ASX: PAA

AGM Investor Update

9 October 2024

Dr Michael Thurn



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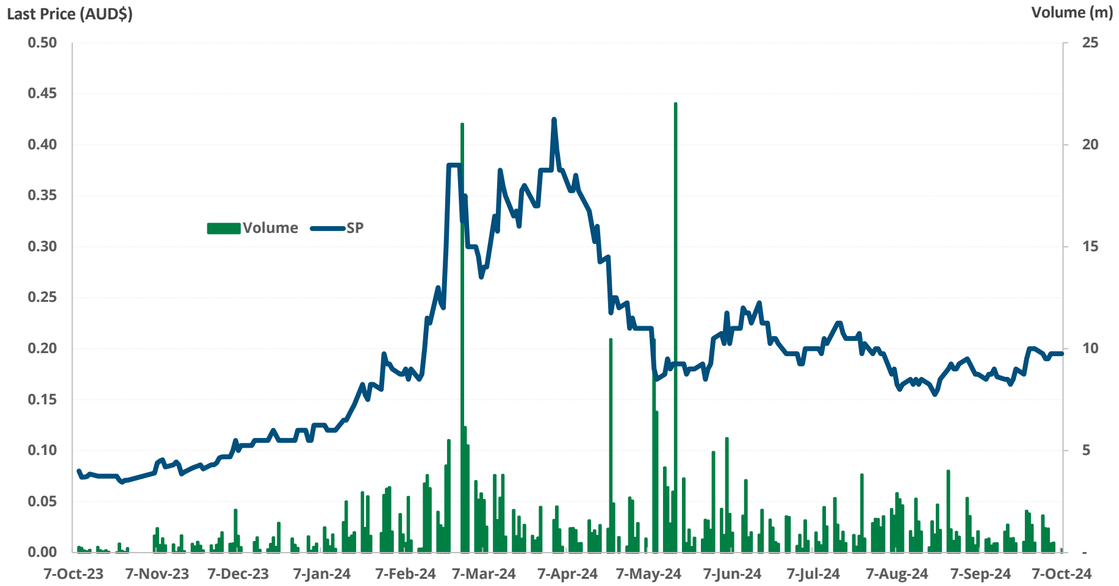
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Corporate Overview

Mid-stage biotechnology company targeting human neurodegenerative diseases

Share Price Performance



Capital Structure (AUD$)

	7 October 2024
Current Share Price (PAA/PAAOA)	$0.20 / $0.10
52 Week Low / High (PAA)	$0.068/ $0.535
No. of Shares (PAA)	486,634,555
Listed Options (PAAOA)	116,315,955
Market Capitalisation	**$94.9m**
Cash (as at 30-Jun-24)	$10.7 m
Debt (as at 30-Jun-24)	Nil
Net Cash	**$10.7m**
Enterprise Value	**$105.6m**
Unlisted Options (10c/15c/17.5c)	11.9 m
Enterprise Value (fully diluted)	**$130.6m**

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>	4.57%
Mr GJ Van & Mrs GV Blommestein <Van Blommestein S/F A/C>	3.80%
Dr Roger Aston	3.09%
Mr Chek Loon Tan	1.80%
Board & Management	5.01%

* As at 7 October 2024

$10 million Placement completed in June, Share Purchase Plan for $7.8 million completed in July

Investment Highlights

Derisked lead program in Amyotrophic Lateral Sclerosis (ALS) with multiple near-term catalysts and potential for use in other neurodegenerative diseases

Positive Phase 1 Data in ALS

- Repurposed drug with excellent long-term safety and tolerability profile
- Monepantel (MPL) and its active metabolite, MPL Sulphone, detectable in cerebrospinal fluid
- Promising early efficacy results showing potential to slow disease progression and increase life expectancy
- Ongoing Open-Label Extension Study
- Granted Orphan Drug Designation (ODD) by the US FDA
- Accepted into the HEALEY ALS Platform Trial

Global Opportunity for ALS

- >200,000 people living with ALS worldwide
- Average life expectancy just over 2 years from diagnosis
- Limited treatment options
- Recent approvals list price >US$160,000

Strong Global IP Position

- Method of use patents issued
- ODD granted
- New manufacturing patent application
- Notice of allowance USPTO – MPL-6 Patent Family

World Class Team

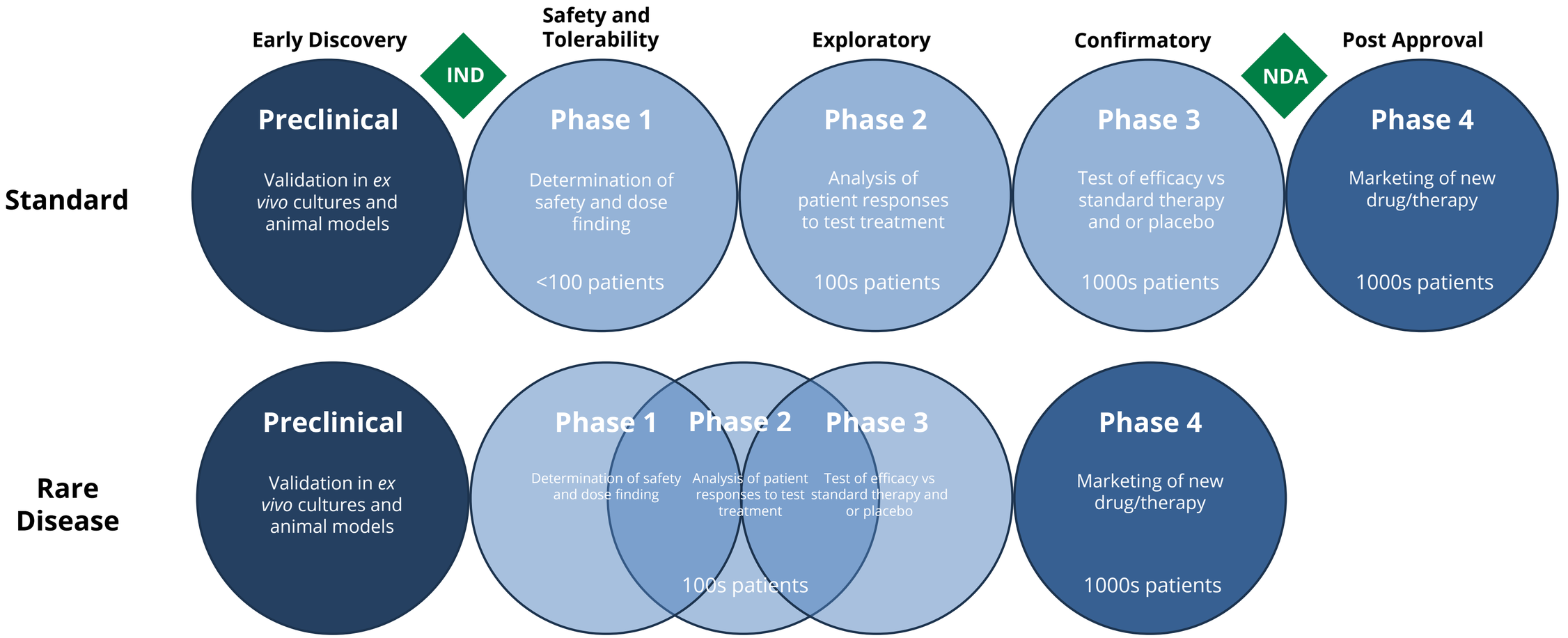
- Experienced Board and management team
- World class Scientific Advisory Board
- Industry leading collaborators and service providers

Neurodegenerative Disease Focus

- MPL has the potential to treat other neurodegenerative diseases
- Accumulation of intracellular misfolded proteins is a hallmark of most neurodegenerative diseases
- Testing underway in a range of preclinical models

Clinical Development Phases

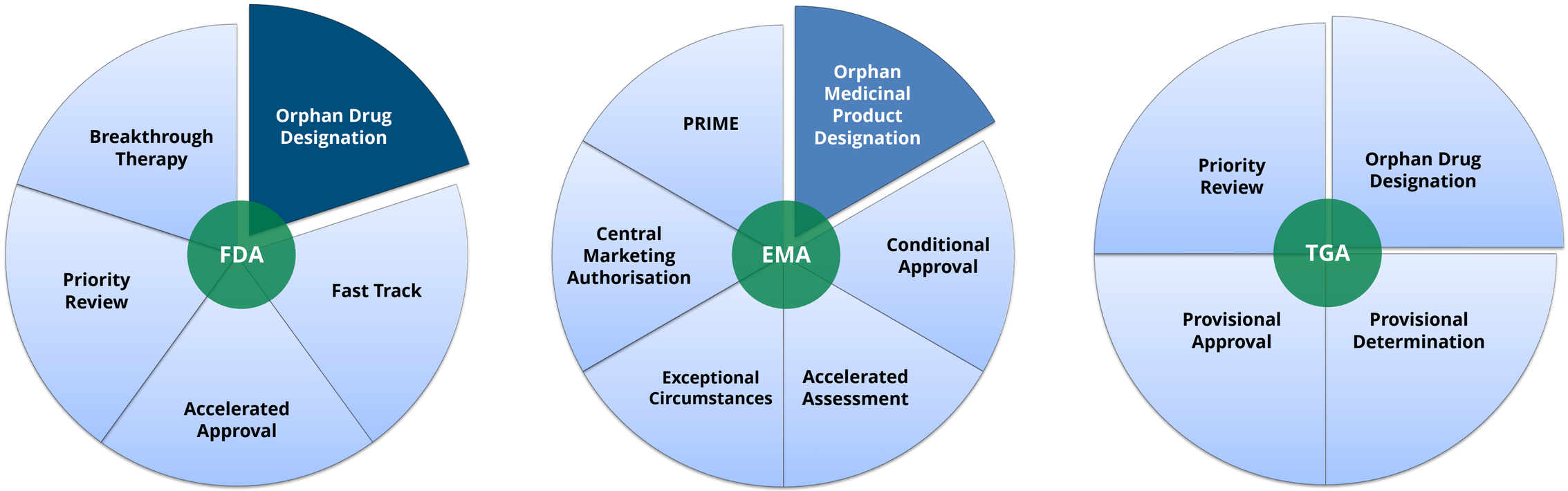
Rare diseases have the advantages of accelerated development timelines and lower development costs



IND – Investigational New Drug; NDA – New Drug Application

Regulatory Designations

Rare diseases have access to broad range of regulatory designations to reduce costs and accelerate development

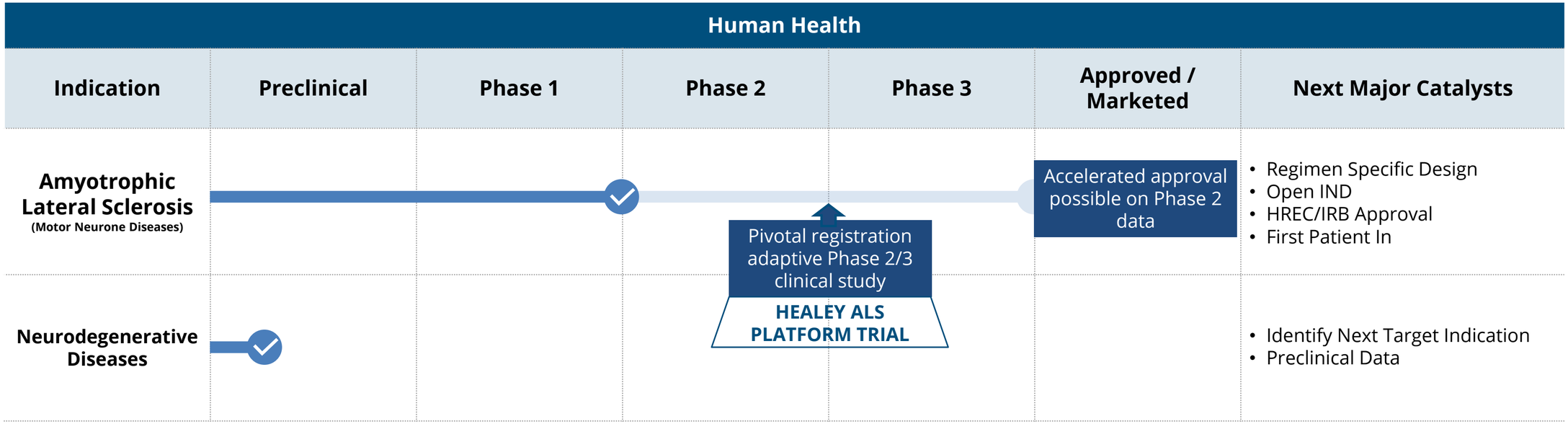


EMA – European Medicines Agency, FDA – Food and Drug Administration, TGA – Therapeutics Goods Administration

Pipeline

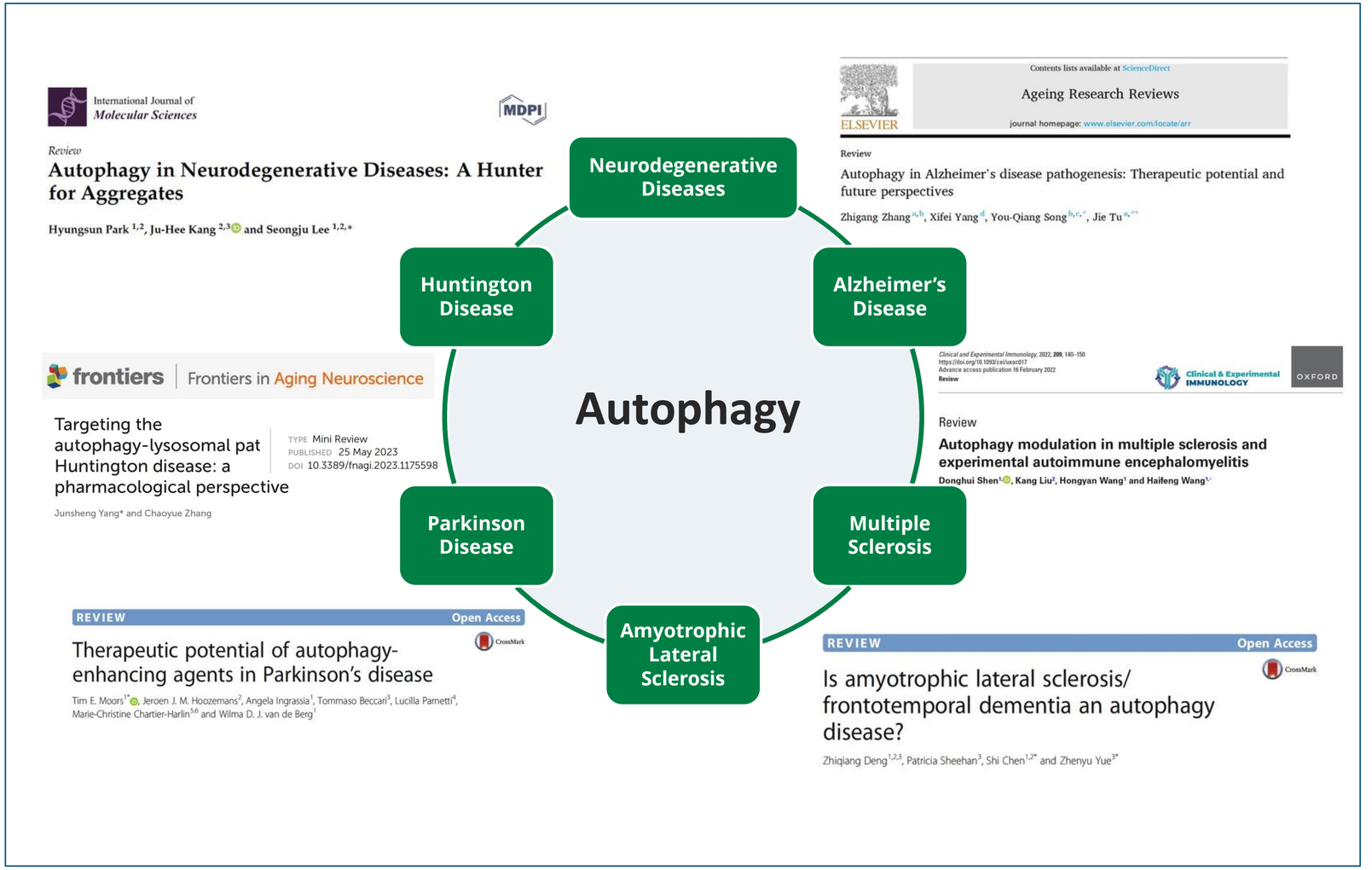
Multiple synergistic product opportunities in neurodegenerative disease by repurposing monepantel

- Single pivotal registration clinical study for ALS
- Targeting accelerated approval from Phase 2 data
- Access to HEALEY ALS Platform Trial reduces study cost and time, and increases patient participation rate
- FDA approval in 2026 possible



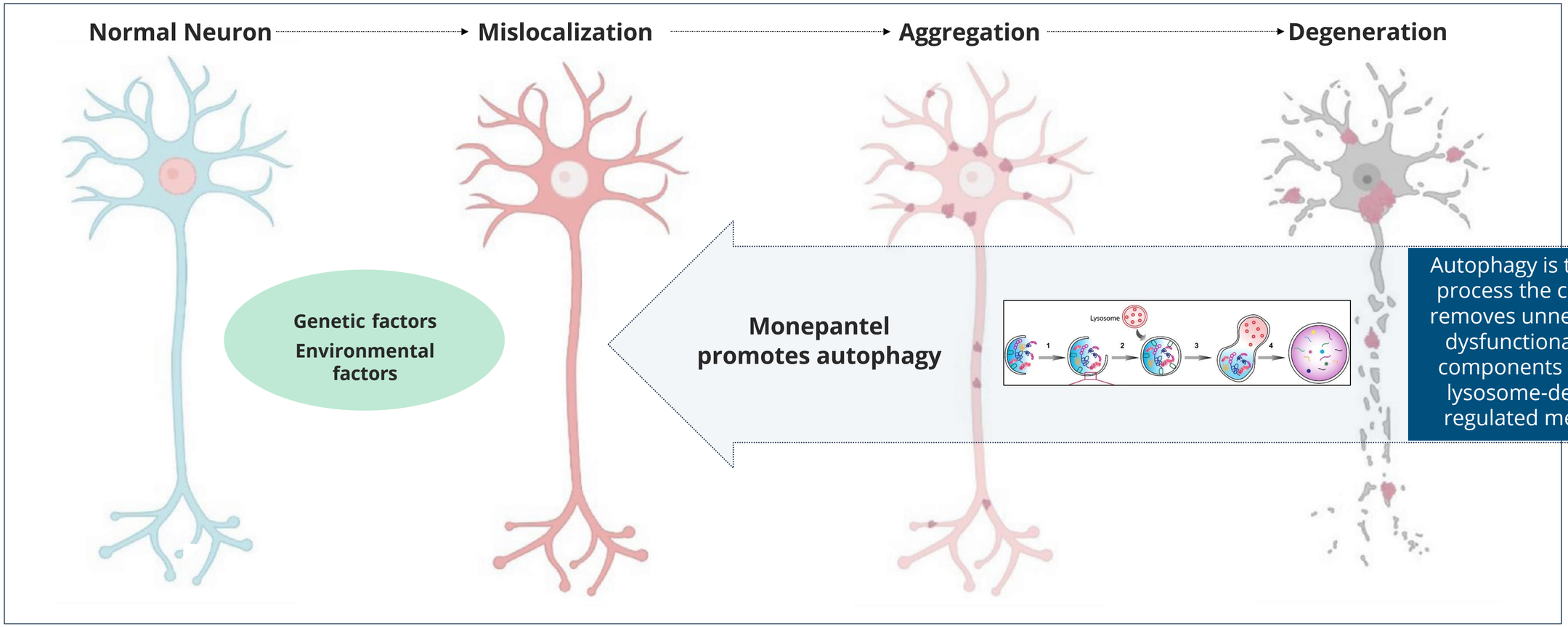
HREC – Human Research Ethics Committee; IND – Investigational New Drug; IRB – Institutional Review Board

Focus on Neurodegenerative Diseases



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

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



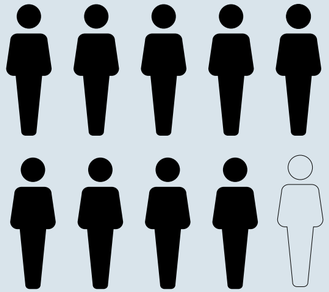
Lidija Damjanovic
Head of Marketing and Corporate Affairs
Lidija brings over 15 years of global experience and passion for launching pharmaceutical products and leading corporate communications and affairs in the biotech and pharmaceutical industry. Her extensive leadership experience in driving commercial growth strategies includes marketing and communications roles in companies such as Merck Sharpe and Dohme, Sartorius, Patheon and other global organizations.

MND / ALS Statistics & Treatments

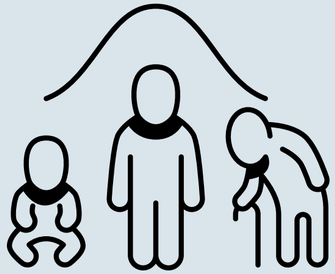
There is no cure and MND/ALS is always fatal



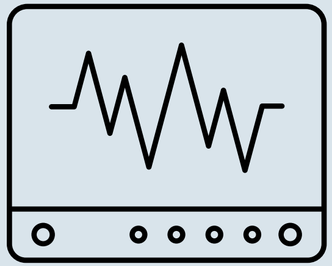
Every **90 minutes** someone is **diagnosed and dies** with MND/ALS



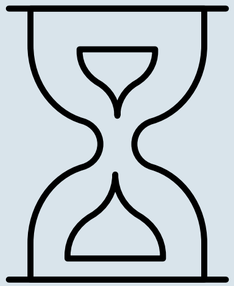
90% of cases occur **without a family history**



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.

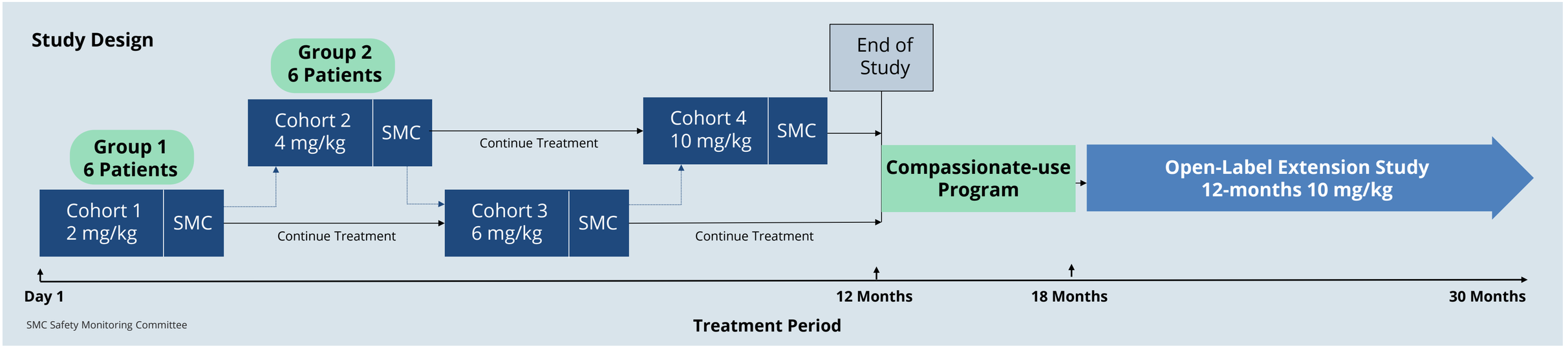
Rilutek (riluzole)
This was the first FDA-approved drug available to treat ALS — in 1995. It inhibits glutamate release and prolongs life ~3 months.

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

Phase 1
ALS MEND Study

The Phase 1 MEND Study was an open label, multicentre study involving 12 patients with 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.
- First group of 6 patients are entering their 24th month of continuous treatment with monepantel
- Phase 1 and baseline OLE data used to design of the protocol specific regimen in the HEALEY ALS Platform Trial

Phase 1
Safety and Tolerability Summary

No deaths, no Serious Adverse Events related to treatment and a very low incidence of Adverse Events

	Incidence of Adverse Event (n)				
	Dose 1 (2 mg/kg)	**Dose 2 (4 mg/kg)**	**Dose 3 (6 mg/kg)**	**Dose 4 (10 mg/kg)**	**Total**
Adverse Events	29	6	12	9	56
Related to Treatment	2	1	-	-	3

- **Only 3 Adverse Events (mild in severity) possibly related to treatment**
  - Raised liver enzymes
  - Increased hair growth
  - Constipation

- **No deaths**
- **No patients withdrew or were discontinued from the study**
- **One Serious Adverse Events (SAEs) reported that was unrelated to treatment**
  - 1 patient (Dose Level 3 – 6 mg/kg) - hospitalised for Intestinal dilatation and Pneumonia

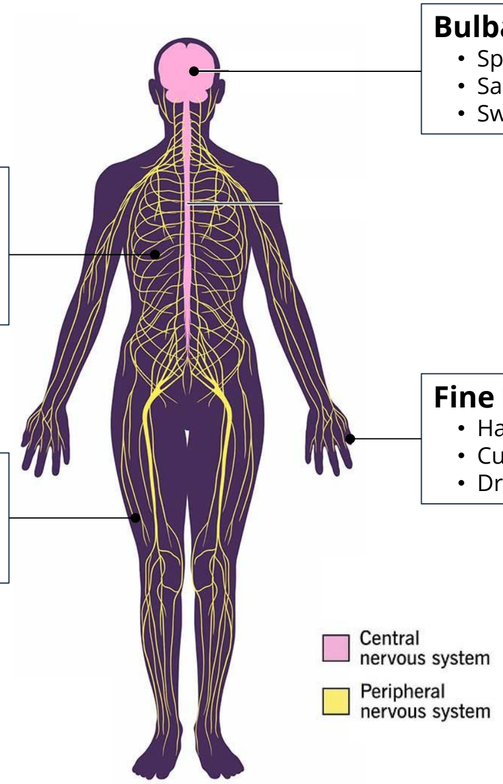


Phase 1

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

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

ALSFRS-R Domains Assessed



Bulbar
- Speech
- Salivation
- Swallowing

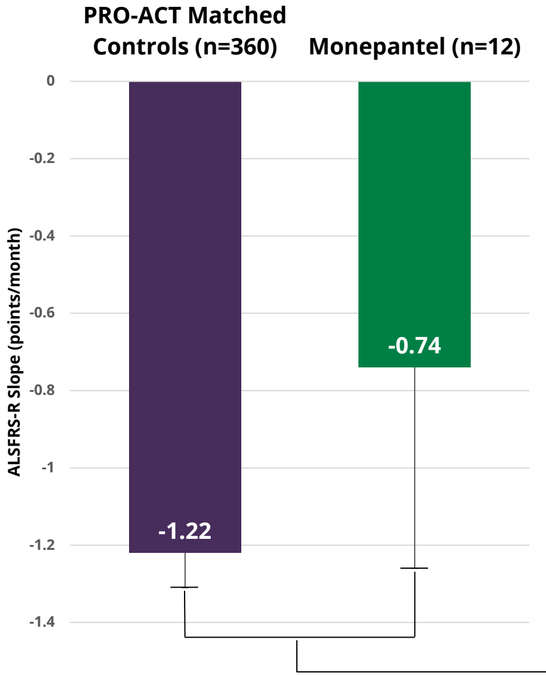
Respiratory
- Dyspnea
- Orthopnea
- Respiratory insufficiency

Fine Motor
- Handwriting
- Cutting food
- Dressing & hygiene

Gross Motor
- Turning in bed
- Walking
- Climbing Stairs

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



Northeast ALS Consortium (NEALS) clinically meaningful = 20% to 25% or greater change in the slope of ALSFRS-R[2]

Difference
0.48 points/month (p=0.08)

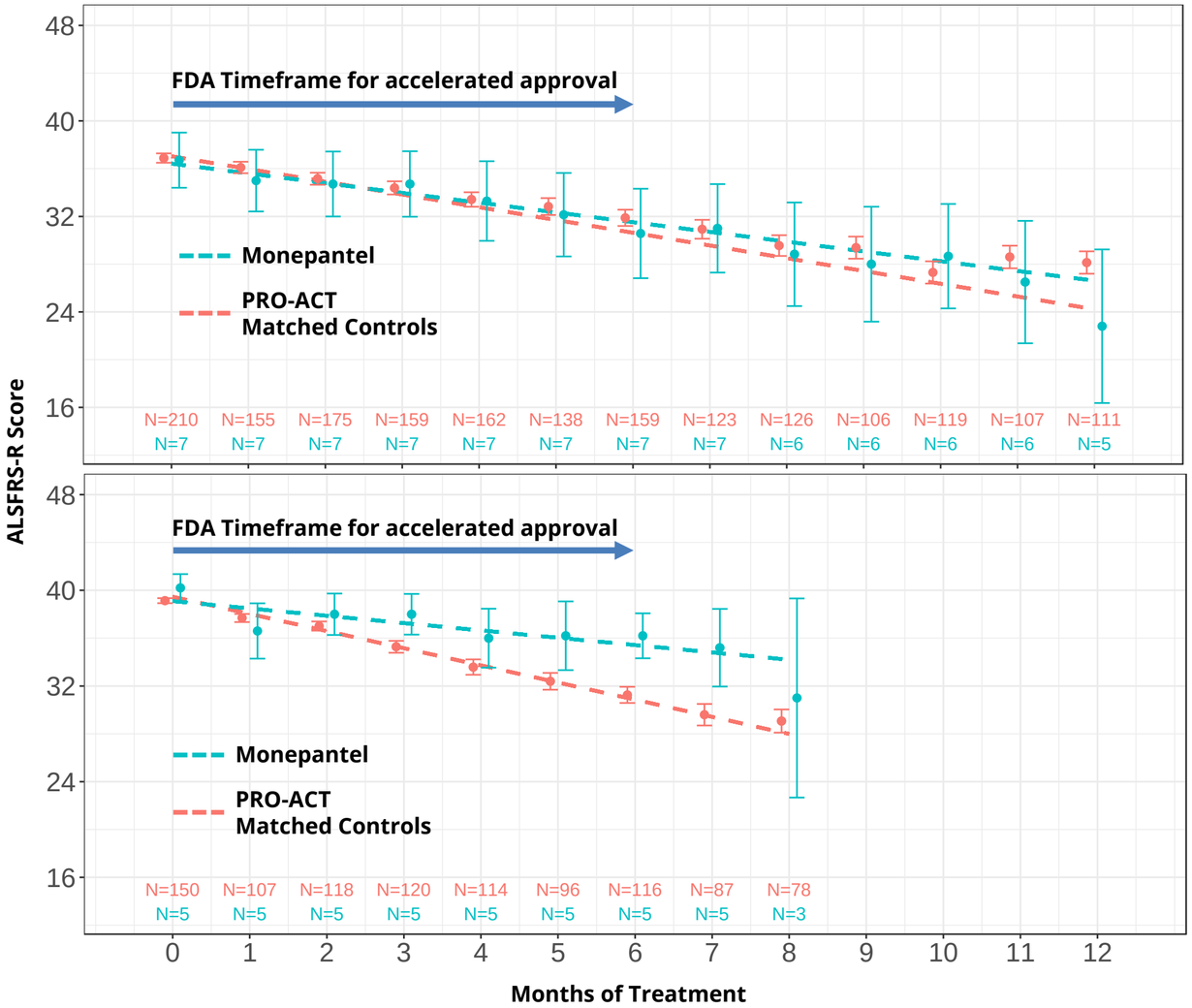
The PRO-ACT database is the largest publicly available repository of merged ALS clinical study data. Data were pooled from 16 completed Phase 2/3 ALS clinical studies and one observational study. Over 8 million de-identified longitudinally collected data points from more than 8,600 persons with ALS, 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.
2Castrillo-Viguera C, Grasso DL, Simpson E, et al. Clinical significance in the change of decline in ALSFRS-R. Amyotroph Lateral Scler. 2010;11(1-2):178-180.

Phase 1

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

Dose response observed between Cohort 1 and 2. Rate of disease progression in Cohort 2 was slowed by an impressive 58% compared to the PRO-ACT database matched controls



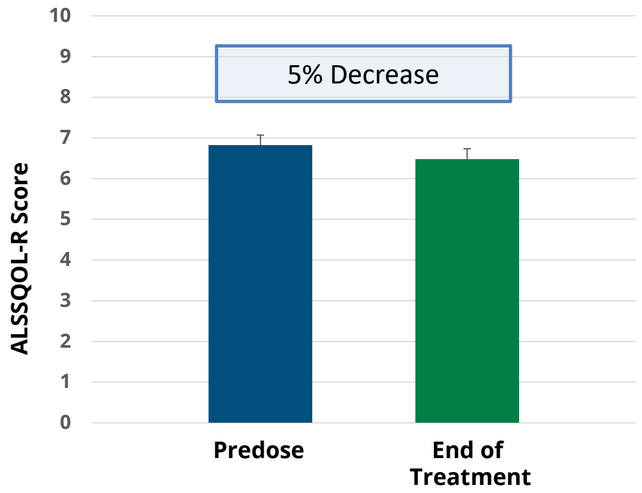
Cohort 1
-0.83 points per month
23% Slower Decline in ALSFRS-R

Cohort 2
-0.60 points per month
58% Slower Decline in ALSFRS-R

Phase 1
Exploratory Endpoints

No significant difference in ALS Quality of Life Questionnaire, Edinburgh Cognitive and Behavioural ALS Screen, and Slow Vital Capacity between predose and end of treatment

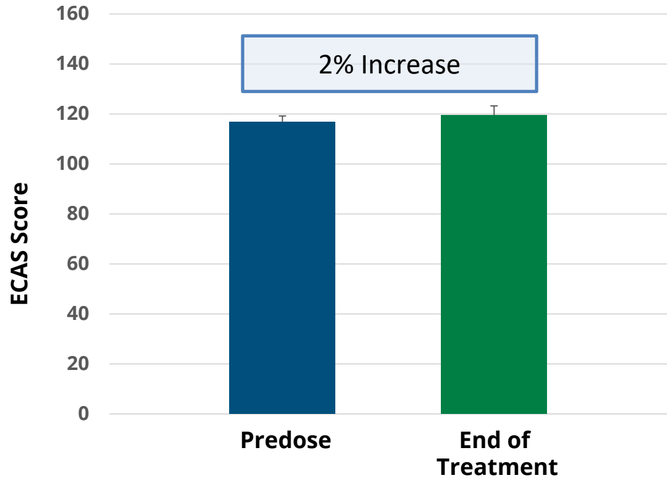
ALSSQOL-R Quality of Life Questionnaire





50-item questionnaire rated on a 10-point scale, across 6 domain scores (negative emotion, interaction with people and environment, intimacy, religiosity, physical symptoms, and bulbar function).

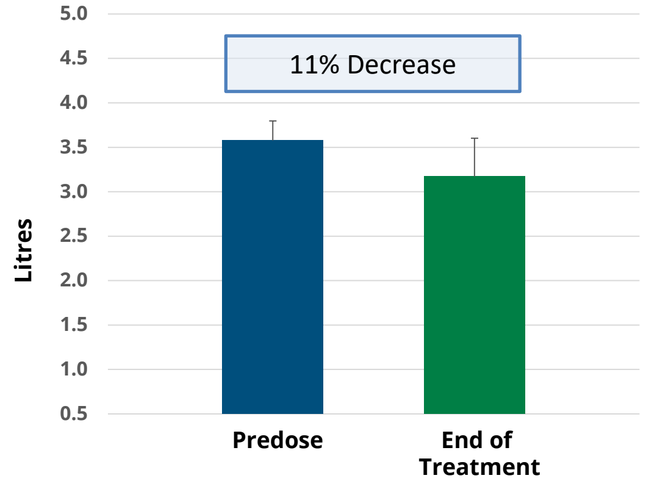
Edinburgh Cognitive and Behavioural ALS Screen

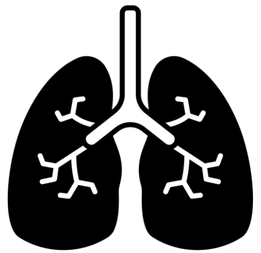




Cognitive screening tool. Includes assessment of fluency, executive functions, language, memory, and visuospatial functions. The total score is 136 points.

Slow Vital Capacity





A lung function test that measures how much air can be exhaled out in a relaxed manner until lungs are completely empty.

Phase 1
ALS Open Label Extension Study

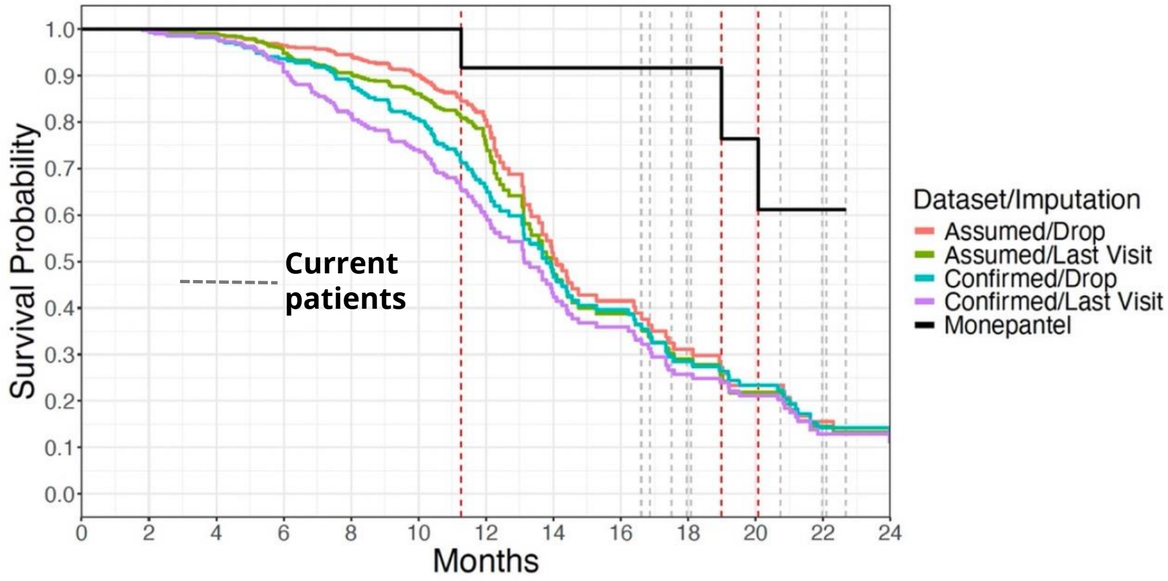
Compared to matched controls from the PRO-ACT Historical Database, treatment with monepantel results in a significantly (X^2=12.83, p=0.0003) longer survival of patients with ALS

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 0.197 (95% CI: (0.062, 0.627), p = 0.0059) indicating that treatment with MPL reduces the risk of death by 80.3%

Analysis Method		Log-Rank Test		Cox Proportional Hazards Model		
Dataset	**Death Time Imputation**	**χ^2**	**p-value**	**Hazard Ratio**	**95% CI**	**p-value**
Assumed	Leave out	12.82	0.00034	0.197	(0.062,0.627)	0.0059
Assumed	Last Visit	14.07	0.00018	0.187	(0.059,0.593)	0.0044
Confirmed	Leave out	14.52	0.00014	0.186	(0.059,0.586)	0.0041
Confirmed	Last Visit	16.35	0.00005	0.173	(0.055,0.546)	0.0028

Overall Survival Probability



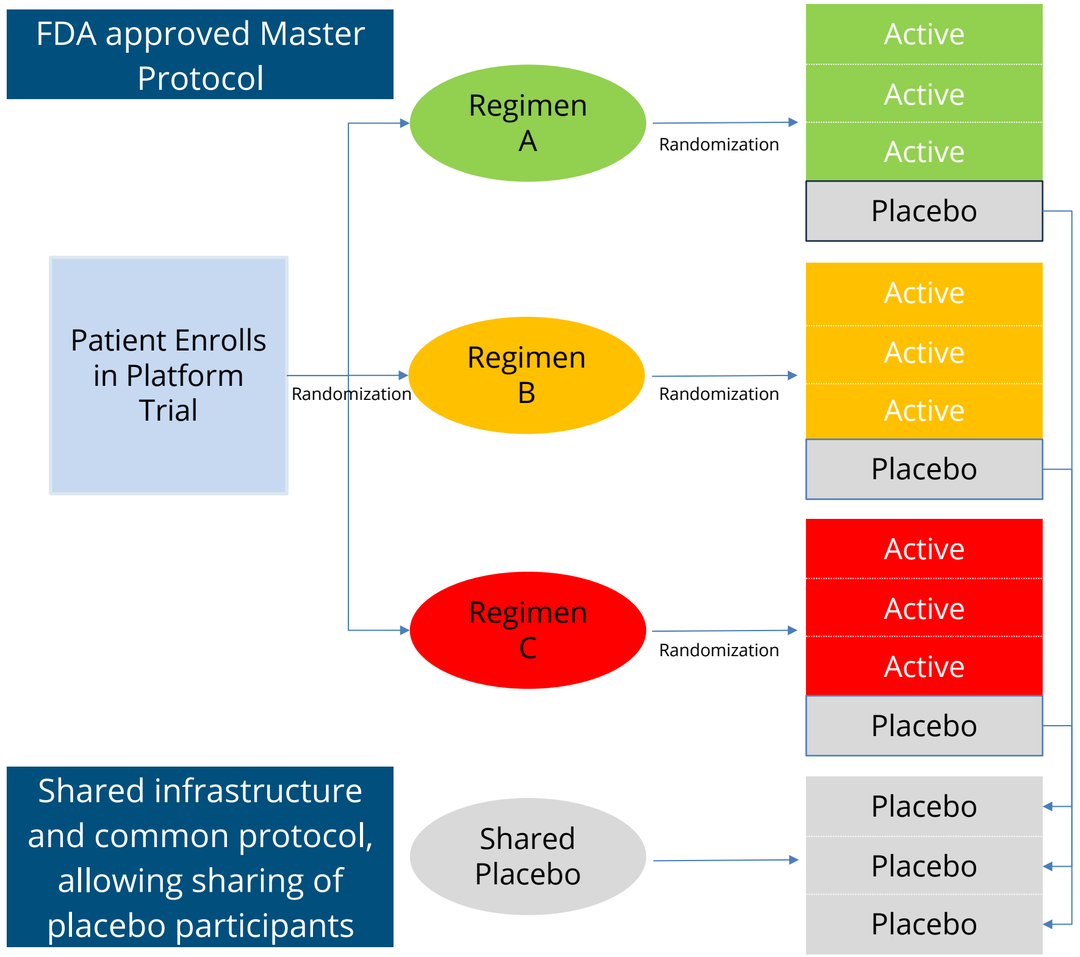
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Monepantel Selected to Enter HEALEY ALS Platform Trial

The HEALEY ALS Platform Trial is a competitive process led by a group of expert ALS scientists and members of the Healey & AMG Center Science Advisory Committee

HEALEY ALS Platform Trial[1]



[1]HEALEY ALS Platform Trial (https://www.massgeneral.org/neurology/als/research/platform-trial)

Massachusetts General Hospital
Founding Member, Mass General Brigham

30% reduction in research cost

- The platform trial tests multiple treatments at once reducing the cost of research

50% faster

- Trial times are cut in half due to the established infrastructure and rapid recruitment

67% more participants

- The platform's broad reach recruits more people and brings them faster access to innovative therapies



Prof Merit Cudkowicz

Director of the Sean M. Healey & AMG Center for ALS at MGH, Chair of the Department of Neurology, and Principal Investigator of the HEALEY ALS Platform Trial



Assoc. Prof Sabrina Paganoni

Co-Director, MGH Neurological Clinical Research Institute (NCRI) and Principal Investigator of the HEALEY ALS Platform Trial

Strategic Importance of the HEALEY ALS Platform Trial

Independent validation of monepantel's potential as a treatment of ALS placing PharmAust in full view of potential pharmaceutical partners

Pivotal Opportunity

- Independent validation of monepantel's potential as an ALS treatment
- Leverages a network of leading ALS Neurologists across the US
- Recognised by industry and the US FDA
- Fastest path to commercialization

Collaboration

- The trial is a large-scale collaboration across multiple clinical trial sites, industry partners, and researchers

Exposure

- Increases reach within the ALS research community, building on an existing partnership with Berry Consultants to create global and US awareness

Funding

- Additional opportunities for non-dilutive and strategic investments

Innovative Trial Structure

Design

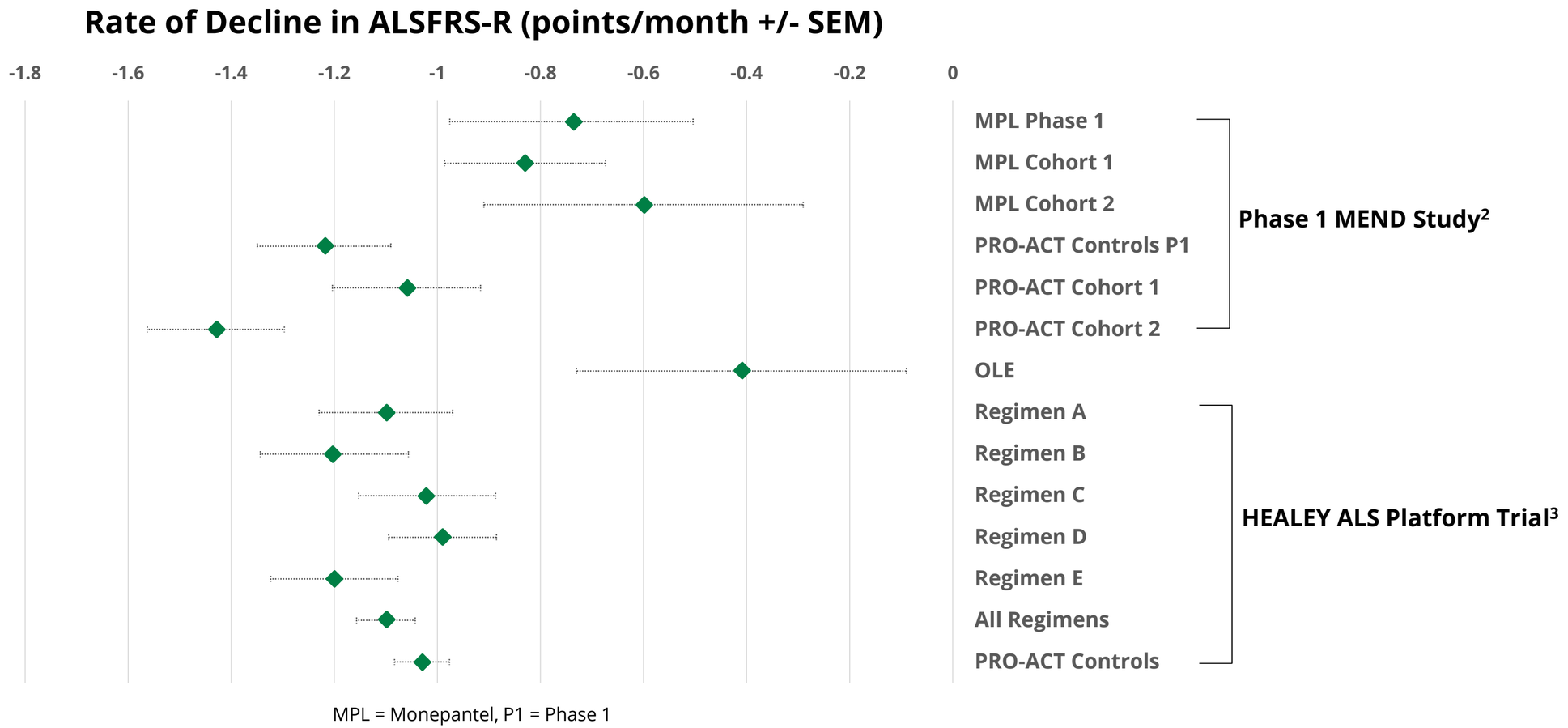
- Shared master protocol
- >70 clinical sites across the US
- 3:1 active drug to placebo ratio
- 160-240 participants per regimen
- 5 regimens completed
- 2 regimens enrolment closed

Next Steps

- Approximately 3-month study design phase to create a regimen-specific protocol amendment
- File master protocol amendment under MGH's IND
- Open US IND for monepantel
- File protocol amendment under MGH's IND
- PharmAust to supply monepantel
- Targeting enrolment Q4 CY 2024

Comparisons of ALSFRS-R Rates of Declines Across Studies

Favourable comparisons to the completed regimens in the HEALEY ALS Platform Trial and PRO-ACT Database[1]



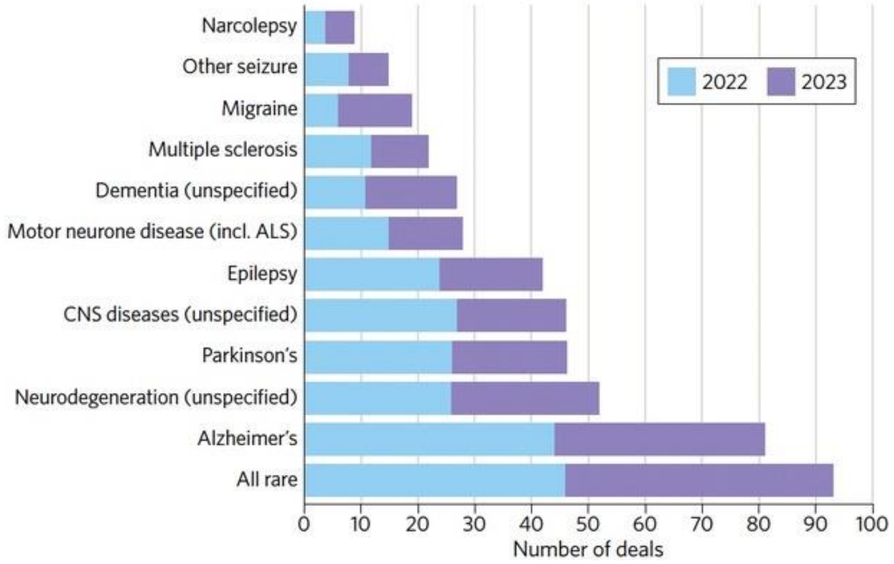
MPL = Monepantel, P1 = Phase 1

[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.
[2]PharmAust Data on file.
[3] Melanie Quintana, Eric Macklin*, Lori Chibnik, Joseph Marion, Anna McGlothlin, Michelle Detry, Matteo Vestrucci, Giorgio Paulon, Jeremy Shefner, Jinsy Andrews, James D. Berry, Marianne Chase, Hong Yu, Alexander Sherman, Sabrina Paganoni, Merit Cudkowicz, for the HEALEY ALS Platform Trial Study Group. Statistical Innovation and Complexities in the HEALEY ALS Platform Trial: Lessons Learned From the First Set of Regimens. Poster Presentation. ENCALS meeting 2024 Stockholm, Sweden June 17-20 2024

Rare Central Nervous System Disease Market

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



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

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

MERCK Preclinical US$505 Million License June 2020 Yumanity Therapeutics	biohaven Preclinical US$970 Million License March 2023 高光制藥 Highlightll Pharma Hangzhou Highlightll	Takeda Preclinical US$580 Million License September 2023 AcuraStem
Dr.Reddy's Phase 1 US$728 Million License December 2023 COYA Therapeutics	ferrer Phase 1 US$122 Million ex-US License March 2024 VERGE genomics	Lilly Preclinical US$612 Million License June 2024 QurAlis



Paul Field
Business Development Officer
Paul brings over 30 years of business development experience across a range of therapeutic areas, including neurodegenerative diseases, and he maintains a deep network in the global biopharmaceutical industry. His experience includes business development roles at Cerecin, Marinova, BioCurate and other companies, and he serves on the Boards of NASDAQ-listed 60 Degrees Pharmaceuticals and Wintermute Biomedical

cerecin BioCurate MARINOVA Pure Source · Pure Science

[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

Research and Development Timeline

Derisked lead program in Amyotrophic Lateral Sclerosis (ALS) with multiple near-term catalysts and potential for use in other neurodegenerative diseases

Timeline

H1 CY2024

- ✓ **Pre-IND Meeting**
- ✓ **OLE HREC Approval**
- ✓ **Phase 1 MEND Study Top-line**
- ✓ **Board & Management Hires**
- ✓ **Orphan Drug Designation**
- ✓ **OLE Update (Survival and ALSFRS-R Analysis)**

H2 CY2024

- ✓ **EMA SME Status**
- ✓ **HEALEY ALS Platform Trial**
- **Design Regimen Specific Protocol**
- **OPEN IND**
- **Preclinical models update**
- **CMC Validation Batches**
- **OMPD**



ALS – Amyotrophic Lateral Sclerosis;; EMA – European Medicines Agency; HREC – Human Research Ethics Committee;
IND – Investigational New Drug; OMPD – Orphan Medicinal Product Designation ; OLE – Open Label Extension; SME – Small and Medium Enterprise

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

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