access the investor hub by scanning the QR code or visiting: https://investorhub.pharmaust.com/

ASX: PAA

Investor Update

21 June 2024

Dr Michael Thurn

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Corporate Overview

Mid-stage biotechnology company targeting human neurodegenerative diseases

Share Price Performance

Capital Structure (AUD$)

	18 June 2024
Current Share Price (PAA/PAAOA)	$0.22 / $0.10
52 Week Low / High (PAA)	$0.06/ $0.53
No. of Shares (PAA)	395,911,235
Listed Options (PAAOA)	116,415,955
Market Capitalisation	**$97.0m**
Cash (as at 31-Mar-24)	$3.9 m
Debt (as at 31-Mar-24)	Nil
Net Cash	**$3.94m**
Enterprise Value	**$100.94m**
Unlisted Options (10c/15c/17.5c)	7.34 m
Enterprise Value (fully diluted)	**$107.7m**

Board & Management

Mr Sergio Duchini	Chairman & Non-Executive Director
Dr Michael Thurn	Chief Executive Officer & Managing Director
Mr Marcus Hughes	Non-Executive Director
Dr Katie MacFarlane	Non-Executive Director
Mr Stefan Ross	Company Secretary

Top Shareholders*

Hybrid Holdings Pty Ltd <Darcy Family Super Fund A/C>	5.6%
Mr Gerald James Van Blommestein & Mrs Gillian Van Blommestein <Van Blommestein S/F A/C>	4.6%
Dr Roger Aston	3.8%
Board & Management	3.1%

* As at 18 June 2024

Product candidates for neurodegenerative diseases

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

Strong IP Position
Strong intellectual property with 6 patent families and protection beyond 2030

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

Pipeline Synergies
Pipeline synergies to leverage commercial infrastructure across development programs

Neurodegenerative Diseases
Exploiting autophagy as a hunter for toxic aggregates, a common pathology in neurodegenerative diseases

Experienced Management
Experienced world-class Board and management team

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

Broad Investor Base
Healthy mix of loyal institutional and retail investors

Meet Our Board of Directors

Sergio Duchini
Chairman & Non-Executive Director
Sergio serves as a Non-Executive Director and Chair of the Audit Committee at Enlitic Inc. Additionally, he holds the position of Chair at Lymphoma Australia, a leading not-for-profit organization. Sergio previously sat on the AusBiotech Board of Directors for nine years. He also served as a Board Director at Deloitte Australia, overseeing the governance, strategy development, and stewardship of the partnership.

Dr Michael Thurn
Managing Director & Chief Executive
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.

Dr Katie MacFarlane
Non-Executive Director
Katie has over 30 years of experience in the development and commercialisation of pharmaceutical products and devices. She has held senior executive positions at Arkayli Biopharma, Agile Therapeutics, Warner Chilcott, Parke-Davis (now Pfizer). Katie currently serves on the Board of Mayne Pharmaceuticals, an affiliate faculty member of the Purdue University School of Pharmacy and a Founding Member and Advisor to IPhO.

Marcus Hughes
Non-Executive Director
Marcus brings more than 20 years' experience with listed companies. He possesses extensive corporate finance experience, having led project financing and capital raisings in the industrial sector. He has held senior managerial, tax and finance roles with multi-national companies including Lend Lease, Fortescue Metals and Rio Tinto

Meet Our Management Team

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 Nicky Wallis
Chief Scientific Officer
Nicky is a neuroscientist and brings over 12 years of global expertise in clinical development, spanning pre-clinical through to Phase 3 drug and device development. Her extensive experience includes roles such as Clinical Trials Program Specialist at the Australian Clinical Trials Alliance, Vice President of Clinical Operations at Lateral Pharma Biotech, and Clinical Project Manager at Orygen Youth Mental Health Research.

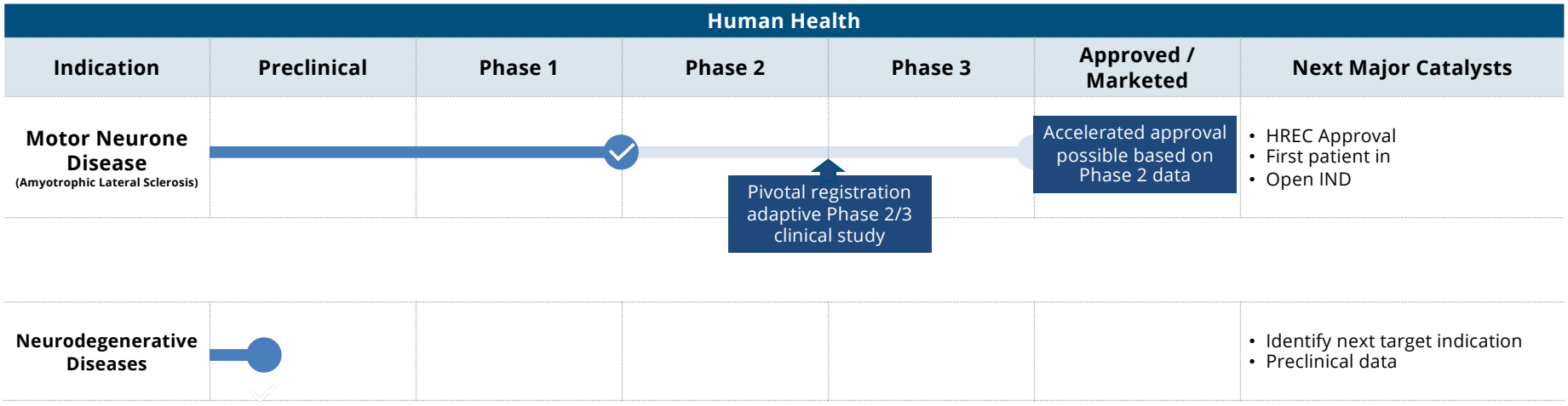
Dr Herbert Brinkman
Head of Manufacturing
Herb has over 30 years of experience in the pharmaceutical industry. He has prepared over 25 Chemistry Manufacturing and Control sections and updates for multiple filings for FDA and EU regulatory agencies. Herb has filed and commercially launched 9 products and contributed to filing 21 ANDAs for various semi-solid and parenteral products. He is also an inventor on 14 patents.

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 health by repurposing monepantel

- Single pivotal registration clinical study or MND/ALS
- Targeting accelerated approval from Phase 2 data
- FDA approval in 2026 possible

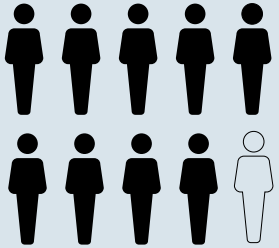


IND – Investigational New Drug
HREC – Human Research Ethics Committee

MND / ALS Statistics & Treatments

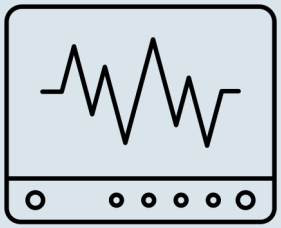
There is no cure and MND/ALS is always fatal

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

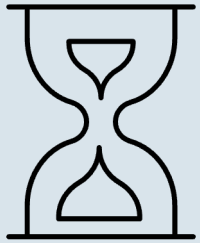


90% of cases occur **without a family history**

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.

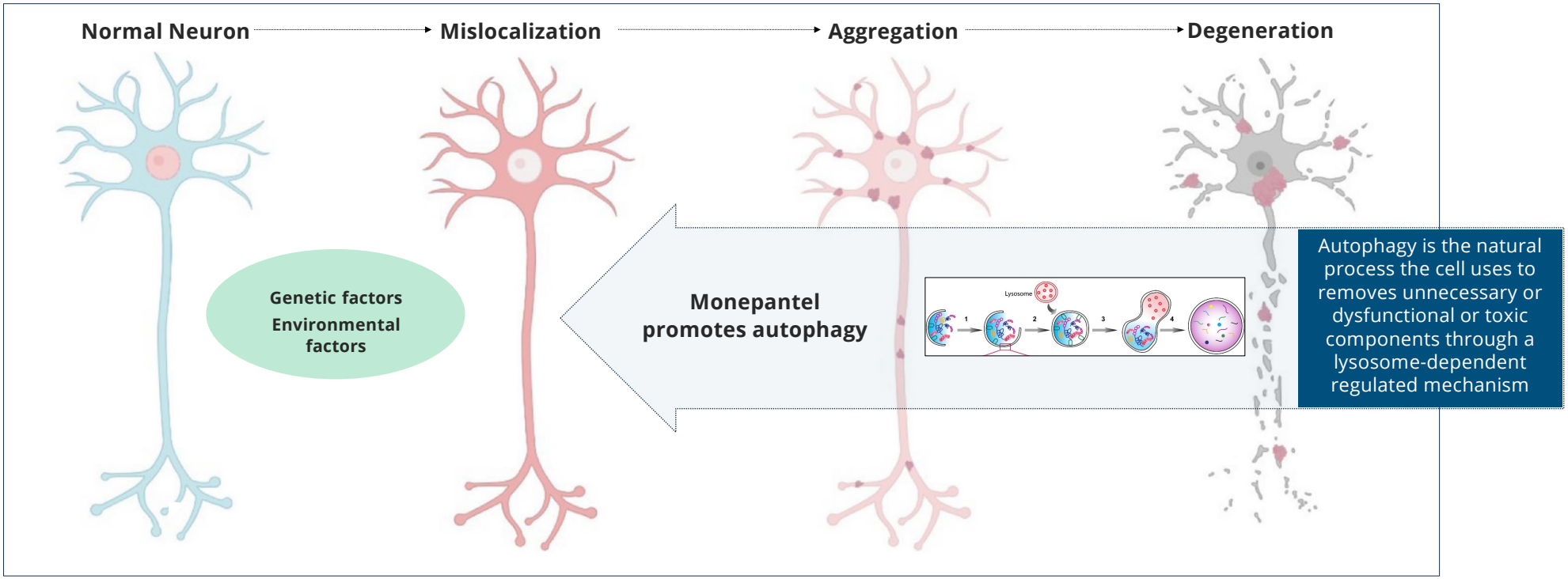
Rilutek (riluzole)
This was the first FDA-approved drug available to treat ALS — in 1995. It inhibits glutamate release and prolongs life ~3 months.

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

These drugs provide limited relief are controversial 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

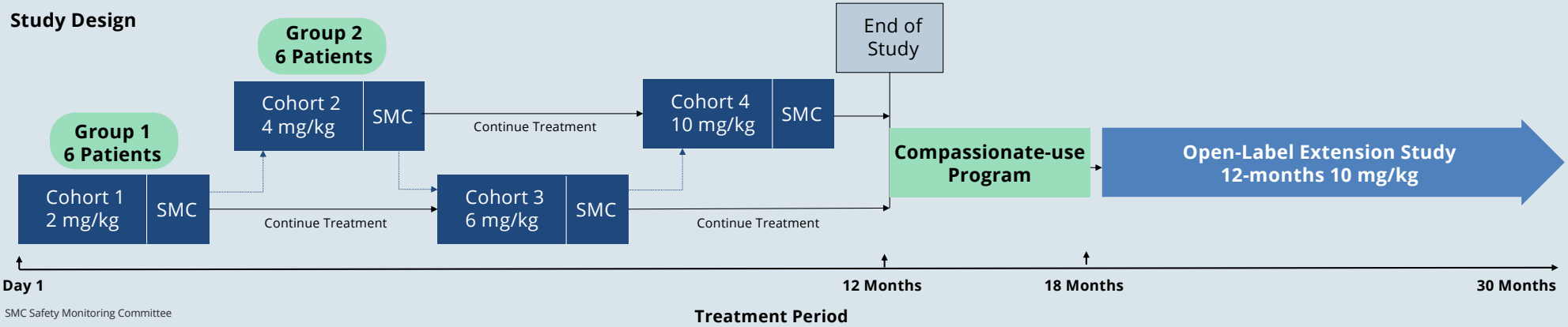


Protein aggregation[1] is an important feature of MND/ALS pathology. Amyloid deposits from different proteins such as TDP-43, C9ORF72 dipeptide repeats, phosphorylated high molecular weight neurofilament protein, rho guanine nucleotide exchange factor, and FUS have been detected in MND/ALS motor neurons. 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

Phase 1
MND/ALS MEND Study

The Phase 1 MEND Study was an open label, multicentre study involving 12 patients with MND/ALS with the goal of determining the recommended Phase 2/3 dose based on safety and preliminary efficacy



Study Update

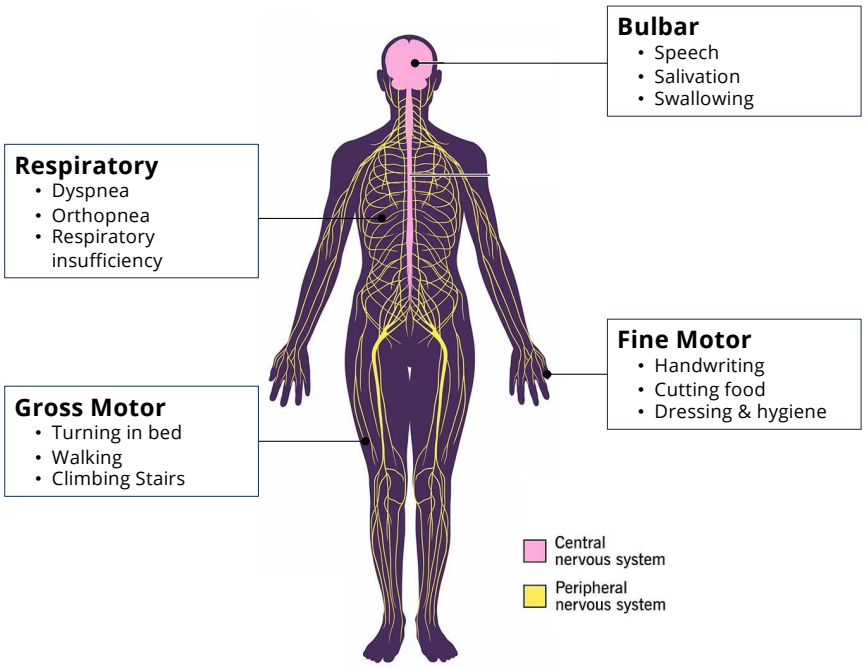
- Positive top-line data released in Q1 CY24
- 12 patients continued treatment with monepantel under a compassionate-use program
- 10 patients have rolled-over into 12-month Open-Label Extension Study. Treatment continues to be very well-tolerated
- Updated ALSFRS-R and Survival Analysis to be generated by Berry Consultants. Update expected in coming weeks
- First group of 6 patients are entering their 20th month of continuous treatment with monepantel
- Phase 1 and baseline OLE data used to design pivotal registration adaptive Phase 2/3 Study, to commence in H2 CY24

Phase 1

Preliminary Efficacy Amyotrophic Lateral Sclerosis Function Rating Scale – Revised (ALSFRS-R)

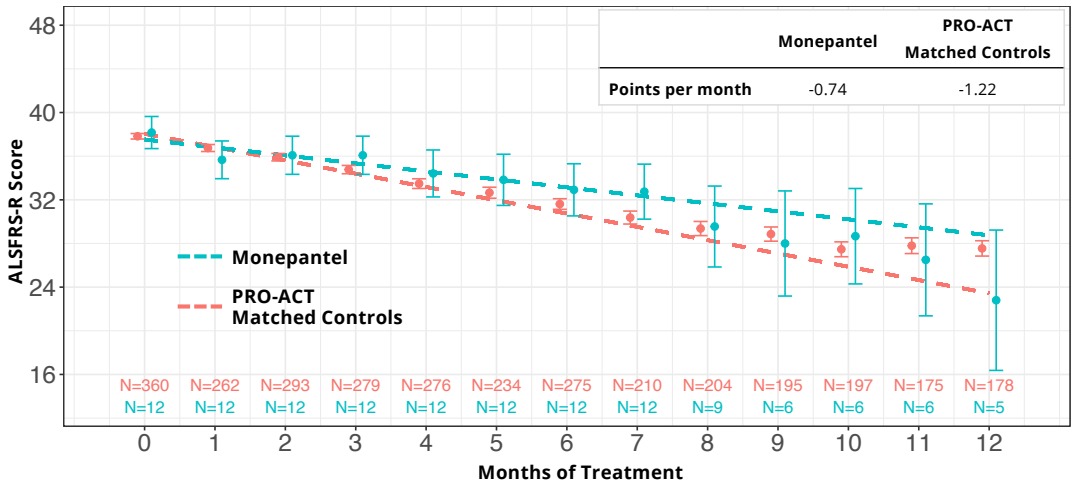
Treatment with monepantel for up to 12 months slowed the progression of MND/ALS in all 12 patients by 39% when compared to matched controls from the PRO-ACT database[1]

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.

MPL – 39% Slower Decline in ALSFRS-R



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.

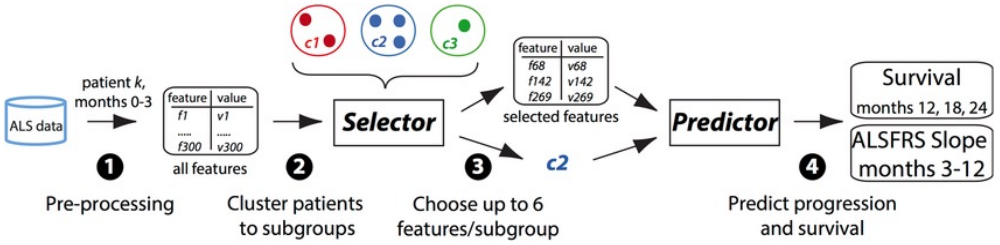
Phase 1
MND/ALS Study

Compared to matched controls from the PRO-ACT Historical Database, treatment with monepantel results in a significantly (X^2=9.39, p=0.0022) longer survival of patients with MND/ALS

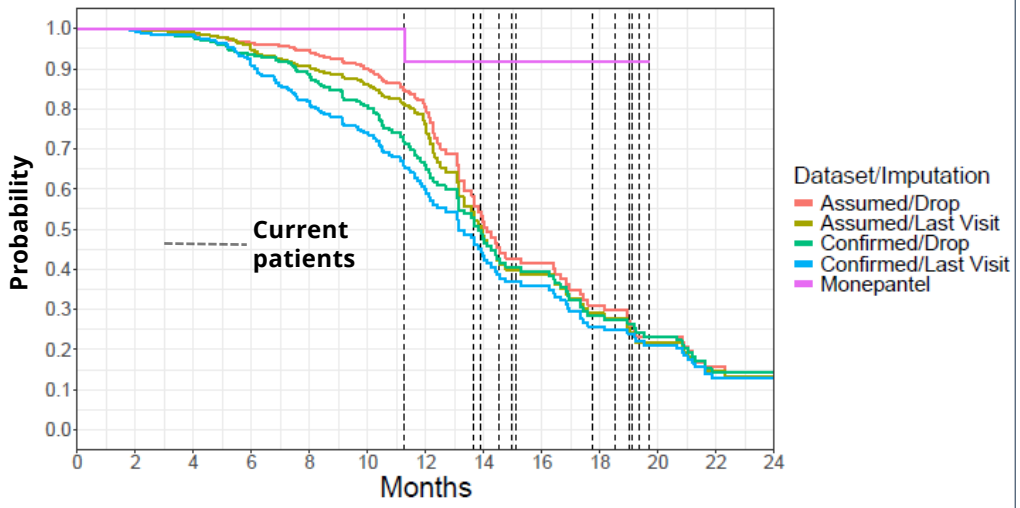
Berry Consultants Statistical Analysis

- 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
- **Hazard ratio** of 0.087 (95% CI: (0.012, 0.627), p = 0.0154) indicating that treatment with MPL reduces the risk of death by 91%

Analysis Method		Log-Rank Test		Cox Proportional Hazards Model		
Dataset	Death Time Imputation	χ^2	p-value	Hazard Ratio	95% CI	p-value
Assumed Survival	Leave out	9.39	0.0022	0.087	(0.012,0.627)	0.0154
	Last Visit	10.19	0.0014	0.081	(0.011,0.585)	0.0127
Assumed Survival	Leave out	10.22	0.0014	0.081	(0.011,0.585)	0.0126
	Last Visit	11.37	0.0001	0.074	(0.010,0.534)	0.0097



Overall Survival Probability



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Phase 2/3
ALS STRIKE Study

The pivotal, adaptive Phase 2/3 STRIKE Study will be a multicenter, randomized, placebo-controlled, parallel adaptive clinical study evaluating the safety and efficacy of Monepantel in subjects with ALS

MAIN INCLUSION CRITERIA:

- Adults with Familial or Sporadic ALS
- Time since onset of weakness due to ALS ≤ 24 months at the time of Screening Visit
- Seated Slow Vital Capacity ≥ 50% of predicted value
- Not take riluzole or be on a stable dose of riluzole for ≥ 30 days prior to the Screening visit
- Not take edaravone or have completed at least one cycle of edaravone prior to Screening visit

STUDY PLAN:

- Pivotal registration study
- Adaptive 24/48-week design
- Interim analysis at Week 24 for success or futility
- 210 participants to be enrolled
- Participants randomised 2:1
- 1st SAB meeting conducted to discuss study design

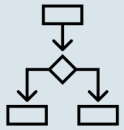
STUDY OBJECTIVES:

- Evaluate the efficacy of MPL, as compared to placebo, on ALS disease progression
- Evaluate the effect of MPL on selected secondary measures of disease progression
- Evaluate the safety of MPL for people with ALS
- Evaluate the effect of MPL on selected biomarkers and endpoints

GEOGRAPHIC LOCATIONS:

~30 sites globally

- 20% AUS
- 40% US (NEALS)
- 40% EU (TRICALS)



PRIMARY & SECONDARY EFFICACY ENDPOINTS:

- Change from baseline through Week 24/48 in disease severity as measured by ALSFRS-R total score & survival
- Change from baseline through Week 24/48 in respiratory function as assessed by slow vital capacity
- Change from baseline through Week 24/48 in disease severity as measured by the ALSFRS-R subdomain scores
- Quality of life from baseline through Week 24/48 as measured by the ALSAQ-40 questionnaire

ALSFRS-R - ALS Functional Rating Scale-Revised; SAB – Scientific Advisory Board; NEALS - Northeast Amyotrophic Lateral Sclerosis Consortium; TRICALS - Translational Research in ALS;

Orphan Drug Designation Granted

FDA granted monepantel orphan drug designation (ODD) status for the treatment of ALS

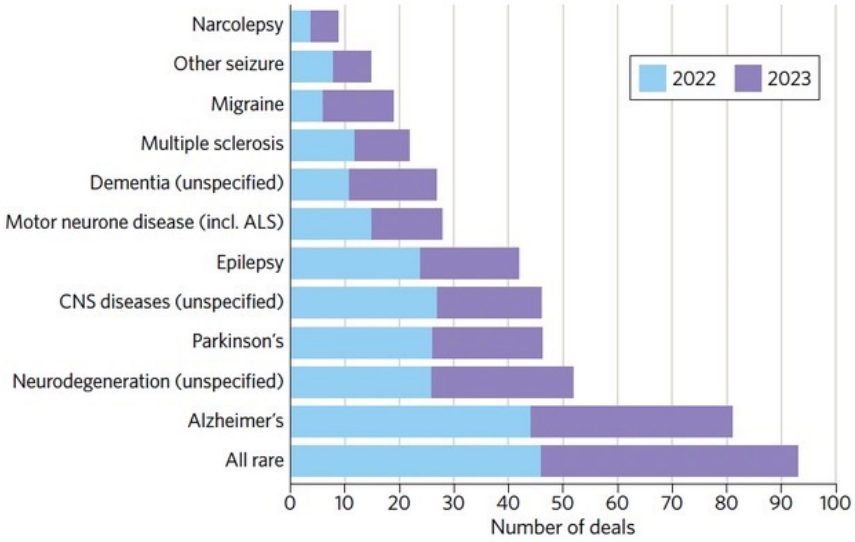
The FDA has authority to grant orphan drug designation to a drug or biological product to prevent, diagnose or treat a rare disease or condition

The ODD status is in place to assist and encourage companies to develop safe and effective treatments for rare diseases and disorders (impacting less than 200,000 persons in the US)

Designation qualifies PharmAust for incentives including:

- Tax credits for qualified clinical trials
- Exemption from user fees
- Seven years of market exclusivity after approval

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

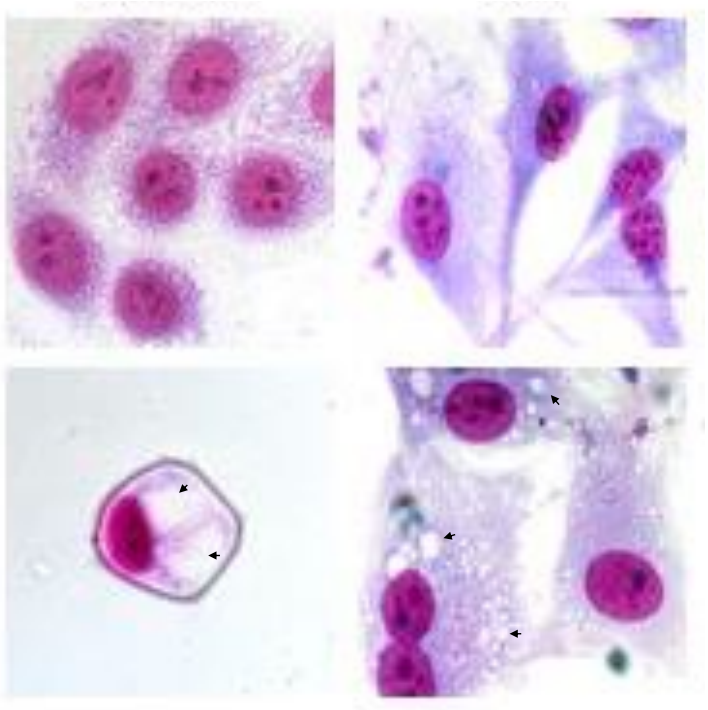


Monepantel Induces Autophagy

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,*]

Contents lists available at ScienceDirect

Ageing Research Reviews

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

ELSEVIER

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

Junsheng Yang* and Chaoyue Zhang

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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)

R&D timeline

Timeline

Q2 CY2023

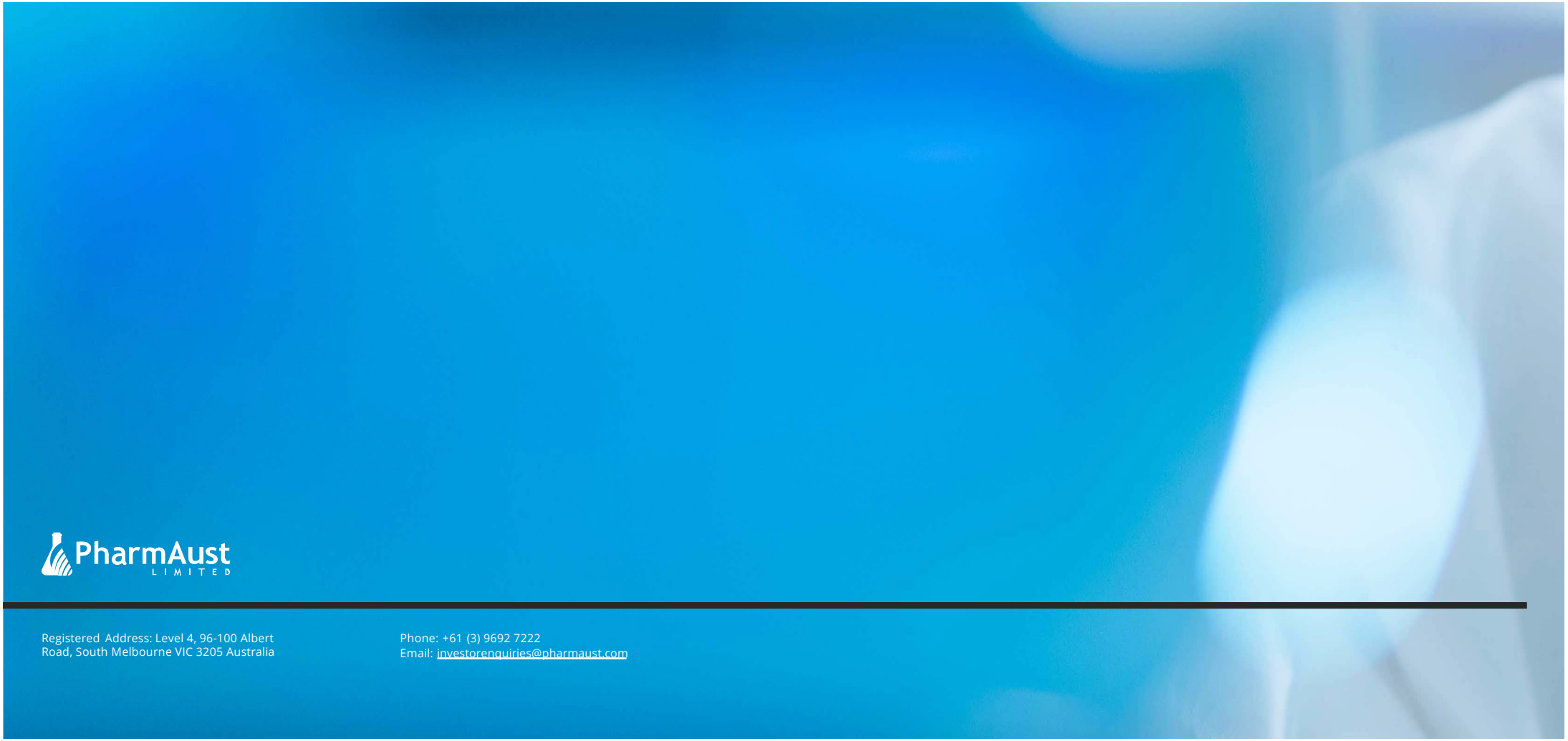
- ✓ Orphan Drug Designation
- ✓ OLE Update (Survival and ALSFRS-R Analysis)
- ✓ Board & Management Hires
- • Pipeline Expansion

Q3 CY2024

- • STRIKE Study HREC Approval
- • EMA CTA
- • Open IND
- • OMPD
- • CMC Validation Batches
- • 1st STRIKE Patient Dosed

CTA – Clinical Trial Application; EMA – European Medicines Agency; HREC – Human Research Ethics Committee; IND – Investigational New Drug; OMPD – Orphan Medicinal Product ; OLE – Open Label Extension;

ASX: PAA



Registered Address: Level 4, 96-100 Albert Road, South Melbourne VIC 3205 Australia

Phone: +61 (3) 9692 7222
Email: investorenquiries@pharmaust.com