ASX RELEASE 31 July 2024

June 2024 Quarterly Activities Report & Appendix 4C

Key Highlights

- **Response Package to US FDA**: Paradigm announced the submission of key documents to the US FDA in April 2024, for review and agreement on the progression of the Phase 3 clinical program for osteoarthritis utilising the optimal dose.
- **Bio International**: Paradigm Biopharma's key executives attended the prestigious Bio International Conference in San Diego in June 2024. The event featured Paradigm's Managing Director, Paul Rennie, along with other top executives, who engaged with global industry leaders, researchers, and potential partners.
- **MPS VI**: Following the conclusion of Paradigm's successful multi-centre phase 2 clinical trial, randomising 13 MPS VI participants to iPPS or placebo, all 13 participants have elected to continue or commence (for the placebo group) ongoing iPPS treatment under the supervision of the treating physician.
- **Quarter Spend**: Cash outflow for the June 2024 quarter was $8.35m, coming in under the guided $10m spend.

Paradigm Biopharmaceuticals Ltd. (ASX:PAR) ("Paradigm" or "the Company") is pleased to provide its quarterly update for the three months ended 30 June 2024 to accompany its Appendix 4C cash flow report for the period.

- Cash balance as of 30 June 2024 was $17.8m (on 31 March 2024 it was $26.2m).
- Research and development expenditure for the quarter of $7.2m was again significantly reduced compared to the previous quarter of $13.1m. In the quarter ending June 2024, Paradigm Biopharmaceuticals reported an outflow of $8.35 million, coming in under the forecasted guidance of $10 million. Major spending areas for the quarter included significant regulatory costs associated with key submissions to the US FDA and Australian TGA. Additionally, expenses were incurred to support the ongoing special access program for MPS VI participants from the phase 2 clinical trial in Brazil, who all opted to continue the iPPS treatment.
- Travel fees were notably higher during this period, driven by key management's attendance at the Bio International Conference in San Diego in July 2024.
- Managing corporate and administrative expenses remains a priority for the Company. Through the cost containment measures introduced in the second quarter of calendar year 2023, expenses were further reduced this quarter. Paradigm is committed to directing funds towards clinical and nonclinical activities that enhance the value of its osteoarthritis clinical program. This prudent financial management underscores Paradigm's commitment to advancing its clinical programs while maintaining fiscal discipline.
- Paradigm forecasts cash outflow for the September 2024 quarter to be under $7 million. This target aligns with strategic financial management practices, ensuring resource allocation towards critical costs related to the osteoarthritis phase 3 program and operational efficiency.

- In accordance with Listing Rule 4.7C.3 and as noted in item 6 of the Appendix 4C Cashflow Statement, payments to related parties and their associates during the quarter ended 30 June 2024 were fees of $46K for payment of Director fees. The quarter also saw a $1K payment for legal fees to Biomeltzer, a company controlled by Non- Executive Director, Amos Meltzer.
- During the quarter the company also paid $75k in ASX fees related to the capital raise completed in late 2023.
- The quarter also saw payments related to continuing activities described in the below.

QUARTERLY ACTIVITIES & OUTLOOK

Paradigm is pleased to provide an update on continuing activities.

Phase 3 Clinical Program

Paradigm met with the US FDA on January 10, 2024, to address the next steps for the Phase 3 clinical program in Osteoarthritis. Paradigm's clinical and regulatory teams have filed the response to the Type D meeting with the US FDA, providing updated nonclinical and clinical data to the Agency. Additionally, a proposed clinical trial protocol utilising a dosage of 2mg/kg twice weekly, was submitted for the next stage of the Phase 3 OA program. The response package was submitted as directed by the Agency through a request for review pathway.

In April, Paradigm Biopharmaceuticals made a comprehensive submission to the US FDA. This response includes the results of five nonclinical studies, data from the successful Phase 2 clinical trial, PARA_OA_008, and clinical data from 600 participants dosed in stage 1 of PARA_OA_002. These data packs were collected following Paradigm's Investigational New Drug (IND) submission to the Agency in March 2021 (see ASX release), with many elements being newly submitted and reviewed by the FDA.

Paradigm also submitted a draft of the Phase 3 pivotal clinical trial protocol for agency review and comment. The response package was submitted through the request for review pathway, which does not have strict Prescription Drug User Fee Act (PDUFA) Agency response timelines, however responses are typically received within three months. Paradigm has been in regular contact with the Agency representative overseeing the review, utilising the benefits provided by the Fast Track designation. Paradigm is expecting an imminent response from the US FDA.

TGA Provisional Approval Determination Application

Paradigm submitted the provisional approval determination application to the TGA at the end of June 2024. The determination application included information from a manuscript detailing the outcomes from the PARA_OA_008 phase 2 clinical trial and a manuscript providing a comparison of iPPS clinical data with other available treatments for osteoarthritis. Paradigm will update investors on the outcome when possible. Should the determination application decision be positive, Paradigm will prepare a full dossier submission for TGA provisional approval marketing authorisation.

Mucopolysaccharidosis (MPS) VI

In Brazil, sponsor companies conducting clinical trials are required to provide an additional five years of the investigational product to participants who choose to continue the treatment after the conclusion of the trial. This regulation ensures that patients who have benefited from the investigational product during the clinical trial can maintain their access to potentially lifesaving or health-improving therapies without interruption. This commitment from sponsor companies underscores their dedication to patient welfare and adherence to ethical standards in clinical research, reflecting the robust regulatory framework governing clinical trials in Brazil.

Following the conclusion of Paradigm's successful multi-centre phase 2 clinical trial, randomising 13 MPS VI participants to iPPS or placebo, all 13 participants have elected to continue or commence (for the placebo group) ongoing iPPS treatment. Paradigm reported during the March 2024 quarter that the phase 2 trial successfully met the primary endpoint and achieved positive results in several of the secondary outcomes. The primary endpoint of the study was the safety and tolerability of iPPS compared to placebo. iPPS was well-tolerated, and all adverse events were mild to moderate. The majority of adverse events were associated with injection site reactions. No adverse events led to discontinuation of the study treatment, nor were there any serious adverse events or adverse events of special interest. Analysis of this phase 2 study demonstrated that iPPS was a safe adjunctive therapy to enzyme replacement therapy for the continual joint pain, stiffness, and functional disability associated with MPS VI.

This outcome demonstrates the perceived benefits of the iPPS treatment from MPS VI participants, physicians and caregivers who participated in the study.

Global Conferences

Paradigm Biopharma's key executives attended the prestigious Bio International Conference in San Diego in June 2024. The event featured Paradigm's Managing Director, Paul Rennie, along with other top executives, who engaged with global industry leaders, researchers, and potential partners. Their participation underscored Paradigm's commitment to advancing iPPS for use in osteoarthritis and strengthening its network within the biotech community. The conference provided an invaluable platform for Paradigm to showcase its latest developments, discuss strategic collaborations, and explore new opportunities in the biotechnology sector.

Other Activities

- Managing Director Paul Rennie attended the Bioshares Biotech Summit in Perth, in July 2024. Paul conducted a presentation to the conference attendees detailing Paradigm's clinical progress utilising iPPS for knee OA and the proposed trial design for the PARA_OA_012 phase 3 study. The Bioshares presentation is available on the Paradigm website.
- The PARA_OA_008 phase 2 clinical trial results manuscript and the comparison manuscript detailing the clinical trial results from the PARA_OA_008 phase 2 trial compared to currently available and pipeline OA therapies have been submitted to separate journals for peer review and publication. A timeline for publication is not available currently however Paradigm expects both manuscripts to be published during CY2024.
- Paradigm Biopharmaceuticals Ltd. has received acceptance for their Australian patent application AU 2021201198 A1, titled "Treatment of bone marrow pathologies with polysulfated polysaccharides," which covers the use of polysulfated

polysaccharides, particularly pentosan polysulfate, for treating bone marrow edema lesions and Modic Endplate Changes Type I, associated with osteoarthritis and chronic low back pain.

- Paradigm Founder and Managing Director Paul Rennie recently conducted a CEO interview with Grafa and a webinar presentation with Sharewise to discuss the current progress with the submission package currently being reviewed by the US FDA. The interview and webinar are available to be viewed through the below links:
    - Grafa – Paradigm Biopharma Interview
    - Sharewise – Paradigm Biopharma Webinar

About Paradigm Biopharmaceuticals

Paradigm Biopharmaceuticals Ltd. (ASX:PAR) is a late-stage drug development company driven by a purpose to improve patients' health and quality of life by discovering, developing, and delivering pharmaceutical therapies. Paradigm's current focus is developing iPPS for the treatment of diseases where inflammation plays a major pathogenic role, indicating a need for the anti-inflammatory and tissue regenerative properties of PPS, such as in osteoarthritis (phase 3) and mucopolysaccharidosis (phase 2).

Forward Looking Statements

This Company announcement contains forward-looking statements, including statements regarding anticipated commencement dates or completions dates of preclinical or clinical trials, regulatory developments, and regulatory approval. These forward-looking statements are not guarantees or predictions of future performance, and involve known and unknown risks, uncertainties and other factors, many of which are beyond our control, and which may cause actual results to differ materially from those expressed in the statements contained in this presentation. Readers are cautioned not to put undue reliance on forward-looking statements.

Authorised for release by the Paradigm Board of Directors.

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Paradigm Biopharma

Appendix 4C

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

Name of entity	
Paradigm Biopharmaceuticals Limited	
ABN	**Quarter ended ("current quarter")**
94 169 346 963	30 June 2024

Consolidated statement of cash flows		**Current quarter $A'000**	**Year to date (12 months) $A'000**
1.	**Cash flows from operating activities**		
1.1	Receipts from customers	53	83
1.2	Payments for		
	(a) research and development	(7,204)	(69,349)
	(b) product manufacturing and operating costs	-	-
	(c) advertising and marketing	(25)	(309)
	(d) leased assets	(20)	(81)
	(e) staff costs	(516)	(2,200)
	(f) administration and corporate costs	(435)	(2,242)
1.3	Dividends received (see note 3)	-	-
1.4	Interest received	78	846
1.5	Interest and other costs of finance paid	(5)	(14)
1.6	Income taxes paid	-	-
1.7	Government grants and tax incentives	-	7,327
1.8	Other (provide details if material)	-	-
1.9	**Net cash from / (used in) operating activities**	**(8,074)**	**(65,939)**

2.	**Cash flows from investing activities**		
2.1	Payments to acquire or for:		
	(a) entities	-	-
	(b) businesses	-	-
	(c) property, plant and equipment	-	-
	(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)	-	-
2.6	**Net cash from / (used in) investing activities**	**-**	**-**

3.	**Cash flows from financing activities**		
3.1	Proceeds from issues of equity securities (excluding convertible debt securities)	-	30,117
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	(75) -	(1,838) -
3.5	Proceeds from borrowings	-	-
3.6	Repayment of borrowings (lease liabilities)	(24)	(102)
3.7	Transaction costs related to loans and borrowings	-	-
3.8	Dividends paid	-	-
3.9	Other (Limited recourse loan repaid under ESP)	-	-
3.10	**Net cash from / (used in) financing activities**	**(99)**	**28,177**

4.	**Net increase / (decrease) in cash and cash equivalents for the period**		
4.1	Cash and cash equivalents at beginning of period	**26,221**	**56,379**
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(8,074)	(65,939)

Consolidated statement of cash flows		Current quarter $A'000	Year to date (12 months) $A'000
4.3	Net cash from / (used in) investing activities (item 2.6 above)	-	-
4.4	Net cash from / (used in) financing activities (item 3.10 above)	(99)	28,177
4.5	Effect of movement in exchange rates on cash held	(181)	(750)
4.6	**Cash and cash equivalents at end of period**	**17,867**	**17,867**

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	17,867	26,221
5.2	Call deposits		
5.3	Bank overdrafts		
5.4	Other (provide details)		
5.5	**Cash and cash equivalents at end of quarter (should equal item 4.6 above)**	**17,867**	**26,221**

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	47
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.

7.	**Financing facilities** *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.*	**Total facility amount at quarter end $A'000**	**Amount drawn at quarter end $A'000**
7.1	Loan facilities	-	-
7.2	Credit standby arrangements	-	-
7.3	Other (please specify)	-	-
7.4	**Total financing facilities**	-	-

7.5	**Unused financing facilities available at quarter end**	-

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.	**Estimated cash available for future operating activities**	**$A'000**
8.1	Net cash from / (used in) operating activities (item 1.9)	(8,074)
8.2	Cash and cash equivalents at quarter end (item 4.6)	17,867
8.3	Unused finance facilities available at quarter end (item 7.5)	-
8.4	Total available funding (item 8.2 + item 8.3)	17,867
8.5	**Estimated quarters of funding available (item 8.4 divided by item 8.1)**	2.21

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.

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:.

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:

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:

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.

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.

Date: ..31 July 2024.....

Authorised by: ...By the board.....
(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.