PharmAust MND Trial Interim Analysis PK Outcomes

- The dosages used for Cohorts 1 and 2 were well tolerated, and no Serious Adverse Events were observed, implying the drug has a good safety profile.
- Quantitative analysis of monepantel (MPL) drug concentrations in patients after 24 hours matched the predicted MPL and MPLS levels.
- Extended data show that MPL levels reached the predicted steady-state therapeutic levels from Day 1, and MPLS reached this state before Day 8.
- The data provide preliminary evidence for a potential linear relationship between patient dosage and MPL and MPLS plasma concentrations.
- Usage of MPL tablets for an extended period provides evidence of accumulation of MPLS in plasma.
- Trial Safety Committee approves Cohort 1 patients to be elevated to Cohort 3 and receive increased dosage.
- Analysis evaluating changes in biomarkers and pharmacodynamics is underway.

7 June 2023 – Perth, Australia: PharmAust Limited (ASX: PAA & PAAO), a clinical-stage biotechnology company, provides a progress update on its clinical trial of its lead drug candidate monepantel (MPL) in Motor Neurone Disease/Amyotrophic Lateral Sclerosis (MND/ALS).

PharmAust completed the interim pharmacokinetic (PK) analysis of plasma MPL and Monepantel Sulphone (MPLS) levels in MND patients who received MPL at a dosage of 2mg/kg for Cohort 1 and 4mg/kg for Cohort 2.

The 24-hour PK data on how MPL was absorbed, distributed, metabolised into MPLS, and eliminated show that tablets perform as expected and are evident in the plasma at the predicted levels for both cohorts. Usage of MPL tablets for an extended period, as recorded for Cohort 1, provides evidence of accumulation of MPLS in the plasma after approximately four months of continual dosing.

MPL levels appear to reach a “steady state” on Day 1, and MPLS levels appear to reach a steady state before Day 8. Given PharmAust’s previous preclinical data from mouse-blood-brain barrier investigations, these data suggest that exposure of MPL to the central nervous system may be achieved.

Within the PK data, the concept of “steady-state” is of fundamental importance in pharmacology. Achieving a "steady-state" suggests a dynamic equilibrium where drug concentrations maintain therapeutic levels for long and potentially indefinite periods.

The Safety Committee has approved dose escalation for patients in Cohort 1 to Cohort 3. Subject to the continued safety of the escalated Cohort 1 patients to level 3, and approval from the Safety Committee, PharmAust will continue with the MPL dose escalation for Cohort 2 to level 4.

***Dr Roger Aston, Executive Chairman of PharmAust, commented**:*
“The outcome is excellent news for PAA, our proprietary tablets formulation shows effective absorption of MPL and the achievement of steady-state levels of MPLS, the active metabolite of MPL.

We are delighted that patients on our drug for over seven months have shown good tolerance and no Serious Adverse Events. We now eagerly await the analysis of the biomarkers.”

The PK results provide good evidence that MPL is being metabolised to MPLS. Additional reporting on the changes in MND biomarkers and pharmacodynamics is still pending, which will determine the activity of MPL and how long MPL stays within therapeutic limits.

The tablets developed by PharmAust deliver MPL to the blood stream as measured in plasma. This is important as MPL is a highly insoluble drug, and the chosen recipients are doing their job of keeping the drug in solution and making it available to the circulation.

The dosages used for Cohorts 1 and 2 were well tolerated and no Serious Adverse Event were observed, implying the drug has a good safety profile. This is very important as patients are potentially expected to take the product for extended periods (MND does not go away and patients are intended to keep taking the drug to slow or stop progression).

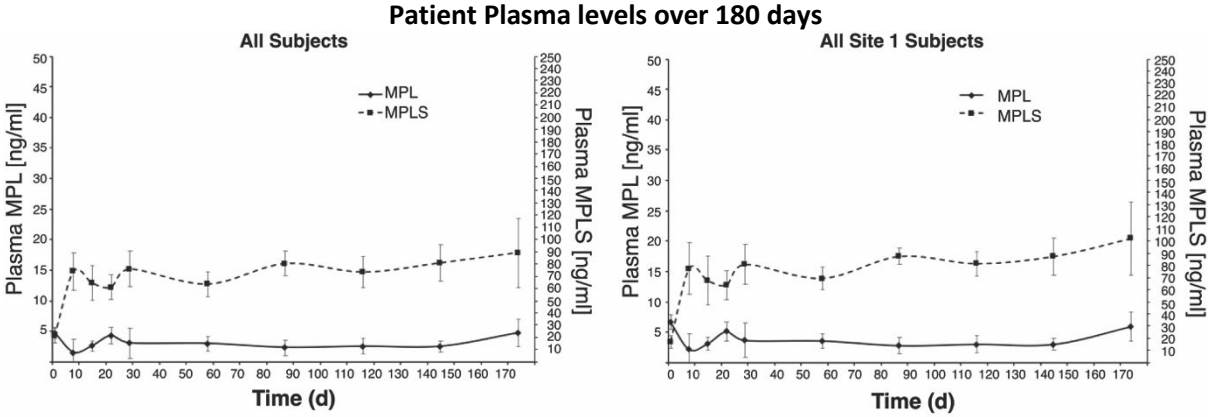

Figure 1. Average MPL and MPLS plasma concentrations plotted for 1) All subjects and 2) Only Site 1 subjects. (d) = days. Note the MPL Y axis is 0 – 50 ng/ml and the MPLS axis is 0 – 250 ng/ml. Y axis upper limit is 250 ng/ml for comparison with Level 2 data.

The variation in individual plasma levels seen in the charts may be explained by patient compliance issues taking the tablets at home instead of when supervised in the clinic.

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 7-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.

The Board authorises this announcement.

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About PharmAust Limited:

PharmAust Limited is listed on the Australian Securities Exchange (code: PAA) and the Frankfurt Stock Exchange (code: 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 which generated $3.4 million in sales of goods & services in FY 2022.

PAA's lead drug candidate is monepantel (MPL), a novel, 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 demonstrated objective anticancer activity in dogs. PAA is uniquely positioned to commercialise MPL for treatment of human and veterinary cancers as well as neurodegenerative disease as it advances a reformulated version of this drug through Phase 1 and 2 clinical trials.