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March 2025 Quarterly Activities Report & Appendix 4C

Key Highlights

- **Ethics Approval:** Secured centralised HREC approval in Australia, enabling multi-site phase 3 trial launch. First patient dosing remains on track for Q2 CY2025.
- **CRO Appointment:** Advanced Clinical selected as CRO following rigorous selection process, supporting global execution of phase 3.
- **R&D Refund:** $6.3 million received under the FY24 R&D Tax Incentive scheme.
- **Cash Position:** Cash balance of $24.56m as of 31 March, with expected inflows and forecast outflows in line with commencement of trial execution.
- **Loyalty Program:** Launch of Loyalty and Piggyback Option Offers to reward shareholders and potentially raise over $110 million in follow-on capital.

Paradigm Biopharmaceuticals Ltd. (ASX: PAR) ("Paradigm" or "the Company") is pleased to provide its quarterly update for the three months ended 31 March 2025 and continuing activities to accompany its Appendix 4C cash flow report for the period.

Operational Update

Paradigm has advanced critical regulatory and operational activities in preparation for its global pivotal phase 3 trial evaluating injectable Pentosan Polysulfate Sodium (iPPS) in knee osteoarthritis (OA).

In October, the updated phase 3 protocol (PARA_OA_012) was submitted to the US FDA and reviewed without further queries, clearing the way for trial initiation. The study (NCT06917404) is now live on the ClinicalTrials.gov registry.

Trial Design Overview

The trial is a global, randomised, double-blind, placebo-controlled study of 466 patients (1:1 randomisation). Participants will receive 12 subcutaneous doses of iPPS over six weeks, administered twice weekly from Day 1 to Day 39.

- **Primary Endpoint:** Change from baseline in average daily pain score at Day 112, measured via patient diaries to reduce recall bias and variability.
- **Key Secondary Endpoints:**
  - WOMAC pain and function scores through Day 404
  - Patient Global Impression of Change (PGIC)
  - OARSI responder rate
  - Paracetamol (rescue medication) usage

The trial also incorporates MRI and X-ray imaging over a 12-month follow-up as secondary endpoints to assess potential structural (disease-modifying) effects of iPPS.

Eligibility Criteria: Adults with Kellgren-Lawrence Grade 2–4 (moderate to severe) knee OA and ≥ 6 months of chronic knee pain.

The study design incorporates insights from Paradigm's phase 2 program and investigator-led studies by Ghosh and Kumagai and reflects feedback from the FDA to align with regulatory expectations for a registration-directed trial.

Operational Progress

Paradigm is actively mitigating placebo response through standardised diary-based pain assessments and rigorous staff training.

- **Australia:** ~10 clinical sites (Melbourne, Sydney, Adelaide, Perth, Brisbane, Gold Coast) are undergoing activation, with enrolment and dosing set to begin in May 2025 (Q2 CY2025). Centralised ethics approval was secured in February 2025 to accelerate site onboarding.
- **United States Sites:** Site start-up activities are expected to begin in Q3 CY2025, ultimately targeting 60 centres across the US and Australia.

Interim Analysis

An interim analysis, led by an independent Data Safety Monitoring Board (DSMB), will occur after 50% of participants reach the Day 112 endpoint. This analysis, planned for mid-2026, includes predefined efficacy thresholds that may support early termination of the study.

Trial Management

Advanced Clinical was appointed as the global CRO during the quarter, selected for its expertise in osteoarthritis trials and patient-centric trial execution.

Paradigm is targeting 50% patient recruitment by end-CY2025, keeping the program on track for interim analysis by mid-CY2026.

Conference and Investor Engagement

During the quarter, Paradigm participated in the Bell Potter Horizon Biotech Summit held in Sorrento, Victoria. The event provided senior management with an opportunity to contribute to panel discussions alongside other leading Australian biotech companies and to engage in one-on-one meetings with institutional investors.

Paradigm also attended the Ignite Investor Summit in Hong Kong from 22–24 March 2025. Managing Director Paul Rennie delivered a company presentation highlighting clinical and corporate progress and met with both existing and prospective investors.

Additionally, Dr Donna Skerrett presented at the NWR Healthcare Conference, delivering an overview of the PARA_OA_012 Phase 3 clinical trial and sharing results from multiple prior Phase 2 studies. These studies continue to support confidence in iPPS as a potential treatment for osteoarthritis. The full presentation, including Q&A, is available on the Paradigm website.

Financial Highlights

Cash and cash equivalents as at 31 March 2025 were $24.56m. Paradigm's cash spending for the March 2025 quarter was $6.49m, which was $5.51m below the forecast $12 million. As at 31 March, the company had approximately $600k in Invoices to be paid in relation to phase 3 startup activities.

In January, Paradigm received a $6.3 million refund under the FY24 R&D Tax Incentive program, enhancing its runway.

To reward long-term holders, during the March 2025 quarter, Paradigm launched a Loyalty Option Offer (1 option for every 4 shares held) with an exercise price of $0.65 and 12-month expiry (February 2026). For every 2 Loyalty Options exercised, shareholders receive 1 Piggyback Option exercisable at $1.00, expiring February 2028. If fully subscribed and exercised, the program could raise up to $111.9 million.

Paul Rennie, MD of Paradigm Biopharma, commented on the quarter:

"This quarter for Paradigm we have successfully transitioned from regulatory clearance into trial execution. Despite a challenging macroeconomic backdrop for biotech, with funding uncertainty in global research institutions, shifting sentiment in Washington, and structural changes within the FDA, we are pleased with our ability to maintain momentum. We now enter the June quarter with clear line of sight to multiple operational milestones, including site activation, first patient enrolment, and dosing in Australia.

As we move forward, we are energised by the robust data we've consistently demonstrated across previous Phase 2 trials and the real-world evidence base built through hundreds of patient experiences with iPPS. Our team remains focused on disciplined execution and maintaining the trust of our shareholders, whose continued belief in the therapeutic potential of iPPS is both acknowledged and deeply appreciated."

Summary of Cash Flow and Quarterly Activity

As of 31 March 2025, Paradigm's cash and cash equivalents totalled $24.56m (on 31 December 2024 it was $24.78m). The net cash outflow for the March 2025 quarter was $121k.The company continues to prioritise resource allocation towards the advancement of its pivotal phase 3 clinical trial for osteoarthritis.

- During the March quarter, Paradigm allocated $5.37m towards research and development activities. Key areas of expenditure included the submission of ethics applications in Australia, site preparation activities, and procurement of clinical trial materials to support the execution of the phase 3 trial locally. These investments reflect Paradigm's continued focus on progressing the Australian arm of the study in alignment with the broader global trial timeline.
- Paradigm continues to explore strategic funding opportunities, including partnerships or licensing agreements, to materially extend the company's cash runway in support of its phase 3 program. The company has a defined timeline for patient recruitment and site activation, including commencement of US operations, and is well advanced in discussions to secure the necessary capital to support these activities and accelerate commercialisation efforts.

- During the March quarter, Paradigm received a $6.3 million rebate under the R&D Tax Incentive scheme. These funds will be directed toward ongoing phase 3 clinical trial operations in Australia, which are expected to continue qualifying for future R&D rebates.
- Paradigm expects a cash outflow of approximately $10–12 million for the June 2025 quarter, primarily driven by clinical site activations, patient recruitment for the Phase 3 trial, and ongoing operational expenses to support trial activities.
- 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 totalled $47K, covering $40K in non-executive Director fees and $7K for legal fees to BioMeltzer, an entity controlled by Amos Meltzer.

OUTLOOK

Phase 3 Trial Launch

Paradigm enters the March 2025 quarter with a strong operational focus on initiating its Australian Phase 3 activities. The Company anticipates activating the first clinical trial sites, enrolling the first subject, and commencing dosing—all within the quarter. This progression marks the formal transition from pre-trial preparation to active patient engagement in Australia. These milestones are critical as they represent the beginning of clinical execution for PARA_OA_012 and form the foundation for broader global activation throughout 2025.

Manuscript Submissions

Editor feedback for two manuscripts based on Paradigm's Phase 2 osteoarthritis (OA) clinical data has been received from their respective journals. Paradigm is working closely with the authors to address the requested revisions, and both manuscripts have now been resubmitted for further editorial consideration.

The manuscripts are as follows:

- **PARA_OA_008 Phase 2 Clinical Trial Results Manuscript** – detailing the outcomes of the Phase 2 study, with updates made to support progression through the peer review process.
- **iPPS Comparison Manuscript** – presenting a comparative analysis of PARA_OA_008 data against existing and emerging OA treatments.

Both manuscripts remain under editorial review. Paradigm expects to update the market once timelines for acceptance and publication become available.

Upcoming Milestones

- **Peer Review Publications:** Two publications from the PARA_OA_008 Phase 2 study are currently under review. One focuses on efficacy outcomes, while the other provides a comparative analysis of the osteoarthritis treatment landscape.
- **First Patient Enrolment (Australia):** First participant enrolment in the PARA_OA_012 Phase 3 trial is expected in Q2 CY2025.

- **First Patient Enrolment (US):** Enrolment of the first US participant is forecast for the second half of CY2025.
- **50% Recruitment Milestone:** Paradigm expects to achieve 50% participant recruitment by end- CY2025, at which point interim analysis preparations will commence.
- **Interim Analysis:** Interim data readout anticipated in mid-CY2026.
- **Full Recruitment Completion:** Full participant recruitment for the PARA_OA_012 study is targeted for H1 CY2026.

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.

FOR FURTHER INFORMATION PLEASE CONTACT:

Simon White
Director of Investor Relations
Tel: +61 404 216 467
Paradigm Biopharmaceuticals Ltd.
ABN: 94 169 346 963
Level 15, 500 Collins St, Melbourne, VIC, 3000, AUSTRALIA
Email: investorrelations@paradigmbiopharma.com

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	31 March 2025

Consolidated statement of cash flows		**Current quarter $A'000**	**Year to date (9 months) $A'000**
1.	**Cash flows from operating activities**		
1.1	Receipts from customers	-	41
1.2	Payments for		
	(a) research and development	(5,468)	(11,676)
	(b) product manufacturing and operating costs	-	-
	(c) advertising and marketing	-	(51)
	(d) leased assets	(18)	(66)
	(e) staff costs	(458)	(1510)
	(f) administration and corporate costs	(584)	(1,569)
1.3	Dividends received (see note 3)	-	-
1.4	Interest received	109	197
1.5	Interest and other costs of finance paid	(2)	(6)
1.6	Income taxes paid	-	-
1.7	Government grants and tax incentives	6,300	6,300
1.8	Other (provide details if material)	-	-
1.9	**Net cash from / (used in) operating activities**	**(121)**	**(8,341)**

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 (9 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)	-	16,000
3.2	Proceeds from issue of convertible debt securities	-	-
3.3	Proceeds from exercise of options	-	1
3.4	Transaction costs related to issues of equity securities or convertible debt securities	(57)	(882)
3.5	Proceeds from borrowings	-	-
3.6	Repayment of borrowings (lease liabilities)	(13)	(71)
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**	**(70)**	**15,048**

4.	**Net increase / (decrease) in cash and cash equivalents for the period**		
4.1	Cash and cash equivalents at beginning of period	**24,778**	**17,867**
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(121)	(8,341)
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 (9 months) $A'000
4.4	Net cash from / (used in) financing activities (item 3.10 above)	(70)	15,048
4.5	Effect of movement in exchange rates on cash held	(27)	(14)
4.6	**Cash and cash equivalents at end of period**	**24,560**	**24,560**

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	24,560	24,778
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)**	**24,560**	**24,778**

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)	(122)
8.2	Cash and cash equivalents at quarter end (item 4.6)	24,560
8.3	Unused finance facilities available at quarter end (item 7.5)	-
8.4	Total available funding (item 8.2 + item 8.3)	24,560
8.5	**Estimated quarters of funding available (item 8.4 divided by item 8.1)**	201

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: ..29 April 2025.....

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.