Preliminary Positive Results for the Treatment of SARS-CoV-2 Viral Infection by Monepantel

- Monepantel treatment reduces SARS-CoV-2 virus replication in tissue culture (based upon preliminary experiments)
- Monepantel treatment reduces SARS-CoV-2 cell-to-cell infectivity in tissue culture (based upon preliminary experiments)
- Promising early data demonstrating suppression of virus by 50-95% requires further confirmation in repeat and more comprehensive studies

4 June 2020 – Perth, Australia: PharmAust Limited (ASX:PAA), a clinical-stage oncology company, is pleased to provide an update on its preliminary work investigating the effects of monepantel (MPL) and monepantel sulfone (MPLS) upon cells infected with SARS-CoV-2 in tissue culture. Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). It was first identified in December 2019 in Wuhan, China and has since spread globally, resulting in an ongoing pandemic.

These experiments have been undertaken for PharmAust by the Walter and Eliza Hall Institute of Medical Research virologists in accredited and controlled safety facilities at the Institute in Melbourne and have demonstrated that both infectivity and replication of SARS-CoV-2 virus particles can be suppressed by between 50%-95% in cell cultures. The lowest inhibition value from the TCID50 assay was approximately 50% and the highest inhibition value was approximately 95%. For the qPCR individual assays, the degree of suppression was up to approximately 55%. Further details of the preliminary experiments are provided overleaf/ on page 2.

Virologists at the Walter and Eliza Hall Institute demonstrated that in preliminary experiments both monepantel and monepantel sulfone reduce the capacity of SARS-CoV-2 to replicate as well as the capacity of SARS-CoV-2 to mature into infectious virus particles. Of note, relatively low concentrations of monepantel blocked the infectious capacity of SARS-CoV-2 in tissue culture. Experimental repeats were conducted for each experiment in quadruplicate.

PharmAust plans further validation of these preliminary results as soon as possible.

Based on the above findings, PharmAust has moved to broaden and extend its Intellectual Property in the area of anti-viral activity through the filing of a patent application specifically covering MPL in the treatment of COVID-19.

Walter and Eliza Hall Institute researcher Professor Marc Pellegrini (*MBBS BSc FRACP PhD FAHMS*), joint head of the Institute's Infectious Diseases and Immune Defence division and an infectious disease clinician at the Royal Melbourne Hospital, stated, "These early signs demonstrating that monepantel can block SARS-CoV-2 infectivity *in vitro* are encouraging".

PharmAust's Chief Scientific Officer Dr Richard Mollard stated, "PharmAust is excited by this early data set and is looking forward to continuing the project with the Walter and Eliza Hall Institute. Continuation will involve repetition of these experiments for validation and comparisons with other mTOR inhibitors and treatments currently in the clinic".

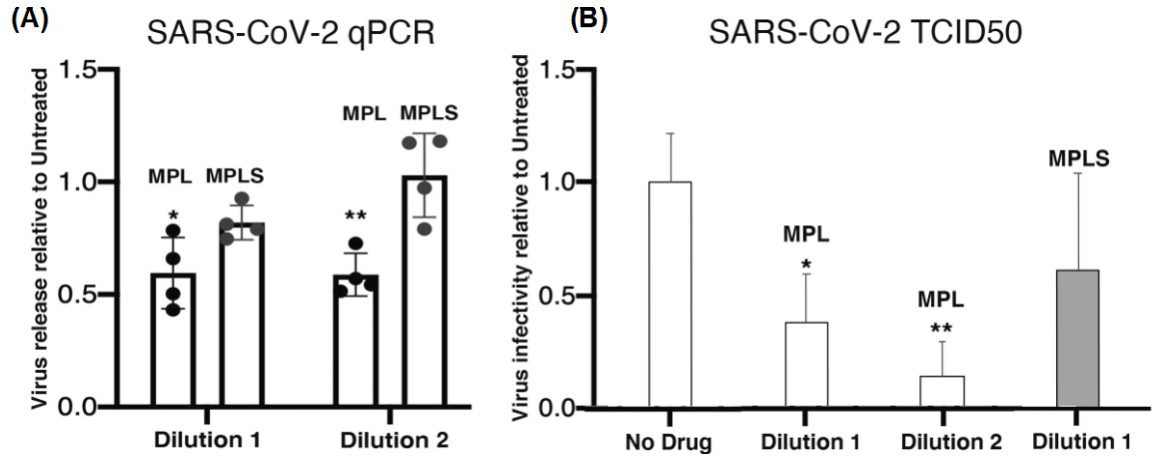
Supplemental technical details of the trial, provided at the request of the ASX:

The nature of the experiments was to test the total amount of virus released from cells into the culture media and also to measure the infectivity of newly released virus during treatment with compounds. To test this, routine assays called quantitative polymerase chain reaction (qPCR) and Median Tissue Culture Infectious Dose (TCID50) were used.

The number of experiments conducted was one of each.

The testing conditions were in vitro using SARS-CoV-2 viral infections of African Green Monkey VERO cells.

The range of suppression related to the individual values used in the quadruplicate repeat of the qPCR and quadruplicate repeat of the TCID50 assays.



(A) qPCR assay inhibition values from two tested and different dilutions (Dilutions 1 and 2) of MPL and MPLS. (B) TCID50 data calculated represented an aggregated score from the experimental wells and dilutions taking into account wells where a cell pathological effect was observed versus wells where no cell pathological effect was observed. Scores were created using the Spearman and Kärber algorithm in Microsoft®Excel® and provided as means +/- standard deviation. ANOVA tests with a Dunnett's post hoc tests demonstrate significance: * $p < 0.05$, ** $p < 0.001$). The value of 1 on the y axes corresponds to no drug.

	Raw SARS-CoV-2 qPCR Data			
	MPL		MpIS	
Repeat No	Dilution 1	Dilution 2	Dilution 1	Dilution 2
0	0.660	0.727	0.812	0.790
Repeat 1	0.785	0.543	0.790	0.973
Repeat 2	0.432	0.514	0.747	1.181
Repeat 3	0.503	0.570	0.927	1.173

	Raw SARS-CoV-2 TDIC50 Data			
	No Drug	MPL		MPLS
	0	Dilution 1	Dilution 2	Dilution 1
Average	1.000	0.378	0.141	0.611
Std	0.215	0.220	0.154	0.434

Raw data used to generate the graphs above. It is important to note that the Spearman and Kärber algorithm used to generate TCID50 data does not give individual data point read outs. It gives averages and standard deviations.

Because TCID50 provides data on infectivity, it is more valuable than qPCR. TCID50 data measures how the virus life-cycle has been inhibited. qPCR data do not measure how the virus life-cycle has been

affected as this method only measures virus RNA content. qPCR tells you whether virus is getting made and released, but not whether that virus is actually capable of infecting new targets.

qPCR and TCID50 methods are according to those previously described: (1) Caly, L., et al., The FDA-approved drug ivermectin inhibits the replication of SARS-CoV-2 in vitro. Antiviral Res, 2020. **178**: p. 104787; (2) Guo, L., et al., Autophagy Negatively Regulates Transmissible Gastroenteritis Virus Replication. Sci Rep, 2016. **6**: p. 23864.

This announcement is authorised by the Board

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About PharmAust (PAA):

PAA is a clinical-stage company developing targeted cancer therapeutics for humans and animals. The company specialises in repurposing marketed drugs lowering the risks and costs of development. PAA's subsidiary, Epichem, is a successful contract medicinal chemistry company.

PAA's lead drug candidate is monepantel (MPL), a novel, potent and safe inhibitor of the mTOR pathway – a key driver of cancer. MPL has been evaluated in Phase I clinical trials in humans and dogs; was well tolerated and produced a significant reduction in key prognostic biomarkers. PAA is uniquely positioned to commercialise MPL for treatment of human and veterinary cancers as it advances the drug in Phase II clinical trials.

About The Walter and Eliza Hall Institute of Medical Research:

The Walter and Eliza Hall Institute is one of Australia's leading biomedical research organisations, with a national and international reputation for performing highly influential basic and translational research. The Institute is addressing some of the major health challenges of our time, with a focus on cancer, immune health and infection, and development and ageing. The Institute is at the forefront of research innovation, with a strong commitment to excellence and investment in research computing, advanced technologies and developing new medicines and diagnostics. For more information visit https://www.wehi.edu.au.