



## Appendix 4C and Quarterly Update

**28 July 2021 – Perth, Australia:** PharmAust Limited (ASX: PAA), a clinical stage biotechnology company, is pleased to present its Appendix 4C and Quarterly Update for the period ended 30 June 2021.

### HIGHLIGHTS:

- Success in Phase IIb Trial in pet dogs with B cell lymphoma
- Phase III trial to proceed with support of administering veterinarians
- PharmAust seeking partners to co-develop and commercialise MPL for treatment of veterinary cancers
- Syngene has commenced manufacture of GMP-Grade Monepantel for Human Clinical Trials
- Leiden University Medical Center (LUMC) confirm antiviral activity
- PharmAust and WEHI to investigate MPL in HTLV-1 viral infections
- PharmAust files patent for monepantel in viral diseases
- PharmAust receives Human Research Ethics approval for FightMND Phase I Clinical trial
- Epichem FY21 Revenue of A\$3.2M with unaudited profit of ~A\$300K
- Epichem pursues build of a benchtop flow reactor to showcase its OHD Technology
- Bank balance of approximately \$3.07 million, enabling pursuit of various pre-clinical and clinical commitments

### ACTIVITY TIMELINE:

Activity	Details	Timing (CY) (est)
Compassionate use in pet dogs	Completed to reserve tablets for further clinical trials	N/A
Phase IIb pet dog cancer trial continuation	Dose optimization trial with current tablets	ongoing
Continuation mechanism of action work with ONJCRI	Looking at MPL effects in gene expression and targets	Q2 – Q4 2021
HTLV-1 testing	WEHI to investigate the effects of MPL upon HTLV-1 infections in vitro	Q3/Q4 2021
Complete manufacture of 10 kg of MPL	For use in Human Clinical Trials: FightMND and COVID-19	Q4 2021
Phase III pet dog cancer trial	After Phase IIb trial completion	Q1 2022
GMP tablet manufacture	Smaller dose tablets for human neurodegeneration and antiviral trials	Q1/2 2022
Complete second manufacture of 10 kg MPL	For use in Human Clinical Trials: cancer and alternative neurodegenerative conditions	Q1/2 2022
Complete second GMP tablet manufacture	Larger dose tablets for anticancer trials	Q2/Q3 2022
Commence FightMND Phase I/II trial	After sufficient tablet stability data	Q2/3 2022
Commence COVID-19 Phase I/II trial	After sufficient tablet stability data	Q2/3 2022
Commence human cancer Phase II trial	After initial PK data from FightMND and Covid-19 trials	Q3/4 2022
Commence alternative Phase II trial in further neurodegenerative diseases	After initial PK data from FightMND and Covid-19 trials	Q4 2022

## **Phase II Canine Cancer Trial**

During the quarter, PharmAust was delighted to announce that following the treatment of 15 pet dogs during its Phase IIa and Phase IIb studies, monepantel (MPL) demonstrated sufficient anti-cancer activity to continue development into Phase III.

Multi-centric high grade B-cell lymphoma is one of the most 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.

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 is now contacting 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.

## **Phase II Human Cancer Trial**

PharmAust continues to take key steps towards progressing the evaluation of MPL in human trials. 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 in Italy and the United Kingdom 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.

PharmAust has had discussions with prospective oncologists in Italy with the aim of undertaking a pancreatic cancer trial in humans. PharmAust has also had discussions with prospective oncologists in the United Kingdom with the aim of undertaking an oesophageal human cancer trial.

Commencement of a human cancer Phase II trial is expected in Q3/4 CY 2022.

## **COVID-19 Testing**

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 models, once again demonstrate their antiviral activity.

Although there have been solubility issues with MPL in certain in vitro model systems, this does not impact the clinical work, either in dogs or humans. For clinical work, PharmAust has resolved the issues of solubility by developing the MPL tablet dosage form which effectively releases MPL into the gut for absorption into the circulation. MPL is quickly and efficiently converted into MPLS in the body, with MPLS representing the dominant form in the plasma.

Researchers at LUMC are part of a consortium called Corona Accelerated R&D in Europe (CARE) which is funded by the EU Innovative Medicines Initiative. The goal of the CARE consortium is to develop solutions for the current COVID-19 pandemic as well as to prevent future coronavirus outbreaks of this magnitude. With a budget of about 4 million euro, LUMC is one of CARE's leading academic partners.

Organoid work is one option for advancing preclinical evidence and we may follow that up if the systems are deemed suitable. If not, PharmAust believes that it has sufficient evidence to continue development in human testing in the clinic.

PharmAust has been actively engaging with clinicians in the United Kingdom, United States as well as Eastern and Caucasus countries and The Balkans about a Phase I trial in human patients to treat COVID-19.

### **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.

PharmAust has already shown in its preclinical programs that MPL has the potential to activate molecular pathways relevant to the treatment of MND. If effective, MPL would reduce the rate of degeneration and loss of motor neurons in the anterior horns and motor nuclei of the brainstem. Furthermore, there are a number of surrogate clinical endpoints that will also be determined during the trial. For the purpose, PharmAust is developing and manufacturing a bespoke monepantel tablet for the trial.

PharmAust completed preparation of the Investigator's Brochure and Protocol for the trial, permitting evaluation and subsequent acceptance by the Monash Human Research Ethics Committee to undertake the trial and the Therapeutics Goods Administration (TGA) of Australia, to undertake the trial according to the Clinical Trial Notification (CTN) scheme. Without these acceptances, the trial would not be permitted to proceed. Acceptance for trial registration on Clinicaltrials.gov at the United States National Library of Medicine at the National Institutes of Health was also obtained. Registration on such a public broadcast platform is required for ethics approval and normally registration is encouraged in the local jurisdiction. Having registration and public broadcast in the US maximally increases the reach and awareness of the trial and facilitates future involvement of US sites for larger Phase II recruiting. All regulatory and ethics requirements to commence the trial are now complete.

The study is a multi-centre open label trial entitled *A Phase I Tolerability, Safety, Pharmacokinetics and Preliminary Efficacy Study of Oral Monepantel in Individuals with Motor Neurone Disease*. It is designed to first test safety in 12 individuals living with ALS/MND according to a conventional dose escalation design, with each level of the dose escalation lasting 28 days. Measures of efficacy are included in the trial design so that where appropriate, this trial can be extended into a Phase II setting. Details of the trial can be found at clinicaltrials.gov using the Identifier code: NCT04894240.

With success in the clinic, PharmAust expects that in due course MPL will receive orphan drug designation by the FDA for the indication of motor neurone disease. Such designations come with a number of financial and supportive benefits. The Orphan Drug Act provides for granting special status to a drug or biological product to treat a rare disease or condition upon request of a sponsor.

PharmAust has not received any funding from FightMND as yet. The first instalment of \$201,615 is due to be received after GMP manufacture of MPL has been completed.

### **Manufacturing of GMP-grade MPL raw compound and GMP-grade MPL tablets**

PharmAust previously announced the commencement of production of 10kg of GMP-grade MPL for research and development (R&D) purposes in 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), a Phase 2 clinical trial examining the effects of MPL-tablets in humans with selected cancers, as well as a Phase 1 clinical trial examining the effects of MPL-tablets in humans with COVID-19. The GMP-grade MPL compound is being manufactured in collaboration with Syngene International Ltd., an integrated research, development and manufacturing services company and Catalent Pharma Solutions (NYSE: CTLT) will perform scaled-up manufacture of GMP-grade monepantel tablets suitable for use in the upcoming human trials.

GMP tablet manufacture is a key component for undertaking GCP (Good Clinical Practice) trials and will enable the data emerging from forthcoming trials to be admissible to the U.S. FDA to support new drug registration programs.

Due to the impact of COVID-19 on global supply chains, Syngene have advised PharmAust that the production of 10kg of GMP-grade MPL has been delayed. Regrettably, the subsequent commencement of human trials in MND, COVID-19 and cancer will therefore be delayed until Q2 CY 2022.

PharmAust Executive Chairman, Dr Roger Aston, said "These are challenging times for our contractors, our partners, our employees and for PharmAust shareholders. Despite the significant challenges ahead, PharmAust is well positioned to work with all parties to address the current challenging environment."

In an effort to ensure PharmAust has more than adequate supplies of MPL going forward for all clinical trials and any potential further trials, the Company will procure an additional 10kg of GMP Grade MPL. This second batch is expected to be manufactured by Q1/2 CY2022. A separate batch of larger dose tablets will be manufactured by Catalent for the human cancer clinical trials.

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

Epichem has reported FY21 Revenue of A\$3.2M with unaudited profit of ~A\$300K.

Epichem secured new projects from new and existing customers in medicinal chemistry, pharmaceutical reference standards, custom synthesis and analytical chemistry and have added additional staff to the Chemistry Team.

The new clients include PYC Therapeutics, where Epichem worked in partnership to develop a world-first treatment for thousands of sufferers of retinitis pigmentosa around the world which could see patients' slow transition into blindness stopped in its tracks. The treatment, which was conceived, researched, developed and will hopefully be trialled in WA, is targeted at retinitis pigmentosa 11 – a degenerative condition which causes a gradual deterioration of vision until a person is completely blind.

Epichem also supported, local WA hand sanitiser and surface spray company Forever and More with the facilitation of the validation of viricidal efficacy against surrogates of COVID-19 in accordance with TGA guidelines and bactericidal efficacy against S.aureus, P.aeruginosa, E.coli and E.hirae.

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.

### **Waste To Fuels Technology**

Epichem continues to pursue its novel, innovative and disruptive Oxidative Hydrothermal Dissolution (OHD) technology to convert and re-purpose biomass and feedstock into valuable end products, recover valuable metals and produce useful high value chemicals with the build of a benchtop flow reactor. The research will be carried out at Epichem's state of the art, purpose built laboratories in Technology Park, Bentley, WA.

OHD is environmentally friendly technology that breaks down solid organic materials (feedstocks) by a direct process based on oxidative bond scission. OHD works by reaction of macromolecular organic solids with dissolve oxygen in superheated (200-370°C), high pressure, liquid water, i.e. not supercritical water.

Feedstocks include anything carbon-based including biomass, coal, oil shale, bituminous sands, plastic, rubber, agricultural waste, and more. Each source material produces a unique mixture of organic components with many potential uses.

Epichem continues its research and development of e-waste using OHD after securing a \$200,000 WasteSorted e-Waste Grant from the Western Australian Government New Industries Fund. The research and development program will support a new and innovative solution to process collected e-waste and reduce the amount of e-waste ending up in landfill.

The WasteSorted e-Waste grants support the WA Waste Avoidance and Resource Recovery Strategy 2030 objectives - to avoid waste, recover more value and resources from waste, and protect the environment from the impacts of waste. The \$16.7 million New Industries Fund was established to support and accelerate new and emerging businesses to diversify the Western Australian economy and create new WA jobs.

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

PharmAust's cash position at 30 June 2021 was \$3.07 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 \$0.154 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.

Cash outflows for the quarter were in line with management expectations. The cash balance at 30 June 2021 was \$3.07 million. Please refer to the attached Appendix 4C for further details on cash flows for the quarter.

#### **Subsequent Events**

Epichem received \$382,856 in July 2021 from DNDi for work continuing on its flagship project on Chagas disease. These funds are not included in this Appendix 4C as they were received after 30 June 2021.

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

#### **Enquiries:**

**Dr Roger Aston**  
Executive Chairman

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

**Mr Sam Wright**  
Finance Director

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

**P +61 (8) 9202 6814**

**F +61 (8) 9467 6111**

**W [www.pharmaust.com](http://www.pharmaust.com)**

**T [@PharmAust](#)**

#### **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.

## 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")**

June 2021

<b>Consolidated statement of cash flows</b>	<b>Current quarter \$A'000</b>	<b>Year to date (12 months) \$A'000</b>
<b>1. Cash flows from operating activities</b>		
1.1 Receipts from customers	403	2,462
1.2 Payments for		
(a) research and development	(154)	(816)
(b) product manufacturing and operating costs	(274)	(1,053)
(c) advertising and marketing	(79)	(206)
(d) leased assets	(23)	(77)
(e) staff costs	(482)	(2,250)
(f) administration and corporate costs	(221)	(622)
1.3 Dividends received (see note 3)		
1.4 Interest received	2	16
1.5 Interest and other costs of finance paid		
1.6 Income taxes paid		
1.7 Government grants and tax incentives	19	1,477
1.8 Other (provide details if material)	13	(9)
<b>1.9 Net cash from / (used in) operating activities</b>	<b>(797)</b>	<b>(1,078)</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	(33)	(67)
(d) investments		
(e) intellectual property		
(f) other non-current assets		

Consolidated statement of cash flows		Current quarter \$A'000	Year to date (12 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>(34)</b>
<b>3.</b>	<b>Cash flows from financing activities</b>		
3.1	Proceeds from issues of equity securities (excluding convertible debt securities)		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	(43)	(207)
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>(43)</b>	<b>1,334</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	3,942	2,879
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(797)	(1,078)
4.3	Net cash from / (used in) investing activities (item 2.6 above)		(34)

Consolidated statement of cash flows		Current quarter \$A'000	Year to date (12 months) \$A'000
4.4	Net cash from / (used in) financing activities (item 3.10 above)	(43)	1,334
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>3,068</b>	<b>3,068</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	3,056	2,430
5.2	Call deposits	12	1,512
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>3,068</b>	<b>3,942</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	148
6.2	Aggregate amount of payments to related parties and their associates included in item 2	
<i>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.</i>		

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	74
7.2 Credit standby arrangements		
7.3 Other (please specify)		
7.4 <b>Total financing facilities</b>	454	74
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)	(797)
8.2 Cash and cash equivalents at quarter end (item 4.6)	3,068
8.3 Unused finance facilities available at quarter end (item 7.5)	
8.4 Total available funding (item 8.2 + item 8.3)	3,068
8.5 <b>Estimated quarters of funding available (item 8.4 divided by item 8.1)</b>	3.8
<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.

28 July 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.

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