Data from Canine Oncology Study Supports Progression to Registration Studies

Highlights:

- **Determination of a clinically safe and efficacious dosing regimen of monepantel (MPL) for the treatment of dogs with B-Cell Lymphoma**
- **Treatment with MPL was safe, well-tolerated and there were no treatment-related deaths or severe adverse reactions to MPL**
- **Overall Clinical Benefit of 35% (14 of 40 dogs) and a median Time to Progression (TTP) of 28 days compares favourably to the most recent United States (US) Food and Drug Administration (FDA) product approved for B-Cell and T-Cell Lymphoma, LAVERDIA™**
- **MPL has a significant competitive advantage in Quality of Life (QoL) and Level of Function (LoF) as assessed by the owner**
- **PharmAust plans to use this data to open an Investigational New Animal Drug (INAD) application with the United States Food and Drug Administration's (FDA) Center for Veterinary Medicine (CVM) and proceed with pivotal studies in 2024 to support product registration**
- **Accompanying video presentation**

9 October 2023 – Perth, Australia: PharmAust Limited (ASX: PAA & PAAO) (Company), a clinical-stage biotechnology company, is pleased to announce positive top-line data from its Phase 2 veterinary clinical study of monepantel (MPL) for the treatment Canine B-Cell Lymphoma. The Company plans to use this data to open an Investigational New Animal Drug (INAD) application with the United States Food and Drug Administration's (FDA) Center for Veterinary Medicine (CVM) and proceed with pivotal studies in 2024 to support product registration. A presentation and a video presentation providing further information about the Phase 2 veterinary clinical study and future directions is attached to this release.

PharmAust Chief Executive Officer Dr Michael Thurn commented: "The potential for PharmAust to achieve a major value inflexion point by advancing MPL through to product registration with the Center of Veterinary Medicine makes good business sense.

The minor investment to conduct the pivotal registration studies could release significant shareholder value through receiving conditional approval for MPL from the CVM. LAVERDIA™, the most recently approved treatment for B-Cell and T-Cell Lymphoma, was acquired by Dechra Pharmaceuticals PLC (LSE:DPH) for US$64.5 million in 2022.

As our MPL tablet has a comparable efficacy profile to LAVERDIA™ and offers significant advantages in quality of life and safety for both the dog and the owner, we are confident in the commercialisation of MPL for canine cancer."

Study Design and Endpoints:

This was a Phase 2, open-label, single-arm, dose-finding study conducted at 9 sites in Australia, New Zealand, and the US. The study's objective was to determine a clinically safe and efficacious dose of monepantel for the treatment of dogs with B-Cell Lymphoma whilst maintaining quality of life (QoL). Dogs received a once-daily treatment of MPL at home for 28 days. Five separate cohorts (See Table 1 below) of dogs received different dosing regimens of MPL before a loading dose of 100 mg/kg body weight (BW) followed by a maintenance dose of 25 mg/kg was selected as the optimal dose based on efficacy and safety data.

Table 1: Dosing Regimens

Dose Regimen	Monepantel Dose, mg/kg BW per day		Dogs Treated
	Loading (Day 1)	**Maintenance** (Day 2–28)	
1	180	180	7
2	10	10	6
3	50	25	5
4	100	50	18
5	100	25	18

Response to MPL therapy was assessed over 28 days following initiation of dosing of MPL. The Overall Response Rate (ORR) was defined as those dogs with Complete Response (CR; the disappearance of all evidence of disease, and all lymph nodes) or Partial Response (PR; a 30% or greater decrease in the mean sum of the longest diameter of all target lesions from baseline). The Overall Clinical Benefit (OCB) was defined as those dogs with CR, PR or Stable Disease (SD; neither sufficient decrease to qualify for PR nor sufficient increase to qualify for Progressive Disease [PD; a 20% or greater increase in the mean sum of the longest diameter of all target lesions with reference to the smallest mean sum longest diameter recorded] of all target lesions). Time to Progression (TTP) was defined as the time from the first date of treatment to the date that the dog developed clinical or radiographic signs of PD or died from any cause, including euthanasia, and QoL was assessed by dog owners using a number ranging from 1 (very poor) to 10 (normal) on initiation of treatment (Day 0) and every day until study completion (Day 28). Overall QoL and the following specific aspects were captured: energy level, appetite, signs of nausea or vomiting, water intake, and general Level of Function (LoF). Dog owners assessed the LoF daily using a visual analogue scale ranking between 1 (normal pet) to 4 (very weak/completely disabled)

Safety was assessed by monitoring haematological, serum chemistry and urine parameters pre-dose at baseline (Day 0), Day 14 and Day 28. Dog owners were required to document all adverse events (AEs) in the study diary. AEs were graded according to the VCOG-CTCAE v1.1.

Study Results

Study Population: A total of 54 dogs of mixed breeds with a median age of 8 years (range 3-13 years) and a median weight of 29.6 kg (range 6.5-87) participated in the study. The majority were neutered males (50%) and spayed females (40.4%) with late-stage disease at diagnosis (61.5% Stage IV; 28.8% Stage V) with prescapular (92.3%), popliteal (90.4%), and submandibular (78.8%) lymphomas.

Safety: Overall, treatment was regarded as safe and well-tolerated. There were no treatment-related deaths and most of the AEs (haematological and serum chemistry) reported were mild to moderate in severity that were self-limiting and responded to supportive care. Weight loss (-0.63% to -3.37%) was minimal during the 28-day treatment period with MPL for 95% of all study dogs.

Efficacy: Of the 40 (14 dogs were excluded from the efficacy evaluation due to protocol violations) dogs evaluable for efficacy, PR to treatment was observed in 2 (5%) dogs, SD in 12 (30%) dogs, PD in 26 (65%) dogs confirming MPL has significant anticancer activity offering disease stabilisation. None of the dogs in this study achieved a CR. The ORR was achieved in 2 (5%) dogs. The OCB was achieved in 14 (35%) dogs, while the median TTP was 28 days. 10 (25%) dogs had a TTP >50 days and 5 (12.5%) dogs had a TTP >80 days.

Comparison to LAVERDIA™: In a field effectiveness study[a] required for product registration, 50 evaluable dogs with B-Cell and T-Cell Lymphoma were treated with LAVERDIA™, the median TTP was 29.5 days. 17 (34%) dogs had a TTP >55 days and 3 (6%) dogs had a TTP >180 days.

Quality of Life (QoL): Owners rated their dogs daily and recorded a score between 1 (very poor) and 10 (normal) on the owner's diary. The median QoL score for the 43 evaluable dogs across the entire study was high at 8. In the study 74.4% of dogs were rated >8 out of 10.

Level of Function (LoF): Owners rated their dogs daily by recording a score between 1 (normal pet) and 4 (very weak/dying). The median LoF score was just below normal at 1.5. No dogs were rated > 2.0.

Post Study: After the Day 28 assessment, Oncologists and owners determined the next phase of therapy for dogs ending the study in sound health. In 19 of the 54 cases, a combination therapy of MPL and Prednisone was selected as the ongoing therapy.

Principal Investigator Dr Kim Agnew commented: "The use of Monepantel for canine lymphoma offers disease stabilisation combined with a canine and owner safety profile which doesn't exist currently in the therapeutic options. I believe as we learn more about how best to manage Canine lymphoma with Monepantel with ongoing studies, dogs and owners have an option to safely medicate their dogs at home. Most importantly, the family will see their pet manage their cancer with an excellent quality of life."

Future Directions:
The encouraging results allow PharmAust to proceed straight to registration studies for MPL as a new treatment for B-Cell Lymphoma in dogs. The Company plans to use this data to open an INAD application with the US FDA's CVM and proceed with pivotal studies in 2024 to support product registration. The planned pivotal field studies to support product registration have been designed to incorporate feedback from potential partners and continue to proceed in parallel with business development efforts.

PharmAust Non-Executive Chairman Dr Roger Aston commented: "Monepantel represents a new treatment approach for the management of B-Cell Lymphomas in dogs by eliminating the need for chemotherapy and allowing dogs to maintain an excellent quality of life for an extended period of time. Approximately 80% of dog owners decline treatment for various reasons including, limited access to specialised veterinary oncologists and veterinary practices that can carry out chemotherapy; concerns over the dog's quality of life due to the often severe side effects that are a cornerstone of chemotherapy treatments; complying with the rigours of the chemotherapy regime once initiated; major safety concerns for owners who handle and/or are exposed to the chemotherapy while caring for their dog; and, the high treatment costs.

MPL is available in tablet form allowing dogs to be treated at home, without the side effects or safety concerns for owners."

This announcement is authorised by the Board.

Enquiries:

Dr Michael Thurn
Chief Executive Officer
investorenquiries@pharmaust.com

P +61 (8) 9202 6814
F +61 (8) 9467 6111
www.pharmaust.com

About Canine Lymphoma

An estimated 6 million dogs are diagnosed with cancer in each year in the US. Lymphoma is the most common haematological neoplasm of dogs, with B-Cell Lymphoma being the most common histologic subtype. B-Cell Lymphoma has a poor prognosis, and without treatment, death can occur within weeks

of diagnosis. Currently, the mainstay of treatment is multiagent chemotherapy, with the most frequently adopted protocol being CHOP (cyclophosphamide, hydroxydaunorubicin, vincristine and prednisone) CHOP has a high response rate, with control of disease in 80% - 95% of cases, resulting in prolonged survival and alleviation of symptoms. However, not all dogs derive meaningful benefits from CHOP, and it can have significant side effects, including gastrointestinal disturbances, bone marrow suppression, and immunosuppression, which vary in severity and may require supportive care or dose adjustments. The overall market for veterinary medical products is more than $22 billion. Key drivers include increasing dog numbers (90 million dogs now in the US) and an increasing willingness for owners to spend more on their pets as they are considered part of the family. According to American Pet Products (2015), almost 80 percent of all dog owners have their dogs treated with drugs, compared to about 50 percent in 1998.

About PharmAust Limited:

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.

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 studies in humans and Phase 2 clinical studies 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 studies.

References:

[a] Center for Veterinary Medicine (2021). Corrected Freedom of Information Summary. Application for Conditional Approval. Application Number 141-526. LAVERDIA™-CA1 verdinexor tablets. Coated Tablet Dogs. Sponsored by: Anivive Lifesciences, Inc. Date of Approval: January 11, 2021. Rockville, MD, Food and Drug Administration, Center for Veterinary Medicine. https://animaldrugsatfda.fda.gov/adafda/app/search/public/document/downloadFoi/10270

PharmAust (ASX: PAA)

Canine Veterinary Product Update

9 October 2023

Dr Kim Agnew

Dr Michael Thurn

Phase 2 Canine Study Overview

Study Design

- Dogs with B-Cell Lymphomas were treated with different dosing regimens of monepantel for 28 days
- Safety was assessed by monitoring haematological, serum chemistry and urine parameters
- Efficacy was assessed using the Response Evaluation Criteria in Solid Tumours (RECIST) after 28 days

Safety and Efficacy Outcomes

- Treatment with MPL was safe, well-tolerated and there were no treatment-related deaths or severe adverse reactions to MPL
- Overall Clinical Benefit of 35% (14 of 40 dogs) and a median Time to Progression (TTP) of 28 days compares favourably to the most recent US FDA product approved for B-Cell and T-Cell Lymphoma, LAVERDIA™
- MPL has a significant competitive advantage in Quality of Life (QoL) and Level of Function (LoF) as assessed by the owner

Future Directions

- Loading dose of 100 mg/kg body weight (BW) followed by a maintenance dose of 25 mg/kg was selected as the optimal dose based on efficacy and safety data
- PharmAust plans to use this data to open an Investigational New Animal Drug (INAD) application with the US Food and Drug Administration's (FDA) Center for Veterinary Medicine (CVM) and proceed with pivotal studies in 2024 to support product registration

Phase 2 Study Design

Population

- 23 Females/ 31 Males
- Treatment naïve B-Cell Lymphoma
- Karnovsky Score <1
- WHO Stage 1-5 Substage a
- Mean age: 8.3 years
- Median weight 29.6kg
- Mixed breeds

Sites

- Australia (7 sites)
- New Zealand (1 site)
- US (1 site)

Study Design

- Phase 2, open-label, single-arm, dose-finding study
- Oral Monepantel (448 mg) tablet
- Treatment duration 28 days
- RECIST – Response Evaluation Criteria in Solid Tumours
- 5 dose regimens tested

Dose Regimen	Monepantel Dose, mg/kg BW per day		Dogs Treated
	Loading (Day 1)	Maintenance (Day 2–28)	
1	180	180	7
2	10	10	6
3	50	25	5
4	100	50	18
5	100	25	18

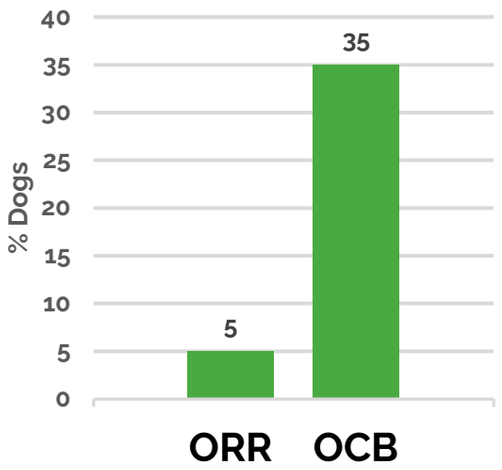
Endpoints

- Overall Response Rate (ORR)
- Overall Clinical Benefit (OCB)
- Time to Progression (TTP)
- Safety
- Quality of Life (QoL)
- Quality of Function (QoF)

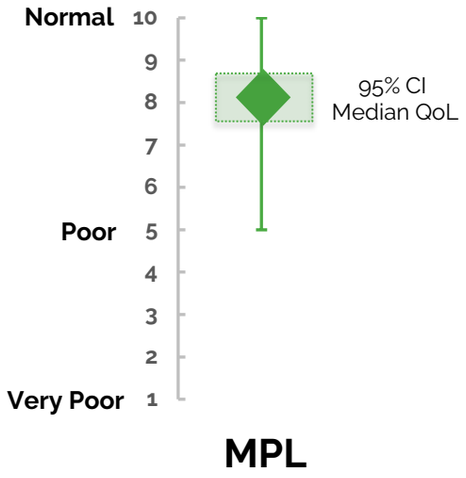
ORR - defined as those dogs with Complete Response (CR; the disappearance of all evidence of disease, and all lymph nodes) or Partial Response (PR; a 30% or greater decrease in the mean sum of the longest diameter of all target lesions from baseline).
OCB - defined as those dogs with CR, PR or Stable Disease (SD; neither sufficient decrease to qualify for PR nor sufficient increase to qualify for Progressive Disease [PD; a 20% or greater increase in the mean sum of the longest diameter of all target lesions with reference to the smallest mean sum longest diameter recorded] of all target lesions).
TTP - defined as the time from the first date of treatment to the date that the dog developed clinical or radiographic signs of PD or died from any cause, including euthanasia.
QoL - was assessed by dog owners using a number ranging from 1 (very poor) to 10 (normal).
QoF – was assessed by dog owners using a visual analogue scale ranking between 1 (normal pet) to 4 (very weak/dying).

Results

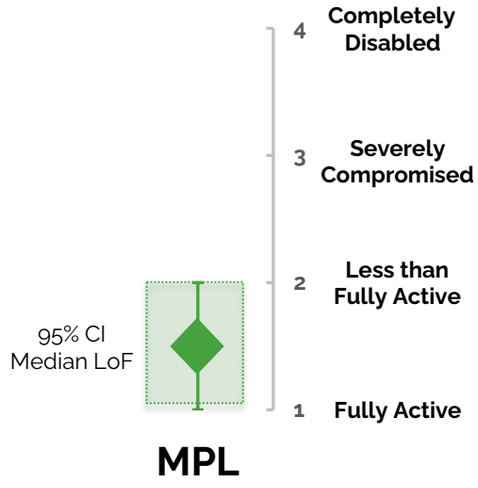
Efficacy



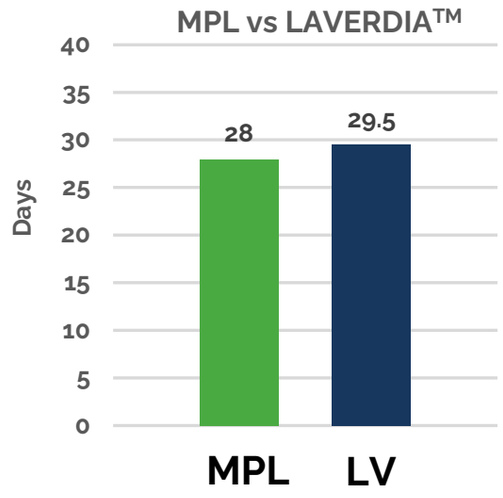
Quality of Life



Level of Function



Time to Progression[a]



Discussion

- PharmAust Overall Clinical Benefit of 35% (14 of 40 dogs) and a median Time to Progression of 28 days compares favourably to the most recent US FDA product approved for B-Cell and T-Cell Lymphoma, LAVERDIA™
- MPL has a significant competitive advantage in QoL and LoF as assessed by the owner

ORR - defined as those dogs with Complete Response (CR; the disappearance of all evidence of disease, and all lymph nodes) or Partial Response (PR; a 30% or greater decrease in the mean sum of the longest diameter of all target lesions from baseline).
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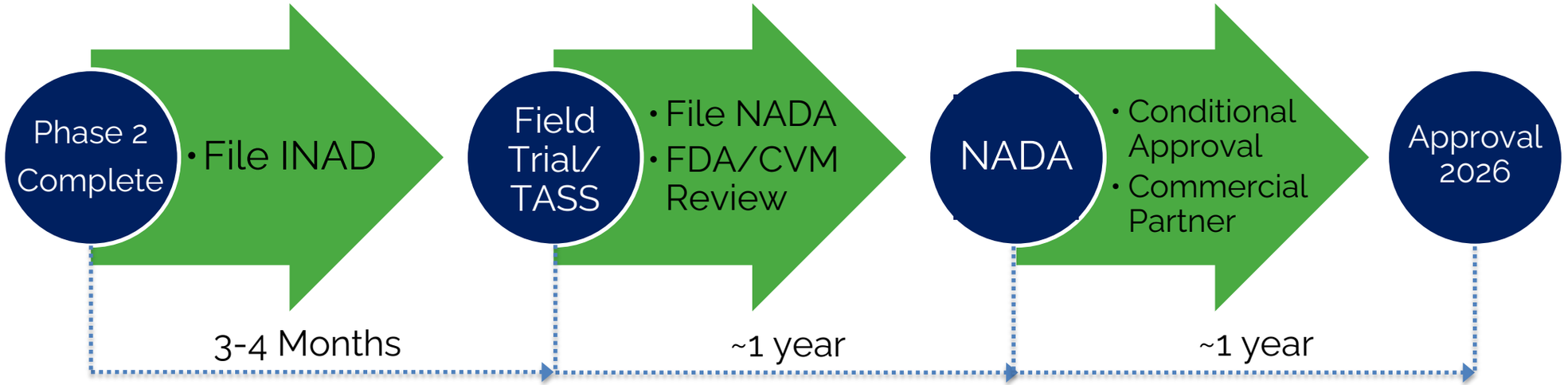
LV - LAVERDIA™

Future Directions

Regulatory Strategy



Discussion

- The potential for PharmAust to achieve a major value inflexion point by advancing MPL through to product registration with the Center of Veterinary Medicine
- The minor investment required over a short period of time to conduct the pivotal registration studies
- LAVERDIA™, the most recently approved treatment for B-Cell and T-Cell Lymphoma, was acquired[1] by Dechra Pharmaceuticals PLC (LSE:DPH) for US$64.5 million in 2022.
- Business development to be conducted in parallel

[1] Dechra Pharmaceuticals PLC acquired Worldwide Rights to Verdinexor from Anivive Lifesciences, Inc. for $64.5 million. Marketscreener January 10, 2022INAD – Investigational New Animal Drug
TASS – Target Animal Safety Trial
NADA – New Animal Drug Application
CVM – Center for Veterinary Medicine

New Treatment Paradigm

Chemotherapy

- Limited access to specialised veterinary oncologists and veterinary practices that can carry out chemotherapy
- Concerns over the dog's quality of life due to the often severe side effects associated with chemotherapy
- Complying with the rigours of the chemotherapy regime once initiated
- Major safety concerns for owners who handle and/or are exposed to the chemotherapy while caring for their dog
- High treatment costs

Monepantel

- Available in tablet form allowing dogs to be treated safely at home
- Offers disease stabilisation eliminating the need for chemotherapy
- Limited side effects for the dog and no safety concerns for owners
- Family sees their pet manage their cancer with an excellent quality of life and quality of function for an extended period of time

Thank you!

Investor Enquires

Registered Address
1 Kyle Way, Suite 116
Claremont WA 6010
Australia

Phone
+61 (8) 9202 6814

Email
investorenquiries@pharmaust.com