Clinical data show MPL suppresses biomarkers associated with motor neurone disease

- Clinical trial results provide preliminary evidence that monepantel (MPL) activity suppresses biomarkers associated with motor neurone disease progression
- MPL significantly decreased $p75^{ECD}$ levels, a biomarker with predictive value in MND/ALS progression
- Results do not show overall disease progression and support proceeding to a Phase 2 trial

11 July 2023 – Perth, Australia: PharmAust Ltd (ASX: PAA & PAAO), a clinical-stage biotechnology company, is pleased to provide this Phase 1/2 trial update on the urinary biomarker data of its lead drug candidate MPL in Motor Neurone Disease/Amyotrophic Lateral Sclerosis (MND/ALS).

Research[2] has demonstrated that people with MND/ALS show significantly higher levels of $p75^{ECD}$ in their urine ($p < 0.0001$).

Significantly reduced $p75^{ECD}$ levels were seen in Cohort 1 participants in PharmAust's Phase 1/2 MND trial. This cohort was on the lowest dosage.

$p75^{ECD}$ and creatinine were measured from all six Cohort 1 participants. $p75^{ECD}$ levels were significantly reduced across the cohort (Mixed Effects analysis, $p < 0.05$, Figure 1), while creatinine levels appeared overall relatively unchanged (Paired tTest, $p > 0.05$). $p75^{ECD}$/ creatinine ratios were reduced for three of six subjects, unchanged for two and increased for one subject.

The data provide preliminary evidence of MPL activity against motor neurone degradation. Importantly, it does not provide evidence of overall disease progression and provide a basis for proceeding to a Phase 2 clinical trial. PharmAust will continue with MPL dose escalation for Cohorts 3 and 4 to determine the optimum dose for Phase 2.

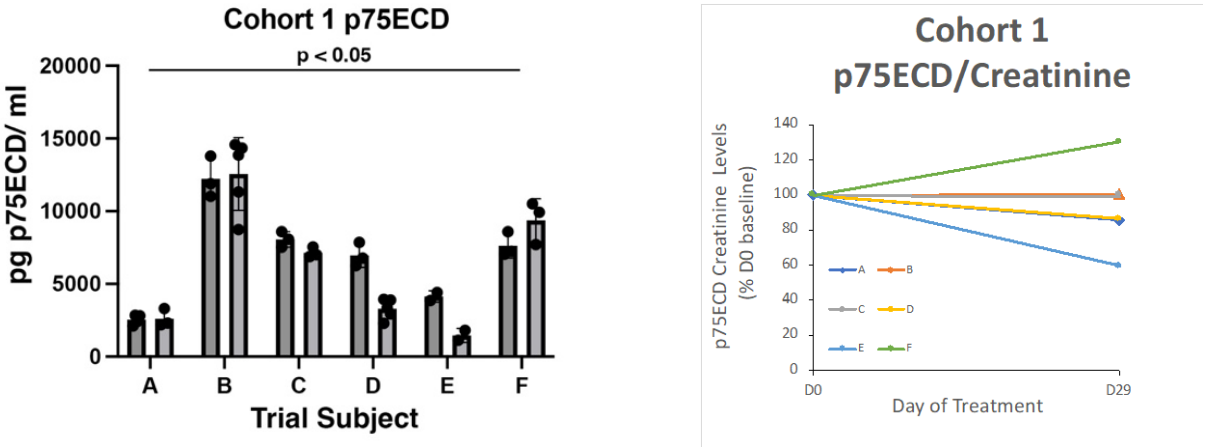

Figure 1. $p75^{ECD}$ levels and $p75^{ECD}$ /creatinine levels in the urine of MND trial subjects

PharmAust Executive Chairman, Dr Roger Aston, added “We are delighted with the results. MND is a disease characterised by progressive, debilitating paralysis due to the loss of motor neurons in the cerebral cortex, brain stem and spinal cord and is fatal. Therapeutic options are limited to Riluzole, which offers a modest 3-6 month survival extension. Baseline urinary $p75^{ECD}$ provides prognostic information and is the only biological fluid–based biomarker of disease progression.”

The Board authorises this announcement.

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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.

[1]References available at:
doi:10.3389/fnmol.2017.00263; doi:10.1016/j.jmb.2019.12.035; doi.org/10.3390/cells11081272; doi:10.3109/17482968.2012.721231B; doi:10.1007/s00401-019-01998-x; doi:10.1016/j.stemcr.2017.12.018; doi:10.1186/s13041-017-0300-4; doi:10.1242/bio.201410066; doi:10.1093/hmg/ddu580
http://dx.doi.org/10.1136/jnnp.2004.048652

[2] Urinary $p75^{ECD}$ | Neurology: https://n.neurology.org/content/88/12/1137#sec-9
“Conclusions: The assay for urinary $p75^{ECD}$ is analytically robust and shows promise as an ALS biomarker with prognostic, disease progression, and potential pharmacodynamic application. Baseline urinary $p75^{ECD}$ provides prognostic information and is currently the only biological fluid–based biomarker of disease progression.”