FDA Outlines Pathway to Accelerated Approval for Monepantel in MND

Highlights:

- **PharmAust has successfully completed a Pre-IND meeting with the FDA**
- **The FDA provided positive feedback and outlined the path required to potentially receive accelerated and full approval of monepantel for the treatment of MND/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 also prepare to launch clinical sites in Europe and Australia where data can also be used to support the FDA drug approval process**

16 February 2024 – Perth, Australia: PharmAust Limited (ASX: PAA & PAAOA) ("PharmAust" or "the Company"), a clinical-stage biotechnology company, is pleased to announce that it has completed a Pre-Investigational New Drug (Pre-IND) meeting for monepantel in the treatment of motor neurone disease/amyotrophic lateral sclerosis (MND/ALS) with the United States (US) Food and Drug Administration (FDA). This represents a significant milestone for the company as it plans to undertake an adaptive Phase 2/3 clinical study in Q2 2024 and potentially only require this clinical study to support accelerated and/or full approval of monepantel for treating MND/ALS.

The pre-IND meeting aimed to formally initiate communication with the FDA and confirm the details and acceptability of PharmAust's proposed ongoing development program, including the requirements for non-clinical and clinical pharmacology, clinical chemistry, and manufacturing controls. PharmAust sought specific guidance from the FDA on the design and overall adequacy of the planned adaptive Phase 2/3 clinical study to enable accelerated and/or full approval. The FDA confirmed that PharmAust may potentially receive accelerated and/or full approval from this single clinical study subject to demonstrating substantial evidence of effectiveness and an adequate database supporting safety.

The FDA also advised that there were no minimum requirements for the number patients and study sites located in the US paving the way for the adaptive Phase 2/3 clinical study to be a global study. Clinical sites and patients from Europe and Australia will be utilised leading to decreased recruitment timelines and allowing PharmAust to also seek approval from the European Medicines Agency (EMA) and Australia's Therapeutic Goods Administration (TGA) following completion of the adaptive Phase 2/3 study.

PharmAust Chief Executive Officer Dr Michael Thurn commented:
"We are highly encouraged by the positive feedback from the FDA. It aligns with our expectations and provides the Company with a clear understanding of the requirements to potentially receive accelerated and/or full approval of monepantel for treating MND/ALS.

This advice truly positions us as a global play following the successful completion of our planned adaptive Phase 2/3 clinical study."

PharmAust's planned adaptive Phase 2/3 clinical study will be a multicentre, randomised, placebo-controlled, adaptive clinical study evaluating the safety and efficacy of monepantel in patients with MND/ALS over 48 weeks. The primary aim will be to assess the efficacy of monepantel, as compared to placebo, on the progression of MND/ALS. This will be evaluated as a change from baseline disease severity measured by the ALS Functional Rating Scale-Revised (ALSFRS-R) total score and survival.

As this is an adaptive study design, an interim analysis will be performed at Week 24 by a team of unblinded statisticians for the potential to receive accelerated approval from the FDA.

The Board authorises this announcement.

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About Motor Neurone Disease:

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 the standard of care treatment, Riluzole, only prolonging life on average by 2-3 months.

The disease is progressive, meaning the symptoms get worse over time. MND has no cure and no effective treatment to reverse its progression. Independent studies have shown that one-third of patients die within 12 months after the first diagnosis.

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 human and animal health applications. The company is focused on repurposing monepantel (MPL) for human neurodegenerative diseases and treating cancer in dogs.

MPL is a potent and safe inhibitor of the mTOR pathway. This pathway plays a central role in cell growth and proliferation of cancer cells and degenerating neurons. The mTOR pathway regulates the cellular “cleaning process”, where toxic protein is broken down into macromolecules to be reused. This autophagic process is disrupted in most neurodegenerative diseases, including motor neurone disease (MND/ALS).

PAA’s lead MPL program is for the treatment of MND/ALS, a rare, incurable disease. The company is currently completing a Phase 1 study in patients with MND/ALS. Top-line results are expected to be announced in Q1 CY2024. PAA anticipates starting an adaptive Phase 2/3 clinical study in H1 2024 that could lead to accelerated approval with the US Food and Drug Administration in 2026. PAA is preparing to begin a pivotal field trial in dogs with B-Cell Lymphoma to enable product registration in the US in 2025. PAA has previously successfully completed a Phase 1 oncology clinical study of monepantel in humans and pilot studies in canine cancer.