Phase IIb Trial in Pet Dogs with B Cell Lymphoma Successfully Achieves Interim Clinical Endpoints

- Monepantel treatment successfully achieves the two interim trial primary endpoints: objective tumour regression and increased progression-free survival
- Administering veterinarians want to now proceed to the Phase III trial
- Data helping define the optimised tolerated dose for the Phase III study
- Clinical outcomes in canines have major implications for progression-free survival and overall survival in humans
- PharmAust will now seek partners to co-develop and commercialise monepantel for treatment of veterinary cancers

28 June 2021 – Perth, Australia: PharmAust Limited (ASX:PAA), a clinical-stage biotechnology company, is delighted to announce that following the treatment of 15 pet dogs during its Phase IIa and Phase IIb studies, monepantel (MPL) demonstrated sufficient and statistically significant anti-cancer activity to continue development into Phase III.

Multi-centric high grade B-cell lymphoma is one of the more aggressive cancers to study in canine oncology. Objective regression in one of the first eight dogs, with some tumours resolving completely, as well as objective stable disease or better in six of the first 15 pet dogs treated over the 28 day trial is a compelling outcome.

Two pet dogs with advanced and extensively disseminated disease and one other dog with advanced and less extensively disseminated disease were treated with lower dose MPL, however, these were withdrawn due to disease progression during the trial. The remaining 12 treated pet dogs completed the full 28 day trial period.

Published mean and median times for untreated dogs show that normally eight of these 15 pet dogs would have been euthanised by day 29/30 with aggressively progressive disease and poor quality of life[1]. Comprehensive data are not available ex-trial, but available reports are that at least six pet dogs continued with either MPL alone or in combination with prednisolone. The inappetence and elevated liver enzymes observed at the higher doses of MPL will not be relevant for Phase III.

This Phase IIb trial also opens the door for PharmAust and its team of vets to explore the value of MPL in other canine cancers. MPL's ability to target a central metabolic pathway associated with tumour growth (mTOR) provides confidence that MPL will have application in other cancers. Furthermore, having evaluated a range of treatment regimens for MPL during the current trial, the Company has established a therapeutic window for clinical trials in human cancers.

Achieving stable disease in primary cancerous lesions as well as in metastatic disease could have substantial value in human cancer therapy particularly if progression-free survival correlates with overall survival. It is noteworthy that achievement of stable disease was observed in PharmAust's previous small Phase I trial in humans where the participants had been admitted with progressive disease following the failure of other treatments.

PharmAust will now contact leading global pharmaceutical companies to seek partners to co-develop and commercialise MPL for treatment of veterinary cancers. Animal healthcare companies in the US and Germany have approached PharmAust for discussions. As previously announced, PharmAust has engaged the services of Dr Kim Agnew (Hon BSc, BVSc, MACVSc) to assist with this process. Dr Agnew worked for 20 years at Elanco Animal Health and for five years at Merial, now Boehringer Ingelheim.

PharmAust's Chief Scientific Officer Dr Richard Mollard stated, "We set the bar very high in our studies of MPL in canine B-Cell lymphoma and we intend that our investment in defining a dosing regimen will now pay dividends in the Phase III and commercialisation programs. With reference to over 50 peer reviewed pet dog lymphoma publications, we adopted a Bayesian method of statistical inference that was approved prior to trial initiation by some big pharma representatives, four independent Australian ethics committees and seven independent practicing veterinarians."

"In addition to the standard measurements of target superficial lymph nodes that are characteristic of many such trials, we incorporated comprehensive thoracic X-ray and abdominal ultrasound analyses into the trial design. This means that designation of stable disease in this trial really means comprehensive stable disease, not superficially stable disease as per many other trials where progression might be hidden somewhere else in the body."

"Many of the pet owners relished the improved quality of life of their dogs on trial. We now wish to formally test this increased quality of life following MPL treatment during the next stages and as a comparator with alternative treatments such as prednisolone. We are confident these interim data indicate meaningful clinical outcomes and now aim to translate all that into commercially valuable outcomes."

"Normally PharmAust would now continue with an extension of the Phase II Bayesian approach, continuing to treat up to 46 dogs according to the prospectively defined full Phase II design. However, advice from the administering veterinarians is to instead immediately commence preparations for Phase III. In these preparations PharmAust will fine tune the optimal dose for the Phase III trial."

The trial's Principal Investigator Dr Kim Agnew stated, "The investigative approach PharmAust has devoted to individual patient diagnostic outcomes is very complete and achievement of this statistically significant study milestone indicates Monepantel can positively impact the lives of canine patients with B Cell lymphoma. Phase III studies enable a deeper investigation of how Monepantel can best become part of a canine oncologist's therapeutic portfolio. This will be a very exciting part of the development."

1. Theilen, 1977. JAVMA 170(6): p607

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