Confirmation of Preliminary COVID-19 Results Following Monepantel Treatment *In Vitro*

- Monepantel and monepantel sulfone treatment both reduce SARS-CoV-2 (COVID-19) cell-to-cell infectivity in cell culture in a repeat preliminary experimental evaluation
- Repeat preliminary experiment data demonstrate suppression of virus infectivity by approximately 95% in cell culture by each drug
- Preparations for Phase 1 trial

18 June 2020 – Perth, Australia: PharmAust Ltd (ASX:PAA), a clinical-stage oncology company, is pleased to provide an update on its repeat cell culture preliminary experiments investigating the effects of monepantel (MPL) and monepantel sulfone (MPLS) upon cells infected with SARS-CoV-2 in cell culture. Replication of the *in vitro* virus infectivity experiment and using the same TCID50 method as that announced on 4 June 2020 confirmed initial findings. qPCR is quicker, cheaper and less labour intensive yet a less informative experiment than TCID50. It is used to check first whether TCID50 should be performed. Given both qPCR and TCID50 both showed monepantel antiviral activity in the previous experimental set, only TCID50 was performed in the repeat here.

These repeat experiments were undertaken for PharmAust by the Walter and Eliza Hall Institute of Medical Research virologists and again demonstrated that infectivity of SARS-CoV-2 virus particles can be suppressed by up to approximately 95% in cell cultures by either MPL or MPLS.

PharmAust is now engaged in further discussions with the Walter and Eliza Hall Institute to investigate key next steps to further explore the significance of this work, including, importantly, comparison with other mTOR inhibitors, such as rapamycin and current anti-viral drugs authorised by the FDA for emergency use to treat COVID-19, such as remdesivir.

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 are encouraging anti-viral profiles. These exciting repeat results validate the results of the initial test and form strong grounds for progressing the drug to the next step. Demonstrating twice that infectivity of SARS-CoV-2 virus particles can be suppressed by up to approximately 95% in cell cultures is a remarkable outcome. We intend to continue collaborating with PharmAust with preclinical experimentation to support their progress." (These statements are the considered view of the principal investigator based on his years of experience in this specialised discipline.)

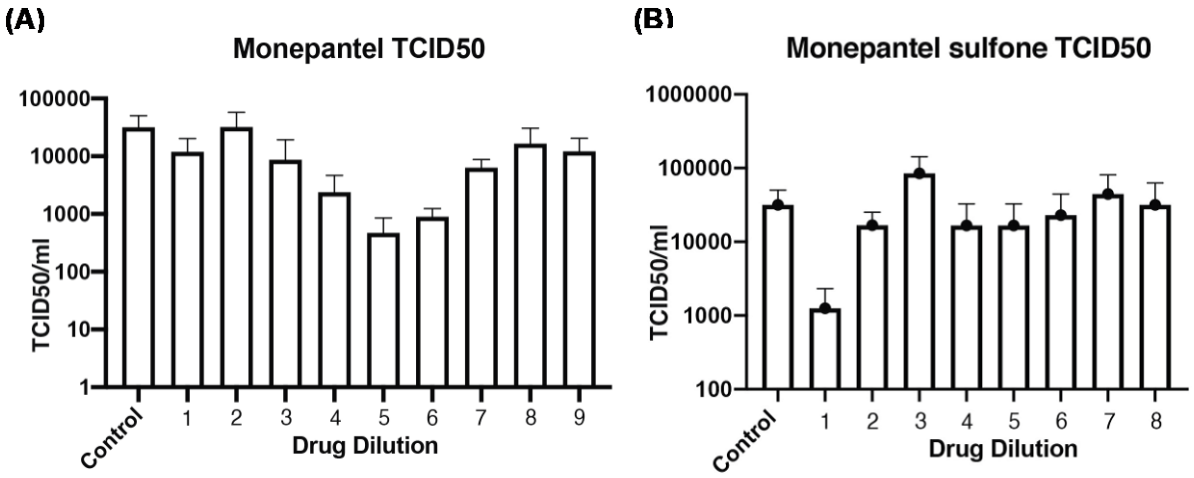
PharmAust's Chief Scientific Officer Dr Richard Mollard stated, "The reproducible nature of this work *in vitro* paves a propitious pathway for continued evaluation. PharmAust is looking forward to building on these experiments with the Walter and Eliza Hall Institute."

PharmAust will prepare an Executive Summary and an Investigator's Brochure to permit discussions with clinicians about a Phase I trial in a small number of human patients to treat COVID-19. Monepantel has already been evaluated in human patients with cancer (ASX announcement 21 October 2015).

Supplemental technical details of the experiment required by the ASX:

The nature of the experiments was to measure the infectivity of newly released virus during treatment with compounds. To test this, routine assays measuring Median Tissue Culture Infectious Dose (TCID50) were performed. Experimental repeats were conducted in sextuplicate.

These experiments are a repeat of the experiments detailed in the announcement dated 4 June 2020.



(A) Monepantel TCID50 data. (B) Monepantel sulfone TCID50 data. TCID50 data calculated represents 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.

	No Drug	Raw SARS-CoV-2 TDIC50 Data for MPL								
	0	Dilution 1	Dilution 2	Dilution 3	Dilution 4	Dilution 5	Dilution 6	Dilution 7	Dilution 8	Dilution 9
Average	31762	12000	32108	8680	2372	469	896	6344	16596	12136
Std	18483	8243	25247	10530	2311	384	343	2430	14112	8337

	No Drug	Raw SARS-CoV-2 TDIC50 Data for MPLS							
	0	Dilution 1	Dilution 2	Dilution 3	Dilution 4	Dilution 5	Dilution 6	Dilution 7	Dilution 8
Average	31762	1254	16784	84951	16596	16596	2295	44408	31748
Std	18483	1066	8513	58360	16173	16173	2166	3648	30937

Raw data used to generate the graphs above. It is important to note that the Spearman and Kärber algorithm used to generate TCID50 data from the 6 experimental repeats for each drug does not give individual data point read outs. It gives averages and standard deviations.

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

TCID50 data measures how the virus life-cycle has been inhibited. TCID50 methods are according to those previously described: 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.