

## Appendix 4C and Quarterly Update

**27 January 2021 – Perth, Australia:** PharmAust Ltd (ASX:PAA), a clinical stage oncology company, is pleased to present its Appendix 4C Quarterly Report and Shareholders' Update for the period ended 31 December 2020.

### HIGHLIGHTS:

- PharmAust commences Phase IIb in pet dogs with B cell lymphoma with monepantel (MPL) tablets with the aim of demonstrating anti-tumour activity at low dose
- NSW, WA and Qld ethics approvals granted for dosing modification (UoM ethics convening for first meeting Q1 2021)
- APVMA approval to use MPL tablets at two additional trial sites
- MPL tablets have arrived at the participating clinics and recruitment of dogs has commenced
- Canine compassionate use treatment with MPL tablets ongoing
- Engaging with leading global veterinary pharmaceutical companies to commercially license MPL for anti-cancer treatments in pet animals
- PharmAust commences manufacture of GMP-Grade Monepantel for Human Clinical Trials
- Following *in vitro* work demonstrating inhibition of SARS-CoV-2 replication in Australia, PharmAust and Leiden University Medical Centre (Netherlands) continue to evaluate MPL suitability for *Ex-Vivo* Human COVID-19 Testing
- PharmAust is increasing its focus on COVID-19 with EU and US collaborators expressing interest in preparing the ground for clinical evaluation of MPL in humans
- PharmAust & Olivia Newton-John Cancer Research Institute to continue MPL preclinical investigations
- Discussions with prospective oncologists in Europe continue with the aim of undertaking a Phase I/II human cancer trial
- Epichem awarded contract extension from DNDi
- Epichem embarks on biofuels and fine chemicals proprietary project, converting carbon-based feedstock into ethanol and valuable organic compounds
- Bank balance of approximately \$3.6 million, enabling pursuit of various preclinical and clinical commitments

### ACTIVITY TIMELINE:

Activity	Details	Timing (CY) (best estimate)
Compassionate use in pet dogs	On-going with current MPL tablets	Q1 2021 and ongoing
COVID-19 pre organoid work	To enable transition to organoids, requirement for COVID-19 Human Clinical Trial	Q1 2021
Phase IIb pet dog cancer trial continuation	Dose optimization trial with current tablets	Q1/Q2 2021
Continuation mechanism of action work with ONJCRI	Looking at MPL effects in gene expression and targets	Q1/Q2 2021
Organoid work	Important precursor for COVID-19 Human Clinical Trials	Q1/Q2/Q3 2021
Complete manufacture of 10 kg of MPL	For use in Human Clinical Trials: FightMND, COVID-19 and Human Cancer.	Q3 2021
Phase III pet dog cancer trial	Current tablets, after Phase II trial continuation	Q3/Q4 2021
Tablet manufacture	Smaller dose tablets for human trials	Q3/Q4 2021
Commence FightMND Phase I/II trial	After 3 month tablet stability data	Q4 2021
Commence COVID-19 Phase I/II trial	After initial PK data from FightMND trial	Q1 2022
Commence human cancer Phase II trial	After initial PK data from FightMND trial	Q1 2022
Commence alternative Phase II trial in further neurodegenerative diseases	After initial PK data from FightMND trial	Q1/Q2 2022

## **Phase II Canine Cancer Trial**

As previously announced, in our recent phase II trial in canines with B-Cell Lymphoma, the most prevalent canine cancer, we observed both tumour regression as well as stable disease. The Company considered these data a sound platform to springboard into undertaking dose optimisation and eventually phase III registration studies.

During the quarter, PharmAust was pleased to announce receipt of ethics approvals from the New South Wales Department of Primary Industry (DPI) and Queensland Department of Agriculture and Fisheries (DAF) to undertake a Phase IIb clinical trial in pet owners' dogs with cancer. Conduct of the trial in WA is covered under an ethics harmonization agreement with NSW.

This extension of the original Phase IIa trial is aimed at demonstrating high efficacy at reduced MPL plasma levels, as well as alleviating the inappetence observed in the previous trial iteration. The approvals cover recruitment at five sites in Sydney, Perth and Brisbane. Another two sites previously involved in the trial await approvals following reconvening of respective ethics committees after the Christmas period.

PharmAust has undertaken detailed analysis of the trial data to understand drug blood level variation and importantly has developed a new dosing methodology that aims to achieve the lower drug blood levels of MPL that are associated with highest anticancer activity ( $\geq 60\%$  reduction in cancer burden, with some cancer lesions disappearing). The trial continuation will involve the same duration and readouts, but just the dosing regimen will be modified.

Additional veterinarians participating in the trial are: Dr Catherine Chan at Veterinary Specialist Services in Brisbane and Dr Jessica Finlay at Perth Vet Specialists. MPL tablets have arrived at the participating clinics and recruitment of dogs has commenced.

PharmAust's Chief Scientific Officer Dr Richard Mollard commented, "PharmAust is pleased to recommence this trial using MPL tablets to treat pet owner's dogs with B cell lymphoma. PharmAust has been testing two independent hypotheses: firstly, that MPL tablets could make cancer disappear and, secondly, that MPL tablets could stop cancer progressing (stable disease). In its human study, PharmAust had demonstrated that MPL liquid formulation stops cancer progressing. The recent set of trial results (announced 12 May 2020) using the MPL tablets exceeded expectations with the demonstration that MPL tablets can make certain cancer lesions disappear. This continuation into Phase IIb is designed to understand and optimise the dosing regimen that will maximise MPL's anticancer activity."

As data emerges, we plan to contact a wider group of leading global pharmaceutical companies to discuss veterinary collaborations and engage in discussions with them on identifying the optimal cancers to target commercially. Animal healthcare companies in the US and Germany have shown initial interest and approached PharmAust for discussions.



*Gypsie successfully completed PharmAust's 28 Day Phase IIa Canine Trial*

## **Phase II Human Cancer Trial**

PharmAust continues to take key steps towards progressing the evaluation of MPL in human trials. The Company received confirmation that the MPL human trial paper was successfully published in a peer review journal describing the historic trial undertaken in Adelaide and the performance of MPL.

PharmAust has conducted further tablet formulation and pharmacokinetic studies aiming to increase uptake of monepantel into the blood and reduce tablet numbers for future human trials.

During the quarter, PharmAust announced the commencement of production of 10kg of GMP-grade monepantel (MPL) for research and development (R&D) purposes in two Phase 1/2 clinical trials in humans. These trials involve a Phase 1/2 clinical trial examining the effects of MPL in patients with motor neurone disease (MND), as well as a Phase 1/2 clinical trial examining the effects of MPL-tablets in humans with selected cancers. MPL will be manufactured in collaboration with Syngene International Ltd., an integrated research, development and manufacturing services company.

The Company is beginning to engage with leading global pharmaceutical companies to discuss human collaborations and engage in discussions with them on identifying the optimal cancers to target. PharmAust has identified suitable Clinical Oncology Units to evaluate the new MPL tablet in humans in a Phase II trial, as a follow on from the Phase I clinical trial undertaken at the Royal Adelaide Hospital in 2015. PharmAust will continue to look for further sites to broaden recruitment possibilities. Supporting data from the current optimization trial in dogs will facilitate further human studies.

Previously, PharmAust demonstrated prevention of tumour progression and suppression of tumour cancer markers associated with the mTOR mechanism of action. The trial was stopped early, however, due to the highly unpalatable nature of the liquid formulation employed at the time. Since then PharmAust has successfully reformulated MPL into a tablet that resolves the palatability issues. Following successful preclinical work in rats and dogs comparing the liquid and tablet formulations, PharmAust can now tailor tablet dosage to achieve more effective target blood levels known to elicit anticancer activity.

PharmAust's wholly owned subsidiary Epichem Pty Ltd has conducted stability shelf-life tests of MPL over two years using feasibility batches manufactured according to the in-house method developed with Syngene. These initial non-GMP tests indicate that the Syngene MPL has demonstrated purity and stability levels compatible with that used in clinical trials. It is therefore anticipated that scaled API (active pharmaceutical ingredient) manufacture for the upcoming clinical R&D trials should demonstrate necessary shelf-life specifications.

Commencement of a human cancer Phase II trial is expected in Q1 CY 2022.

## **PharmAust & Olivia Newton-John Cancer Research Institute to Continue MPL Preclinical Investigations**

PharmAust announced an agreed extension of work being conducted at the Olivia Newton-John Cancer Research Institute (ONJCRI) investigating the mechanism of action of monepantel (MPL) upon cancer cells.

As announced on 29 September 2020, researchers in the Cell Death and Survival Laboratory at the ONJCRI led by Associate Professor Doug Fairlie conducted a comprehensive RNA-Seq (RNA sequencing) screen investigating how the entire genome of cancer cells responds when treated with MPL. A select subset of genes was found to be either switched on or off by MPL in cancer cells, but not in non-cancer cells. The mRNA profiles of non-cancer cells were relatively unaffected by MPL treatment, consistent with the possible low level of toxicology observed for MPL.

Using state-of-the-art techniques, the ONJCRI researchers will now examine these genes in greater detail and match changes in their activity with changes in associated protein signalling pathways. These experiments are aimed at determining what happens within the cancer cell once MPL interacts with its primary molecular targets and then exerts its downstream and definitive anti-cancer activity. Establishing MPL's mechanism of action in this detail will enable differentiation of MPL's effects upon cancer cells as compared to other anti-cancer drugs, thus assisting with regulatory submissions and facilitating licensing and marketing as we move towards Phase III and IV trials.

The work to be conducted by the ONJCRI will be funded by PharmAust.

PharmAust's Chief Scientific Officer Dr Richard Mollard stated "PharmAust is pleased to continue this productive relationship with the ONJCRI. PharmAust is looking forward to seeing at the molecular level how MPL works in cells to combat disease, especially in terms of how MPL's mechanism of action differs to other mTOR inhibitors presently in the clinic."

## **COVID-19 Testing**

Having undertaken our studies at the Walter and Elisa Hall Institute for Medical Research in Melbourne and then confirmatory work at 360biolabs Pty Ltd, which provides quality assured services in virology and immunology, we are confident that we are seeing meaningful anti-viral activity.

During the Quarter, PharmAust entered into a Service Agreement with researchers in the Netherlands to test the effects of monepantel and monepantel sulfone on the replication of SARS-CoV-2 in cell lines. The purpose is to determine their applicability for testing these compounds in ex-vivo human SARS-CoV-2 infection models (cultured human airway epithelial tissue/organoids). The studies have now commenced and the final data report is expected imminently. The work is being overseen by molecular virologist Professor Martijn van Hemert, Principal Investigator of Antiviral Drug Development at Leiden University Medical Center.

The only anti-viral drug on the market currently approved for the treatment of COVID-19 infection is remdesivir (Gilead Science, Inc). Remdesivir is not a cure and in a clinically controlled trial it reduced time to recovery of hospitalised patients in intensive care from 15 to 11 days. With this success, early predictions were for annual sales of US\$2-7.7 billion by 2022.

MPL may have a distinct advantage over many other drugs in development given that it has already been used in human clinical trials and is a very well-known drug with a high safety profile. Remdesivir is an intravenous therapy whereas MPL can be administered orally in tablet form. This means patients could be treated earlier when they first test positive rather than intensive care patients hospitalised with COVID-19.

PharmAust has prepared an Executive Summary, is preparing an Investigator's Brochure and has been engaging with clinicians about a Phase I trial in human patients to treat COVID-19.



*Dr. M.J. (Martijn) van Hemert*

## **Phase I/II Human Trial in Motor Neurone Disease**

PharmAust previously announced it has received funding of A\$881,085 for a Phase I trial examining the effects of monepantel (MPL) in Motor Neurone Disease (MND), otherwise known as Lou Gehrig's disease or Amyotrophic Lateral Sclerosis (ALS).

These funds have been granted by FightMND, the largest independent funder of MND research in Australia. The trial will be overseen by Dr Susan Mathers of Calvary Health Care, Bethlehem, Melbourne and will include a second trial site headed by Professor Dominic Rowe of the Centre for Motor Neurone Disease Research Faculty of Medicine and Health Research at Macquarie University in Sydney.

Preparations for the trial have already commenced and while remaining subject to approval from the Institutional Human Research Ethics Committees, Phase I trial recruitment will commence as soon as possible in CY 2021, likely to be Q4 after PharmAust has 3 months of tablet stability data. The funding agreement provides that PharmAust shall own all intellectual property generated from the study.

### **Epichem Pty Ltd (100% wholly owned subsidiary)**

Epichem continues to support the PharmAust drug development pipeline with lead drug development and validation, drug candidate pipeline manufacture and analysis, drug reformulation, GMP synthesis and stability support as well as drug inventory dispensing to clinical trial centres.

Epichem continues to pursue opportunities to create its own IP portfolio with the assignment of specific projects to individual chemists. This will also allow Epichem to maximise the R&D Tax Incentive as well as act as an R&D project incubator for PAA.

Epichem entered into a HoA to develop and commercialise the biomass/feedstock oxidative process that can turn waste into fuels. The technology is a world-first because of its potential to turn a wide range of waste and biomass feedstock into valuable fuels, fine chemicals, agricultural growth stimulants and ethanol. The Company sees this as a low cost but high potential initiative in a very scalable and disruptive business that may have multiple uses and customers.

### **Appendix 4C – Quarterly Cash Flow Report**

PharmAust's cash position at 31 December 2020 was \$3.6 million. The company is adequately funded to continue its current activities during these uncertain times and will continue to demonstrate appropriate fiscal restraint.

During the quarter, payments for Research and Development of \$0.170 million represented costs involved with the development of the Company's primary drug candidate, Monepantel (MPL) and salary allocations of Dr Richard Mollard who is 100% focused on R&D activities.

Payments for Product Manufacturing and Operating Costs represent wholly owned subsidiary Epichem Pty Ltd's expenditure allocated to manufacturing and operating.

Payments for Staff Costs represent salaries for laboratory, administration, sales and general management activities.

Payments for Administration and Corporate Costs represent general costs associated with running the Company, including ASX fees, legal fees, rent, etc.

The aggregate amount of payments to related parties and their associates included in the current quarter Cash flows from operating activities were \$0.161 million comprising Directors fees, salaries and superannuation.

\$0.041 million was raised during the quarter from the exercise of options.

Cash outflows for the quarter were in line with management expectations. The cash balance at 31 December 2020 was \$3.6 million. Please refer to the attached Appendix 4C for further details on cash flows for the quarter and subsequent events outlined below.

### **Subsequent Events**

Epichem received \$510,475 in January 2021 from DNDi for work continuing on its flagship project on Chagas disease.

Epichem was awarded a \$200,000 WasteSorted e-Waste Grant from the Western Australian Government New Industries Fund in January 2021.

These funds are not included in this Appendix 4C as they were received after 31 December 2020.

**This announcement is authorised by the Board.**

#### **Enquiries:**

**Dr Roger Aston**  
**Executive Chairman**

[rogeraston@pharmaust.com](mailto:rogeraston@pharmaust.com)

**Tel: 0402 762 204**

**Mr Robert Bishop**  
**Executive Director**

[robertbishop@pharmaust.com](mailto:robertbishop@pharmaust.com)

**Tel: 0417 445 180**

## Appendix 4C

### Quarterly cash flow report for entities subject to Listing Rule 4.7B

**Name of entity**

PharmAust Limited

**ABN**

35 094 006 023

**Quarter ended ("current quarter")**

December 2020

<b>Consolidated statement of cash flows</b>	<b>Current quarter \$A'000</b>	<b>Year to date (6 months) \$A'000</b>
<b>1. Cash flows from operating activities</b>		
1.1 Receipts from customers	549	1,321
1.2 Payments for		
(a) research and development	(170)	(296)
(b) product manufacturing and operating costs	(158)	(506)
(c) advertising and marketing	(19)	(85)
(d) leased assets	(28)	(28)
(e) staff costs	(672)	(1,276)
(f) administration and corporate costs	(86)	(204)
1.3 Dividends received (see note 3)		
1.4 Interest received	9	14
1.5 Interest and other costs of finance paid		
1.6 Income taxes paid		
1.7 Government grants and tax incentives	145	427
1.8 Other (provide details if material)	5	(14)
<b>1.9 Net cash from / (used in) operating activities</b>	<b>(358)</b>	<b>(648)</b>
<b>2. Cash flows from investing activities</b>		
2.1 Payments to acquire or for:		
(a) entities		
(b) businesses		
(c) property, plant and equipment	(13)	(34)
(d) investments		
(e) intellectual property		
(f) other non-current assets		

For personal use only

Consolidated statement of cash flows		Current quarter \$A'000	Year to date (6 months) \$A'000
2.2	Proceeds from disposal of:		
	(a) entities		
	(b) businesses		
	(c) property, plant and equipment		
	(d) investments		
	(e) intellectual property		
	(f) other non-current assets		
2.3	Cash flows from loans to other entities		
2.4	Dividends received (see note 3)		
2.5	Other (provide details if material)		
<b>2.6</b>	<b>Net cash from / (used in) investing activities</b>	<b>(13)</b>	<b>(34)</b>
<b>3.</b>	<b>Cash flows from financing activities</b>		
3.1	Proceeds from issues of equity securities (excluding convertible debt securities)	41	1,542
3.2	Proceeds from issue of convertible debt securities		
3.3	Proceeds from exercise of options		
3.4	Transaction costs related to issues of equity securities or convertible debt securities		
3.5	Proceeds from borrowings		
3.6	Repayment of borrowings	(36)	(128)
3.7	Transaction costs related to loans and borrowings		
3.8	Dividends paid		
3.9	Other (provide details if material)		
<b>3.10</b>	<b>Net cash from / (used in) financing activities</b>	<b>5</b>	<b>1,413</b>
<b>4.</b>	<b>Net increase / (decrease) in cash and cash equivalents for the period</b>		
4.1	Cash and cash equivalents at beginning of period	3,976	2,879
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(358)	(648)
4.3	Net cash from / (used in) investing activities (item 2.6 above)	(13)	(34)

Consolidated statement of cash flows		Current quarter \$A'000	Year to date (6 months) \$A'000
4.4	Net cash from / (used in) financing activities (item 3.10 above)	5	1,413
4.5	Effect of movement in exchange rates on cash held		
<b>4.6</b>	<b>Cash and cash equivalents at end of period</b>	<b>3,610</b>	<b>3,610</b>

5. Reconciliation of cash and cash equivalents at the end of the quarter (as shown in the consolidated statement of cash flows) to the related items in the accounts		Current quarter \$A'000	Previous quarter \$A'000
5.1	Bank balances	598	964
5.2	Call deposits	3,012	3,012
5.3	Bank overdrafts		
5.4	Other (provide details)		
<b>5.5</b>	<b>Cash and cash equivalents at end of quarter (should equal item 4.6 above)</b>	<b>3,610</b>	<b>3,976</b>

6. Payments to related parties of the entity and their associates		Current quarter \$A'000
6.1	Aggregate amount of payments to related parties and their associates included in item 1	161
6.2	Aggregate amount of payments to related parties and their associates included in item 2	

*Note: if any amounts are shown in items 6.1 or 6.2, your quarterly activity report must include a description of, and an explanation for, such payments.*

Director's Salaries & Superannuation



7. <b>Financing facilities</b> <i>Note: the term "facility" includes all forms of financing arrangements available to the entity. Add notes as necessary for an understanding of the sources of finance available to the entity.</i>	<b>Total facility amount at quarter end \$A'000</b>	<b>Amount drawn at quarter end \$A'000</b>
7.1 Loan facilities	454	146
7.2 Credit standby arrangements		
7.3 Other (please specify)		
7.4 <b>Total financing facilities</b>	454	146
7.5 <b>Unused financing facilities available at quarter end</b>		
7.6 Include in the box below a description of each facility above, including the lender, interest rate, maturity date and whether it is secured or unsecured. If any additional financing facilities have been entered into or are proposed to be entered into after quarter end, include a note providing details of those facilities as well.		

8. <b>Estimated cash available for future operating activities</b>	<b>\$A'000</b>
8.1 Net cash from / (used in) operating activities (item 1.9)	(358)
8.2 Cash and cash equivalents at quarter end (item 4.6)	3,610
8.3 Unused finance facilities available at quarter end (item 7.5)	
8.4 Total available funding (item 8.2 + item 8.3)	3,252
8.5 <b>Estimated quarters of funding available (item 8.4 divided by item 8.1)</b>	9.1
<i>Note: if the entity has reported positive net operating cash flows in item 1.9, answer item 8.5 as "N/A". Otherwise, a figure for the estimated quarters of funding available must be included in item 8.5.</i>	
8.6 If item 8.5 is less than 2 quarters, please provide answers to the following questions:	
8.6.1 Does the entity expect that it will continue to have the current level of net operating cash flows for the time being and, if not, why not?	
Answer: N/A	
8.6.2 Has the entity taken any steps, or does it propose to take any steps, to raise further cash to fund its operations and, if so, what are those steps and how likely does it believe that they will be successful?	
Answer: N/A	
8.6.3 Does the entity expect to be able to continue its operations and to meet its business objectives and, if so, on what basis?	
Answer: N/A	
<i>Note: where item 8.5 is less than 2 quarters, all of questions 8.6.1, 8.6.2 and 8.6.3 above must be answered.</i>	

**Compliance statement**

- 1 This statement has been prepared in accordance with accounting standards and policies which comply with Listing Rule 19.11A.
- 2 This statement gives a true and fair view of the matters disclosed.

27 January 2021

Date: .....

By the board

Authorised by: .....  
 (Name of body or officer authorising release – see note 4)

**Notes**

1. This quarterly cash flow report and the accompanying activity report provide a basis for informing the market about the entity's activities for the past quarter, how they have been financed and the effect this has had on its cash position. An entity that wishes to disclose additional information over and above the minimum required under the Listing Rules is encouraged to do so.
2. If this quarterly cash flow report has been prepared in accordance with Australian Accounting Standards, the definitions in, and provisions of, *AASB 107: Statement of Cash Flows* apply to this report. If this quarterly cash flow report has been prepared in accordance with other accounting standards agreed by ASX pursuant to Listing Rule 19.11A, the corresponding equivalent standard applies to this report.
3. Dividends received may be classified either as cash flows from operating activities or cash flows from investing activities, depending on the accounting policy of the entity.
4. If this report has been authorised for release to the market by your board of directors, you can insert here: "By the board". If it has been authorised for release to the market by a committee of your board of directors, you can insert here: "By the [name of board committee – eg Audit and Risk Committee]". If it has been authorised for release to the market by a disclosure committee, you can insert here: "By the Disclosure Committee".
5. If this report has been authorised for release to the market by your board of directors and you wish to hold yourself out as complying with recommendation 4.2 of the ASX Corporate Governance Council's *Corporate Governance Principles and Recommendations*, the board should have received a declaration from its CEO and CFO that, in their opinion, the financial records of the entity have been properly maintained, that this report complies with the appropriate accounting standards and gives a true and fair view of the cash flows of the entity, and that their opinion has been formed on the basis of a sound system of risk management and internal control which is operating effectively.