Leiden University Testing Indicates Monepantel and Monepantel Sulphone SARS-CoV-2 Antiviral Activity

- Previously PAA reported to shareholders that monepantel (MPL) and monepantel sulfone (MPLS) demonstrate antiviral activity in cultured cell infection models of SARS-CoV-2, the virus causing COVID-19
- Leiden University Medical Center (LUMC) has generated indicative data that MPL and MPLS again demonstrate antiviral activity in non-human primate systems
- High insolubility of MPL in these systems was challenging and required several analyses
- LUMC is now moving forward and transitioning to human cultured cells

7 April 2021 – Perth, Australia: PharmAust Limited (ASX:PAA), a clinical-stage oncology company, is pleased to provide an update on its antiviral program investigating the development of MPL and its metabolite MPLS as antiviral therapeutics for the prevention and treatment of COVID-19 disease.

PharmAust previously demonstrated MPL's antiviral activity in two independent laboratories in Australia in both primate and non-primate cell cultures (announced on 4 June, 18 June, 25 August and 9 September 2020). Data from extensive testing at LUMC, examining the effects of MPL and MPLS in specialised COVID-19 non-human primate systems, once again indicate their antiviral activity. The nature of the testing and conditions, the testing context and the number of tests with a data summary, are provided to assist in understanding the indicated antiviral activity (Supplemental technical details below).

Solubility issues of MPL in these *in vitro* systems remain challenging yet do not impact PharmAust's clinical programs. PharmAust has resolved the issues of solubility for administration to patients by developing the MPL tablet dosage form. MPL is quickly and efficiently converted into MPLS in the body, with MPLS representing the dominant form in the plasma. PharmAust and LUMC will now progress the antiviral development program to testing in human cells.

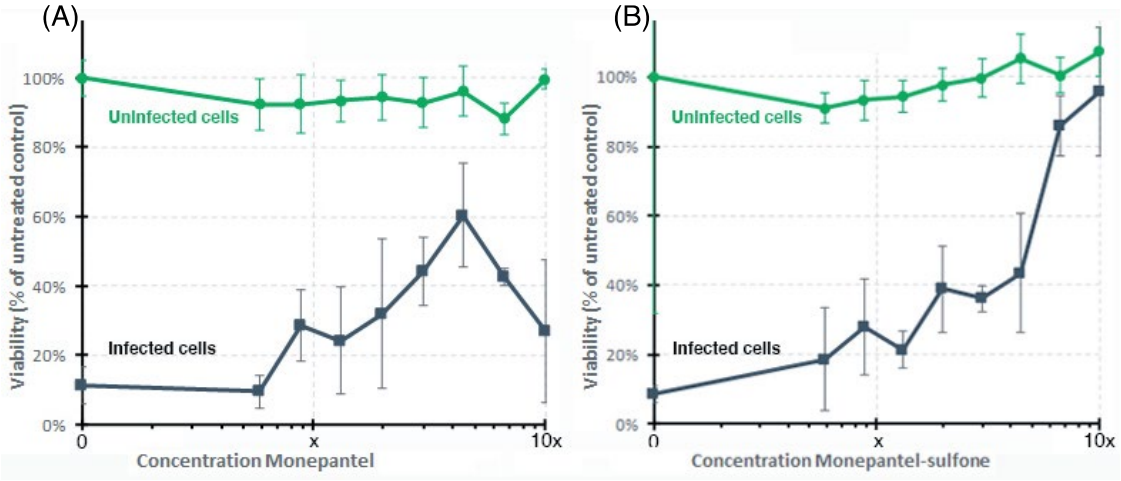
Associate Professor Martijn van Hemert, principal investigator at LUMC stated, "There are indications for an antiviral effect in these assays, but solubility issues under the conditions required for cell-based screening complicate analysis. Additional experiments will now be performed on SARS-CoV-2 infected human lung cell lines."

PharmAust's Chief Scientific Officer, Dr Richard Mollard stated, "Testing highly insoluble drugs such as MPL in established complex culture conditions is notoriously difficult. PharmAust is very grateful to Associate Professor van Hemert and his team for their extensive and exhaustive efforts with MPL. We look forward to updating the market as these programs continue."

GMP-quality MPL production for human clinical trials has commenced at Syngene International Ltd (India).

Overall timing of PharmAust's clinical development plans remains unchanged.

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



Nature of the testing and conditions: *in vitro* viability of non-human primate Vero cells infected with SARS-CoV2 (black) and not infected with SARS-CoV2 (green; appropriate control conditions) and treated with either monepantel (A) or monepantel sulfone (B) at increasing concentrations. **Testing context**: Monepantel (A) shows signs of antiviral activity (protection against cell death) at lower concentrations, but at higher concentrations loses effect for unknown reasons. It is currently supposed this is due to monepantel's very low solubility in aqueous media. Monepantel sulfone shows signs of antiviral activity reaching levels > 95% at higher concentrations. The protective effect against SARS-CoV2 appears attributable to the addition of each drug because uninfected cells treated with the same concentration of drug remain viable at all concentrations tested here. **Number of tests**: Experiments were performed three times (two repeats) with quadruplicate tests in each experiment.

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.

About LUMC:
Leiden University Medical Center (7,000 employees, >700 million annual turnover) is a modern and internationally renowned biomedical research center. LUMC integrates research, education and patient care with a high-quality profile and a strong scientific orientation, ranging from basic to applied and clinical research. LUMC offers state-of-the-art research facilities to contribute to innovation and scientific research, i.e. Leiden Genome Technology Center, Flow Cytometry Core Facility, Center for Proteomics and Metabolomics, Light and Electron Microscopy, Bioinformatics - Data Analytics - Computational Biology, GMP-facility, Leiden Stem Cell Hotel, Central Animal and Transgenic Facility, Preclinical Imaging Facility, Biosafety level-3 Facility, and Biobank Facility.

The Molecular Virology team (~35 scientific and supporting staff members) of the LUMC department of Medical Microbiology studies the molecular biology of +RNA virus replication and uses this knowledge to develop novel antiviral strategies. The group has worked on coronaviruses for over 30 years, and was and is deeply involved in the characterisation of the emerging SARS- and MERS-coronaviruses in 2003 and 2012, and SARS-CoV-2 since the beginning of 2020. Key contributions were made to the functional characterization of the coronavirus replicative enzymes, RNA synthesis, replication organelles, and innate immune evasion strategies. Moreover, the group has identified and studied the mechanism-of-action of a wide variety of compounds with antiviral activity.