Inhibition of SARS-CoV-2 by Monepantel in Preliminary Studies of Human Respiratory Calu-3 Cells *In Vitro*

- Monepantel and monepantel sulfone treatment both inhibit SARS-CoV-2 (COVID-19) in preliminary work on cultured human lung adenocarcinoma epithelial cells (Calu-3 cells).
- Data demonstrate inhibition of virus by approximately 90 - 95% in Calu-3 cells by each drug.
- Monepantel and monepantel sulfone in preliminary work have now been demonstrated to reduce SARS-CoV-2 infectivity in two independent cell lines: one non-human primate kidney (VERO) and one human lung (Calu-3).
- This work requires repetition and robust verification

25 August 2020 – Perth, Australia: PharmAust Limited (ASX:PAA), a clinical-stage oncology company, is pleased to provide an update on its further preliminary work investigating the effects of monepantel (MPL) and monepantel sulfone (MPLS) upon cultured cells infected with SARS-CoV-2. 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 global pandemic.

The research program undertaken for PharmAust by the Walter and Eliza Hall Institute of Medical Research in Melbourne has now demonstrated in preliminary findings that SARS-CoV-2 virus particle counts in human Calu-3 lung adenocarcinoma epithelial cells in culture can be suppressed by up to approximately 95% by both monepantel and monepantel sulfone application. This work in this cell type has not been repeated and is therefore not as yet verified. Importantly in this early work, the degree of anti-viral activity was similar to the previous evaluation of MPL and MPLS in African Green Monkey VERO cells yet at higher drug concentrations.

Non-human primate VERO cell lines may not reflect how SARS-CoV-2 replicates and infects human tissue, so it is important to test the effects of MPL in human lung epithelial cells, such as Calu-3 cells. However, it is also important to note that infectivity of human Calu-3 cells in culture may not necessarily reflect how SARS-CoV-2 infects and replicates in human organs under physiological conditions and how the constituent cells infected with SARS-CoV-2 react to treatment with MPL or MPLS. Sequential testing of MPL and MPLS through *in vitro* organoid and *ex-vivo* organotypic systems from patients of diverse ages, sexes and underlying disease conditions may be required to better understand how MPL and MPLS affect SARS-CoV-2 infectivity prior to formalised clinical studies[1]. In the interests of completeness, the latter studies will be pursued as a matter of course by PharmAust subject to the timely availability of organoid samples. PharmAust has commenced discussions with several groups that may be able to assist with these experiments.

PharmAust's Chief Scientific Officer Dr Richard Mollard stated, "Further preliminary confirmation of the activities of MPL and MPLS against SARS-CoV-2 in alternative, and especially human, cellular models is an encouraging step. These data will fuel further development of the effects of monepantel administration upon SARS-CoV-2 for clinical application".

[1] Chu et al, 2020. The Lancet, 1(1):E14; https://doi.org/10.1016/S2666-5247(20)30004-5

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.