PharmAust files positive clinical data with FDA to support Orphan Drug Designation request

Highlights:

- **Clinical data showing monepantel has the potential to delay the progression of MND/ALS and provide patients with a survival benefit was submitted to the FDA**
- **Response from the FDA expected within 90 days**
- **Recent clinical trial failures by leading FDA approved drugs highlights the significant unmet global need for safe and effective drugs for the treatment of MND/ALS**
- **PharmAust remains on track to commence a pivotal registration Phase 2/3 Study for MND/ALS in H1 CY24**

14 March 2024 – Perth, Australia: PharmAust Limited (ASX: PAA & PAAOA) ("PharmAust" or "the Company"), a clinical-stage biotechnology company, is pleased to announce that it has filed supplementary clinical data from its recently completed Phase 1 MEND Study with the United States (US) Food and Drug Administration (FDA) Office of Orphan Products Development in support of its recent request for Orphan Drug Designation (ODD) for monepantel (MPL) for the treatment of Motor Neurone Disease (MND) / Amyotrophic Lateral Sclerosis (ALS).

PharmAust initially submitted the request for ODD to the FDA's Office of Orphan Products Development early in November 2023. In January 2024, the FDA responded, requesting further supporting data, either preclinical or clinical, to establish the drug's potential for effectiveness in MND/ALS.

PharmAust recently announced positive top-line data from its Phase 1 MEND Study involving 12 patients with MND/ALS. Daily administration of MPL over a 7 to 12-month period was well-tolerated and did not result in any dose-limiting toxicities or serious adverse effects. Daily administration of MPL resulted in a clinically meaningful therapeutic effect as evidence by by a small and non-significant numerical reduction in ALS Functional Rating Scale-Revised (ALSFRS-R) scores from baseline to end of treatment. Quality of life (ALSSQOL-R Quality of Life Questionnaire) and cognitive and behavioural (Edinburgh Cognitive and Behavioural ALS Screen) function were also not significantly impacted, and there was no change in respiratory function (Slow Vital Capacity). The effects of treatment with MPL on biomarkers demonstrated a large reduction in cerebrospinal fluid (CSF) NfL, which supported a meaningful clinical effect.

Comparisons to matched controls from the PRO-ACT database for the decline in ALSFRS-R scores and overall survival provided confirmatory evidence of the potential efficacy of MPL in prolonging the survival of patients with MND/ALS.

This data has been packaged in a formal amendment to the original ODD request and successfully submitted to the FDA. The timeline for granting the ODD is up to 90 days.

Recent Trial Failures of FDA Approved Drugs

Amylyx Pharmaceuticals (NASDAQ:AMLX) recently announced[1] the top-line results from PHOENIX, a global, 48-week, randomised, placebo-controlled Phase 3 clinical trial of RELYVRIO® (AMX0035 - sodium phenylbutyrate and taurursodiol) involving 664 people living with ALS. PHOENIX did not meet its primary endpoint of reaching statistical significance (p=0.667) as measured by change from baseline in the ALSFRS-R total score at Week 48, nor was there statistical significance seen in secondary endpoints. Amylyx plans to engage with regulatory authorities, which may include the voluntary withdrawal of RELYVRIO® from the market.

Ferrier International S.A. also recently announced[2] the top-line results from ADORE, a multicentre, multinational, 48-week, double-blind, randomised, placebo-controlled Phase 3 study of edaravone (100 mg, FAB122, once daily as oral formulation) in patients with ALS. Edaravone did not show significant benefit over placebo in patients with ALS in slowing the disease progression as measured by change from baseline in the ALSFRS-R score after 48 weeks. No improvement over placebo on long-term survival was observed at 48 weeks and 72 weeks for a subgroup of patients. Edaravone is currently approved by the FDA in two different formulations: RADICAVA® IV administered through intravenous (IV) infusions, and RADICAVA® Oral Suspension, an oral suspension taken by mouth or via a feeding tube. Both formulations are distributed by the pharmaceutical company Mitsubishi Tanabe Pharma.

PharmAust Chief Executive Officer Dr Michael Thurn commented:
"Based on the strength of the Phase 1 MEND Study outcomes we are very confident that FDA will grant monepantel an ODD for the treatment of MND/ALS. Receiving ODD status from the FDA will come at an opportune time for PharmAust given the recent clinical trial failures of the 2 leading FDA drugs for MND/ALS. At a time of need, monepantel offers much needed hope for patients with this severely debilitating disease.

The Company is in the process of finalising our exciting plans for its pivotal registration Phase 2/3 study and is on track to commence the study during the middle of this year."

About Orphan Drug Designation

The FDA has the authority to grant ODD to a drug to prevent, diagnose or treat a rare disease or condition, defined as any disease or condition that affects less than 200,000 persons in the US. An ODD qualifies sponsors for incentives, including tax credits for qualified clinical trials, exemption from user fees, and the potential for seven years of market exclusivity after approval.

The Board authorises this announcement.

Enquiries:

Dr Michael Thurn
Chief Executive Officer
investorenquiries@pharmaust.com

Media:

Matthew Wright
NWR Communications
matt@nwrcommunications.com.au
0451 896 420

P +61 (8) 9202 6814
F +61 (8) 9467 6111
www.pharmaust.com

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.

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 recently announced positive top-line results for its Phase 1 study in patients with MND/ALS. PAA anticipates starting an adaptive Phase 2/3 clinical study in H2 CY 2024 that could lead to accelerated approval with the US Food and Drug Administration in 2026.

The Neurodegenerative Disease Market size is estimated at USD 55.12 billion in 2024, and is expected to reach USD 77.82 billion by 2029, growing at a CAGR of 7.14% during the forecast period (2024-2029).[3]

[1] https://investors.amylyx.com/news-releases/news-release-details/amylyx-pharmaceuticals-announces-topline-results-global-phase-3
[2] Ferrer Reports Top-Line Results from Phase 3 ADORE Study in ALS. News Release. Ferrer. Published January 10, 2024. Accessed January 15, 2024. https://ala.associates/clinical/ferrer-reports-top-line-results-from-phase-iii-adore-study-in-als/
[3] https://www.mordorintelligence.com/industry-reports/neurodegenerative-disease-market

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