PARADIGM BIOPHARMA

ASX RELEASE 31 October 2024

September 2024 Quarterly Activities Report & Appendix 4C

Key Highlights

- **Phase 3 Protocol Submission:** Paradigm submitted the final Phase 3 protocol for the PARA_OA_012 trial to the US FDA on 29th October 2024. The 30-day review period is expected to conclude on 28th November 2024, marking a critical milestone for the company.
- **Advancing Trial Design:** Protocol adjustments have been made to improve patient convenience and optimise trial efficiency. Global CRO selection is nearing completion, further preparing Paradigm for Phase 3 enrolment in early 2025.
- **Strong Regulatory Alignment:** Paradigm continues to work closely with the FDA and commercial parties to ensure regulatory success and a clinical protocol designed to achieve the best possible label for iPPS once approved.
- **Quarter Spend**: Net cash outflows for the September 2024 quarter were $4.72m, coming in under the guided $7m spend with normalised accounts payable.
- **R&D Incentive Rebate:** Paradigm is finalising its R&D incentive rebate and anticipates a refund of between $5-6 million, providing additional support for ongoing research and development activities.

Paradigm Biopharmaceuticals Ltd. (ASX: PAR) ("Paradigm" or "the Company") is pleased to provide its quarterly update for the three months ended 31 September 2024 and continuing activities to accompany its Appendix 4C cash flow report for the period.

Phase 3 Clinical Program

Paradigm has made substantial progress in its Phase 3 clinical trial preparations for the treatment of knee osteoarthritis with iPPS. In January 2024, Paradigm held a Type D meeting with the US FDA to discuss Stage 1 results of PARA_OA_002 and determine the optimal dosing strategy for progressing the development program. Following this, in April 2024, Paradigm submitted key documents to the FDA, including the results of five nonclinical studies, data from the successful Phase 2 trial (PARA_OA_008), and clinical data from 600 participants dosed in Stage 1 of PARA_OA_002. This submission also included a draft of the Phase 3 pivotal trial protocol for agency review and feedback. In September 2024, Paradigm received a response from the US FDA, which provided guidance on the progression of the Phase 3 knee OA program, allowing the company to refine and finalise the trial protocol.

The Type D meeting response from the FDA provided positive feedback and several key recommendations:

- The FDA confirmed the acceptability of the 2 mg/kg dosing regimen.
- Suggested reductions in safety monitoring and mitigation requirements compared to prior study stages, streamlining the trial process.
- Provided recommendations for statistical analysis, including guidance on the timing of planned assessments for the Phase 3 study.

- Agreed to proceed with the final submission of the protocol, contingent on implementing the recommended changes.

Subsequently, the updated protocol was submitted to the FDA on 29th October 2024. This submission incorporates the FDA's feedback, including a dosing regimen of 2 mg/kg iPPS administered twice weekly. Paradigm expects the FDA review period to conclude by 29th November 2024, enabling the initiation of pre-screening and enrolment activities at up to 10 Australian trial sites in Q1 2025.

PARA_OA_012 is a phase 3, randomised, double-blind, placebo-controlled multicenter study designed to evaluate the efficacy and safety of PPS 2 mg/kg administered via subcutaneous injection twice weekly for 6 weeks compared to placebo in patients with knee osteoarthritis. The study will include a 6-week treatment period followed by a 52-week follow-up period to assess long-term outcomes.

Enhancements to Trial Design

The PARA_OA_002 clinical trial provided valuable data that has informed the design of the new Phase 3 study, PARA_OA_012. The Paradigm clinical team has applied the learnings from PARA_OA_002 to enhance patient convenience and experience in the PARA_OA_012 study. Many of the adjustments, recommended through FDA discussions, aim to streamline the trial process, and reduce the burden on participants, enhancing patient retention. These modifications are also expected to positively impact the overall trial budget by potentially reducing costs. Additionally, design changes have been made to better address variability in patient responses, aiming for more consistent outcomes across different patient groups. This approach can increase the sensitivity of detecting changes in pain levels over time, making it easier to assess the efficacy of a treatment. Paradigm aims to achieve a more accurate and nuanced understanding of treatment effects, potentially enhancing the reliability and relevance of trial outcomes.

These enhancements are expected to support a more efficient and effective Phase 3 trial, aiding in the collection of robust data for global regulatory submissions. Paradigm continues to align closely with the FDA and engage with commercial partners to ensure both regulatory success and a clinical protocol designed to achieve the best possible label for iPPS upon approval.

Paul Rennie, MD of Paradigm Biopharma, commented on the quarter: *"The submission of our phase 3 protocol to the FDA is a significant milestone for Paradigm. It represents the culmination of extensive work by our team and close collaboration with the FDA. We are confident that this progress, combined with the anticipated TGA response and our ongoing engagement with funding partners, positions us strongly as we move into this pivotal phase. Our focus remains on delivering outcomes that will benefit patients and create long-term value for our shareholders."*

Summary of Cash Flow and Quarterly Activity

As of 30 September 2024, Paradigm's cash and cash equivalents totalled $13.14m (on 30 June 2024 it was $17.8m). During the quarter, the company allocated a significant portion of its expenditure towards research and development, reflecting the focus on advancing the Phase 3 clinical trial.

- Research and development expenditure for the quarter of $3.79m was again significantly reduced compared to the previous quarter of $7.2m. In the quarter ending September 2024, Paradigm reported an outflow of $4.72 million, coming in

under the forecasted guidance of $7 million. Major spending areas for the quarter included significant regulatory costs associated with key submissions to the US FDA with normalised accounts payable at the end of the quarter.

- Paradigm is in the process of finalising its R&D incentive rebate and expects a refund for activities of between $5-6 million. This rebate will provide additional support for ongoing research and development activities.
- Paradigm forecasts cash outflow for the December 2024 quarter to be under $7.0million, similar to the guidance for September 2024 quarter. This target aligns with strategic fiscal 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 31 September 2024 were fees of $65K for payment of Director fees.

OUTLOOK

Board Update

Dr. Donna Skerrett will transition away from her role as Executive Director as announced on 21st October, to focus solely on her responsibilities as Chief Medical Officer (CMO) after the 2024 Annual General Meeting. Dr. Skerrett will focus exclusively on her responsibilities as Chief Medical Officer (CMO) and the successful execution of Paradigm's pivotal phase 3 clinical trial. Her deep expertise and commitment to advancing the trial remain a crucial asset as Paradigm moves toward this key milestone. This change aligns with Paradigm's focus on advancing the pivotal phase 3 trial.

TGA Provisional Approval Determination Application

Paradigm has engaged with the TGA following the US FDA's agreement on the dosing regimen and anticipates a response to its provisional approval determination application during the December quarter. Paradigm will keep investors informed as soon as the outcome is available. Should the determination be positive, Paradigm is prepared to proceed with a full dossier submission for TGA provisional approval and marketing authorisation.

Manuscript Submissions and Peer Review

Paradigm has completed two manuscripts, based on the phase 2 OA clinical data:

- *PARA_OA_008 Phase 2 Clinical Trial Results Manuscript*: This manuscript details the outcomes from the Phase 2 clinical trial and has been planned for publication in the *Osteoarthritis and Cartilage* journal once peer review and editing is completed.

- *iPPS Comparison Manuscript*: This manuscript provides a comparative analysis of clinical trial results from the PARA_OA_008 Phase 2 trial against currently available and pipeline therapies for osteoarthritis. It has been submitted to the *Arthritis and Rheumatology* journal, where it has received minor edits from the editor and is now awaiting acceptance for publication. These publications aim to enhance the visibility and scientific validation of iPPS's clinical data.

Upcoming Milestones

- **FDA Review Conclusion** (29th November 2024): Paradigm anticipates the conclusion of the FDA's 30-day review of the submitted Phase 3 protocol for the PARA_OA_012 trial on 29th November 2024, pending no further comments. A positive outcome will allow Paradigm to commence patient pre-screening and enrolment activities at up to 10 Australian trial sites, with enrolment expected to begin in Q1 2025. This milestone is critical as it advances the trial towards pivotal data collection.
- **TGA Determination Response** (Q4 2024): Paradigm awaits the TGA's response to the provisional approval determination application, this determination is a significant step toward securing regulatory approval in Australia for iPPS.
- **CRO Selection and Trial Preparation** (Q4 2024): Paradigm is in the final stages of selecting a Contract Research Organisation (CRO) to manage the global Phase 3 trial. The selection will ensure that the trial is conducted to the highest standards, supporting a successful regulatory submission. Paradigm expects to finalise the CRO by the end of Q4 2024 and proceed with preparations for the trial launch in early 2025, including site readiness and training for clinical staff.
- **R&D Incentive Rebate Finalisation** (December 2024): Paradigm is in the final stages of securing an R&D incentive rebate, expected to be between $5-6 million. This rebate will provide additional financial support for Paradigm's ongoing research and development activities, contributing to a robust cash position as the company advances through key trial phases.
- **Commencement of Phase 3 Patient Enrolment** (Q1 2025): Subject to a positive FDA review and site readiness, Paradigm is targeting the start of patient enrolment for the Phase 3 trial in Q1 2025. The initial focus will be on Australian trial sites, with plans to expand globally as part of a comprehensive effort to gather pivotal data on the safety and efficacy of iPPS in treating knee osteoarthritis.

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 September 2024

Consolidated statement of cash flows		**Current quarter $A'000**	**Year to date (3 months) $A'000**
1.	**Cash flows from operating activities**		
1.1	Receipts from customers	41	41
1.2	Payments for		
	(a) research and development	(3,794)	(3,794)
	(b) product manufacturing and operating costs	-	-
	(c) advertising and marketing	(5)	(5)
	(d) leased assets	(15)	(15)
	(e) staff costs	(568)	(568)
	(f) administration and corporate costs	(351)	(351)
1.3	Dividends received (see note 3)	-	-
1.4	Interest received	52	52
1.5	Interest and other costs of finance paid	(2)	(2)
1.6	Income taxes paid	-	-
1.7	Government grants and tax incentives	-	-
1.8	Other (provide details if material)	-	-
1.9	**Net cash from / (used in) operating activities**	**(4,642)**	**(4,642)**

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 (3 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)	-	-
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 (lease liabilities)	(34)	(34)
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**	**(34)**	**(34)**

4.	**Net increase / (decrease) in cash and cash equivalents for the period**		
4.1	Cash and cash equivalents at beginning of period	**17,867**	**17,867**
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(4,642)	(4,642)
4.3	Net cash from / (used in) investing activities (item 2.6 above)	-	-

Consolidated statement of cash flows		Current quarter $A'000	Year to date (3 months) $A'000
4.4	Net cash from / (used in) financing activities (item 3.10 above)	(34)	(34)
4.5	Effect of movement in exchange rates on cash held	(44)	(44)
4.6	**Cash and cash equivalents at end of period**	**13,147**	**13,147**

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	13,147	17,867
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)**	**13,147**	**17,867**

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	65
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)	(4,642)
8.2	Cash and cash equivalents at quarter end (item 4.6)	13,147
8.3	Unused finance facilities available at quarter end (item 7.5)	-
8.4	Total available funding (item 8.2 + item 8.3)	13,147
8.5	**Estimated quarters of funding available (item 8.4 divided by item 8.1)**	2.83

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 October 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.