Monepantel Trial Achieves Successful Anti-Cancer Outcome

- Pet dogs with treatment naive B cell lymphoma successfully treated with new MPL tablets demonstrated an overall strong anti-cancer trend
- Monepantel "tablet trial" outperforms original monepantel "liquid trial"
- One pet dog achieved greater than 60% reduction in tumour burden, with one of its tumours regressing completely
- Higher efficacy observed at lower plasma MPL levels provides a strong basis for target dose reduction in future Phase III trials and facilitates path to commercialisation
- The high dose of MPL adopted caused some inappetence and elevated liver enzymes
- Trial outcomes will be presented to Elanco

12 May 2020 – Perth, Australia: PharmAust Ltd (ASX:PAA), a clinical-stage oncology company, is pleased to advise that its monepantel canine trial achieved a successful outcome. The Company now provides an Interim Trial Update for its veterinary Phase II clinical trial investigating the anti-cancer effects of monepantel tablets in dogs with treatment naïve B cell lymphoma.

A total of six of seven eligible and enrolled pet canine patients have completed assessment following "at home" treatment by their owners. One dog failed to medicate in accordance with the study protocol and was removed from trial assessment early on. This dog, however, continued receiving monepantel tablets and has now reached over 120 days of treatment with prednisolone added to the treatment regimen by the veterinary surgeon.

Following 14 days of monepantel tablet treatment, the veterinarians reported that one dog achieved a partial response with a greater than 60% reduction in total tumour burden and with one lymph node tumour regressing completely. Four dogs achieved stable disease and progressive disease was seen in one dog. This outcome provides a meaningful trend, comparing favourably with the treatment used in the original "liquid" monepantel formula reported on 3 December 2017, where six of seven dogs achieved stable disease and progressive disease was seen in one dog.

After 14 days of treatment, one dog with progressive disease and the one dog with a partial response but elevated liver enzymes, discontinued monepantel tablet treatment. All four remaining pet dogs completed the 28-day treatment schedule, with all four pet dogs achieving stable measured lymph nodes. A new lesion, however, became apparent in two of these dogs and some elevated liver enzyme values not resulting in clinical illness were also noted.

Plasma MPL levels were recorded for all dogs and reached levels up to 50 times higher than those recorded in the human trial undertaken at the Royal Adelaide Hospital in 2014/2015. Some variability was observed in plasma levels and, unexpectedly, at the lower blood levels of MPL there were better outcomes. This observation may be consistent with the mechanism of action of mTOR inhibitors and lends itself to reducing and optimising the future dosing of monepantel tablets.

University of Melbourne and U-Vet Werribee's Dr Claire Cannon, the principal investigator overseeing the trial, stated "Monepantel appears to be showing anti-cancer activity in dogs with lymphoma and I believe that controlled Phase III trials are now warranted to investigate the efficacy and safety of lower dose monepantel. The Phase II trial results suggest that monepantel, perhaps in combination with standard of care lymphoma therapy, may represent a future prospect for treatment of dogs with this disease".

The current trial has provided a strong basis for further evaluation of this new approach to canine cancer therapy.

An unexpected outcome was that at these high dosing levels, some pet dogs developed inappetence and lost weight. Furthermore, inappetence caused pet owners some difficulties in administering tablets, so reducing the target dose in future trials is anticipated to result in better outcomes in terms of efficacy, safety and dosing pets.

Based on the above, the Phase II trial is now on hold while an Interim Report is finalised for Elanco US Inc, highlighting both the efficacy parameters as well as the induction of inappetence and elevated liver enzymes at very high dosage levels of MPL.

PharmAust's Chief Scientific Officer Dr Richard Mollard stated "Having the monepantel tablets achieve a 60% reduction in tumour burden in one dog, with one lymph node returning to normal, is a terrific and unexpected outcome. The correlation of lower MPL blood levels with superior outcomes is also a very positive trend, providing flexibility for better outcomes in a future Phase III trial."

Dr Richard Mollard further commented "We had a number of key goals for this trial including:

- Determining the safety and efficacy of monepantel tablets as compared with previous canine and human studies
- Evaluating the drug delivery capabilities of the newly developed monepantel tablets in pet dogs with cancer
- Deriving sufficient positive and indicative data to enable Phase III trials
- Producing sufficient data to enable further discussions with Elanco US Inc with which PharmAust has an Option Agreement.

PharmAust considers these goals have been met".

This announcement is authorised by the Board

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About this Clinical Trial
This clinical trial is being conducted under permit PER 7250 issued under section 114 of the Agvet Codes, allowing the conduct of small-scale trials with AGVET chemicals.

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 U-Vet:
The University of Melbourne's U-Vet Werribee Animal Hospital is one of Australia's leading veterinary hospital facilities, based in Werribee. U-Vet offers complete animal care to the public including general practice (primary and preventative care, exotic pet care), a suite of specialist referral services, specialist support services, 24-hour emergency care and specialist referral equine services. The hospital also trains the next generation of veterinarians and veterinary specialists with the assistance of its academic staff, who are world leaders in clinical excellence and research.

About University of Melbourne:
Established in 1853, the University of Melbourne is a public-spirited institution that makes distinctive contributions to society in research, learning and teaching and engagement. It's consistently ranked among the leading universities in the world, with international rankings of world universities placing it as number 1 in Australia and number 32 in the world (Times Higher Education World University Rankings 2017-2018). The University's distinctive Melbourne experience helps graduates become well-rounded, thoughtful and skilled professionals – making a positive impact across the globe. Its research helps solve social, economic and environmental challenges the world is facing today and into the future.