Motor Neurone Disease Phase 1/2 Clinical Trial Update

- **All 12 patients in Cohort 3 have received initial escalated dose of MPL**
- **The dosages used for Cohorts 1, 2 & 3 have been well tolerated, and no Serious Adverse Events were observed, implying the drug has a good safety profile**
- **Analysis evaluating changes in biomarkers and pharmacodynamics is well underway**
- **PharmAust expects to proceed to Phase 2 with favourable efficacy biomarker results under the interim analysis**

27 June 2023 – Perth, Australia: PharmAust Limited (ASX: PAA & PAAO), a clinical-stage biotechnology company, is pleased to announce that all 12 patients in Cohort 3 have received an initial escalated dose in its Phase 1/2 clinical trial of its lead drug candidate monepantel (MPL) in Motor Neurone Disease/Amyotrophic Lateral Sclerosis (MND/ALS).

The patients are enrolled at two sites: Calvary Health Care Bethlehem, Statewide Progressive Neurological Disease Service, Caulfield South in Victoria and The Centre for Motor Neurone Disease Research, Faculty of Medicine and Health Research Macquarie University in NSW.

The Phase 1/2 clinical study aims to determine the tolerability, safety, pharmacokinetics and preliminary efficacy of oral MPL in individuals living with MND. The trial is open label and comprises four cohorts with escalating MPL doses.

So far the MPL tablets have been well tolerated by all patients in the trial and the Safety Monitoring Committee will continue the assessment of safety and efficacy for each dosage.

Progress update on Phase 1/2 MND interim analysis

As previously announced, interim analysis of biomarkers and pharmacodynamics through the current Phase 1/2 study is well underway. These highly specialised assays are being performed by three independent Australian institutions to explore how MPL is acting on the mTOR signalling pathway in MND patients to slow disease progression. It is hoped that biomarker analysis will confirm MPL's ability to cross the blood-brain barrier and to aid in clearing protein aggregation that is the hallmark of neurodegenerative diseases through the induction of autophagy in nerve cells.

Biomarker research in MND has led to the identification of the protein p75 ECD in urine, demonstrating people with MND show significantly higher levels of that protein compared to those without MND (reference: https://pubmed.ncbi.nlm.nih.gov/28228570/).

The p75 ECD study results have now been received from Flinders University in Adelaide and will be formally interpreted by a pharmacologist and will be announced as soon as possible.

An analysis being conducted at the Florey Institute in Melbourne evaluating p-RPS6KB1 and p-EIF4EBP1 is still pending. Further, highly specialised testing of Neurofilament Light Chain (NfL) is being conducted at the University of Tasmania which is expected in the coming weeks.

About Motor Neurone Disease/Amyotrophic Lateral Sclerosis and the trial

According to the International Alliance of ALS/MND Associations, MND affects over 350,000 people globally and kills more than 100,000 people yearly. The disease is invariably fatal, with the average life expectancy of someone with MND being around 27 months. The MND/ALS addressable market is US$3.6Bn per annum, with Riluzole reaching ~US$1Bn annual sales.

The disease is progressive, meaning the symptoms get worse over time. MND has no cure and no effective treatment to reverse its progression. PharmAust notes that five patients have surpassed the 8-month mark on MPL without any safety issues, and one patient appears “stable”.

PharmAust demonstrated in its preclinical programs that MPL has the potential to activate molecular pathways relevant to the treatment of MND. MPL could reduce the rate of degeneration and loss of motor neurons in the brainstem's anterior horns and motor nuclei. There are also several surrogate clinical endpoints to be determined during the trial. PharmAust has developed and manufactured a bespoke MPL tablet for the trial.

The Phase 1/2 study is being funded by a commitment of $881,085 by FightMND, Australia's largest independent funder of MND research.

With success in the clinic, PharmAust hopes that MPL could receive orphan drug designation by the TGA and FDA for MND. Such designations come with financial and supportive benefits and PAA is evaluating this opportunity.

This announcement is authorised by the Board.

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About PharmAust Limited:

PharmAust Limited is listed on the Australian Securities Exchange (PAA) and the Frankfurt Stock Exchange (ECQ). PAA is a clinical-stage company developing therapeutics for both humans and animals. The company specialises in repurposing marketed drugs lowering the risks and costs of development. These efforts are supported by PAA’s subsidiary, Epichem, a highly successful contract medicinal chemistry company that generated $3.4 million in sales of goods & services in FY 2022.

PAA’s lead drug candidate is monepantel (MPL), a novel, a potent and safe inhibitor of the mTOR pathway – a pathway having key influences in cancer growth and neurodegenerative diseases. MPL has been evaluated in Phase 1 clinical trials in humans and Phase 2 clinical trials in dogs. MPL treatment was well-tolerated in humans, demonstrating preliminary evidence of anticancer activity. MPL showed objective anticancer activity in dogs. PAA is uniquely positioned to commercialise MPL for treating human and veterinary cancers and neurodegenerative diseases as it advances a reformulated version of this drug through Phase 1 and 2 clinical trials.