Monepantel and monepantel sulfone COVID-19 anti-viral update

- Three individual laboratories have now examined the effects of monepantel (MPS) and monepantel sulfone (MPLS) upon SARS-COV2 infection, the causal agent of COVID-19 disease
- MPL and MPLS significantly protect against COVID-19 virus mediated cell death
- MPL and MPLS appear to inhibit viral infection by targeting late-stage events in the COVID-19 virus life-cycle
- Evaluation of MPL in COVID-19 patients is being assessed in Europe for when GMP grade tablets are manufactured
- PharmAust will continue to build its anti-viral preclinical data package by additionally investigating MPL in HTLV-1 viral infections

26 July 2021 – Perth, Australia: PharmAust Limited (ASX:PAA), a clinical-stage biotechnology company, is pleased to provide an update on its anti-viral program investigating the development of monepantel (MPL) and its metabolite monepantel sulfone (MPLS) as anti-viral therapeutics against SARS-CoV2, the causal agent of COVID-19 disease.

In collaboration with three independent laboratories, PharmAust has investigated the capacity of MPL and MPLS *in vitro* to inhibit:

i) SARS-CoV2-induced cell death,
ii) SARS-CoV2 RNA release from the cell, and
iii) SARS-CoV2 RNA infection of neighbouring cells.

All three laboratories demonstrated that both MPL and MPLS protect against cell death *in vitro* following infection with SARS-CoV2. Furthermore, two laboratories investigated the effects of MPL and MPLS upon the early stages of the SARS-CoV2 virus lifecycle by examining RNA release into the culture media.

In one study both MPL and MPLS showed an approximate 50% decrease of SARS-CoV2 viral RNA. In another study, investigating MPLS only, SARS-CoV2 virus RNA in the media was decreased 60-70% (Figure 1, Supplementary technical details below). On their own, these reductions in SARS-CoV2 viral RNA release in the media are considered moderate. Most significantly and as announced on 4 June 2020, 18 June 2020 and 9 September 2020, however, two laboratories investigated the infectivity of SARS-CoV2 virus particles using extended culture TCID50 (Tissue Culture Infective Dose) assays. Both laboratories showed significant suppression of infectivity following MPL or MPLS treatment. In one laboratory, suppression of approximately 99% and 75% was observed for MPL and MPLS respectively and in two different cell lines, while in the second laboratory, suppression was approximately 95% for both MPL and MPLS on one cell line.

While preparing for clinical trials PharmAust will continue to analyse TCID50 data to understand optimal use of MPL as an anti-viral therapeutic.

The data from these three independent investigations support the hypotheses that both MPL and MPLS:

i) significantly protect cells *in vitro* against SARS-CoV2-induced cell death,
ii) significantly inhibit completion of the SARS-CoV2 life cycle, by blocking transmission of virus to neighbouring cells,
iii) may act later in the SARS-CoV2 virus life cycle than well characterised drugs ie Remdesivir.

The potentially distinct mechanism by which MPL and MPLS inhibit viral replication may offer the opportunity to generate “combination cocktails” with other anti-virals to simultaneously block multiple points of the virus life cycle to strengthen anti-viral activity.

In moving its programs towards the clinic PharmAust has been actively engaging with contract research organisations (CROs) exploring European and United Kingdom evaluations for a Phase I trial in human patients to treat COVID-19 once manufacture of GMP-grade monepantel tablets is completed.

As announced on 12 July 2021, PharmAust is continuing to build its anti-viral preclinical data package by studying the effects of MPL and MPLS in models of human T cell leukaemia virus-1 (HTLV-1). While also broadening the scope of MPL and MPLS potential anti-viral activity, the HTLV-1 models are considered by PharmAust to offer greatest relevance for translation into the clinic for both SARS-CoV2 and HTLV-1 infections.

Supplemental technical details
The nature of the experiments was to test the total amount of virus released from cells in the culture media. To test this, a routine assay called quantitative qPCR was used. The testing conditions were *in vitro* using SARS-CoV-2 viral infections of human Calu respiratory cells. The range of suppression relates to a repeat of experiments performed in triplicate.

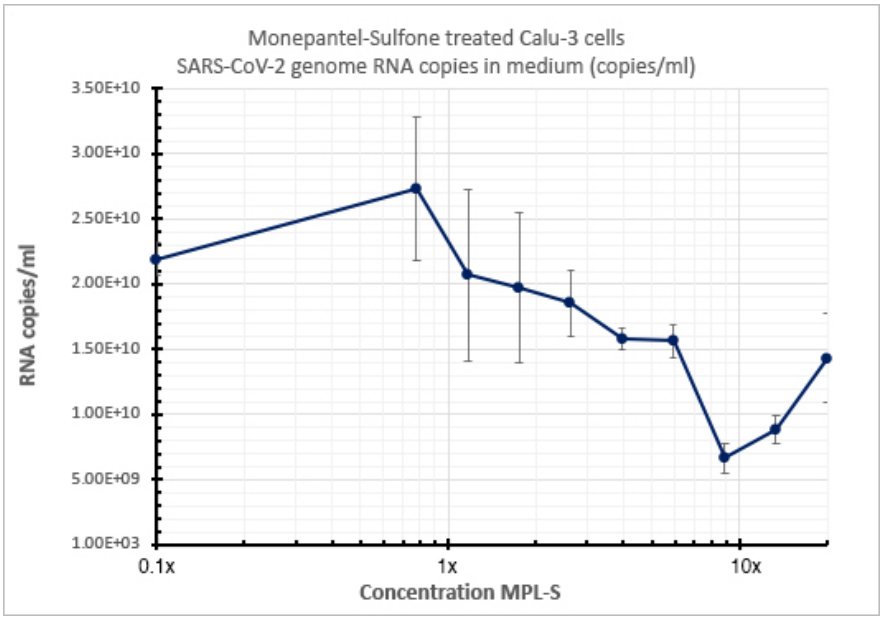

Figure 1. qPCR assay inhibition values from triplicate repeats. MPLS moderately decreases the SARS-CoV-2 genomic RNA copy number in the medium (~60-70%). Previous experiments suggest that monepantel renders the RNA released into the medium is not infectious.

This announcement is authorised by the Board

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About PharmAust (PAA):
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 that generated $3.5 million in revenue in FY 2020.

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, neurodegenerative diseases and viral infections. 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 and antiviral disease as it advances a reformulated version of this drug through Phase 1 and 2 clinical trials.