ASX RELEASE 30 January 2025

December 2024 Quarterly Activities Report & Appendix 4C

Key Highlights

- **Phase 3 Clearance:** Paradigm's revised protocol for the phase 3 PARA_OA_012 trial successfully completed the FDA's 30-day review period without any questions or comments. As a result, Paradigm is entitled to proceed with the phase 3 trial as planned.
- **Centralised Ethics Submission:** Paradigm submitted its Australian ethics application through the centralised HREC pathway in Q4, with approval expected in Q1, ensuring a streamlined process and timely study initiation.
- **Successful $16m Placement:** Paradigm raised $16 million through a placement to institutional and sophisticated investors, through the issue of 40 million shares at $0.40 each.
- **Quarter Spend**: Operating expenses for the December 2024 quarter were $3.58m, significantly under the guided $7m.
- **R&D Incentive Rebate:** $6.3m received from the Australian Government for the FY24 R&D Tax incentive rebate.

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

Phase 3 Clinical Program

FDA Protocol Submission and Review

On October 29, 2024, Paradigm submitted the revised protocol for the phase 3 PARA_OA_012 clinical trial to the U.S. Food and Drug Administration (FDA). The submission included a comprehensive package reflecting detailed feedback from prior engagements with the FDA.

The FDA's 30-day review period officially commenced on October 29 and concluded successfully on November 27, 2024, without additional questions or concerns. This clearance marks a significant regulatory milestone, enabling Paradigm to proceed with the phase 3 clinical trial.

Centralised Ethics Submission in Australia

As part of its preparatory activities, Paradigm also submitted the centralised ethics application for the PARA_OA_012 trial in Australia during the quarter. Centralised ethics approval is a critical step in streamlining the initiation of clinical sites across the country. By leveraging this centralised process, Paradigm aims to significantly accelerate the activation of trial sites and the recruitment of participants in Australia. Approval is expected in the coming weeks, enabling the company to commence site and recruitment activities in Q1 CY2025.

Financial Highlights

Paradigm successfully completed a $16 million capital raise in December through a placement to institutional and sophisticated investors. The placement involved issuing 40 million shares at $0.40 per share, representing a 2.9% premium to the 30-day volume-weighted average price (VWAP). Following the placement the Company anticipates sufficient funding to commence phase 3 activities in Australia, and runway into the second half of CY2025.

The raised funds will be allocated strategically to support the company's key initiatives. This includes $5.5 million for the setup of global phase 3 clinical trial, $6.1 million for site recruitment, $1.5 million for manufacturing and inventory preparation, $1.2 million for regulatory-enabling studies, and $1.7 million for working capital and associated costs of the capital raise.

Additionally, Paradigm has recently advised that it has received a $6,300,438 Research and Development (R&D) Tax Incentive refund for the 2024 financial year. This refund significantly bolsters the company's financial position, bringing its current cash balance to approximately $31 million. These funds ensure the company remains capitalised to commence its pivotal phase 3 trials and other strategic initiatives.

TGA Provisional Approval Determination

During the December quarter, Paradigm was informed by the Therapeutic Goods Administration (TGA) of its determination regarding the clinical development of PPS for knee osteoarthritis. The TGA acknowledged that preliminary clinical results for PPS demonstrated clinically meaningful benefits for patients suffering from moderate to severe OA of the knee. The TGA noted that such benefits are not considered significant for patients with minor or mild OA, as these conditions are not deemed seriously debilitating.

Following a review of the available clinical data, the TGA concluded that PPS is suitable to enter the therapeutic landscape through the traditional registration pathway (CTX), rather than a provisional determination application. This decision reflects the TGA's recognition of the comprehensive data provided by Paradigm, supporting the safety and efficacy of PPS. Furthermore, the TGA confirmed that the proposed phase 3 OA program, if successfully executed, will generate the necessary evidence to support full registration of PPS in Australia.

Paul Rennie, MD of Paradigm Biopharma, commented on the quarter: *" This quarter has been a transformative period for Paradigm as we advance our pivotal phase 3 clinical program for knee osteoarthritis. The successful submission and approval of the trial protocol by the FDA, along with the centralised ethics submission in Australia, highlights the progress we are making toward delivering a meaningful treatment option for patients living with this debilitating condition.*

With the phase 3 trial on track to commence recruitment initiatives in Q1 CY2025, we are now fully focused on executing site activations and patient enrolment firstly in Australia. This milestone, combined with our improved financial position, provides the foundation to achieve our clinical and commercial objectives. I am incredibly proud of the dedication and persistence of our team, and I am optimistic about the opportunities ahead."

Summary of Cash Flow and Quarterly Activity

As of 31 December 2024, Paradigm's cash and cash equivalents totalled $24.78m (on 30 September 2024 it was $13.14m). This increase reflects the successful $16 million (before costs) capital raise during the quarter. The company continues to prioritise resource allocation towards the advancement of its pivotal phase 3 clinical trial for osteoarthritis.

- During the December quarter, Paradigm allocated $3.58 million towards operating activities. Key areas of expenditure included preparatory activities for phase 3 clinical trial initiation, regulatory costs associated with submissions to the FDA, TGA, and centralised ethics, and expenses related to the capital raise. This expenditure demonstrates Paradigm's focus on ensuring the timely initiation of its phase 3 trial.
- Paradigm received a $6.3 million refund under the R&D Tax Incentive program after the end of the quarter. This refund provides additional financial support for ongoing research and development activities, further strengthening the company's ability to execute its strategic objectives.
- The company continues to explore funding opportunities, including potential partnerships or licensing agreements, to extend its financial runway and accelerate commercialisation efforts.
- Paradigm forecasts a cash outflow of approximately $12 million for the March 2025 quarter. This projection includes clinical site activations, patient recruitment for the phase 3 trial, and continued regulatory and operational expenses to support trial progress. The company remains committed to maintaining strategic fiscal management while prioritising critical 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 $42K, covering $41K in non-executive Director fees and $1K for legal fees to BioMeltzer an entity controlled by Amos Meltzer.

Paradigm's financial position, supported by strategic expenditure, the successful capital raise, and ongoing funding initiatives, ensures the company is well-positioned to advance the phase 3 clinical trial and deliver on its long-term goals.

OUTLOOK

Preparations for Phase 3 Trial Launch

With regulatory and ethics submissions progressing smoothly, Paradigm is on track to initiate patient enrolment in Q1 CY2025. Initial trial activities are expected to begin with up to 10 clinical sites in Australia. Preparatory activities are well underway, and the company is actively engaging with stakeholders, including key potential partners, to support the trial and future commercialisation.

The phase 3 clinical trial will enrol approximately 466 participants in a 1:1 randomisation design, using the 2mg/kg twice weekly iPPS dosing regimen. The primary endpoint of the study will focus on changes in pain from baseline, with key secondary endpoints including functional assessments, patient-reported outcomes, and structural changes as measured by MRI and X-ray. An interim analysis will be conducted when 50% of participants complete 112 days of follow-up.

Loyalty Option

Paradigm has previously announced its intention to introduce a loyalty option program for shareholders. In line with this commitment, the Company currently plans to issue one (1) listed option for every four (4) shares held as of the Record Date ("Loyalty Options"). These Loyalty Options will have an exercise price of $0.65 and will expire 12 months from the Record Date.

The Record Date for the Loyalty Options is expected to be four business days after the lodgement of a prospectus ("Record Date"). Additionally, for every two (2) Loyalty Options exercised, holders will receive one (1) piggyback option, which will have an exercise price of $1.00 and an expiry date 24 months after the Loyalty Options expire.

A prospectus detailing the offer is expected to be available shortly.

Manuscript Submissions

Editor comments for the two manuscripts submitted to separate journals have been received. Paradigm is now working with the authors of the manuscripts to incorporate the necessary changes for further review by the respective journals.

The manuscripts, based on the phase 2 osteoarthritis (OA) clinical data, are as follows:

- **PARA_OA_008 Phase 2 Clinical Trial Results Manuscript**: This manuscript details the outcomes of the phase 2 clinical trial. Necessary edits and updates are being addressed to facilitate the peer review process.
- **iPPS Comparison Manuscript**: This manuscript provides a comparative analysis of the PARA_OA_008 phase 2 trial results against current therapies and emerging treatments for osteoarthritis.

These publications are expected to further enhance Paradigm's credibility and the scientific visibility of iPPS's clinical data, reinforcing its potential as a novel treatment for osteoarthritis.

Upcoming Milestones

- **CRO Selection** (Q1 2025): Paradigm is finalising the agreement with its selected Contract Research Organisation (CRO) to manage the global phase 3 trial. Paradigm undertook an extensive due diligence and selection process to ensure that the phase 3 clinical trial will be conducted to the highest standards.
- **Australian Centralised Ethics Approval** (Q1 CY2025)**:** Paradigm anticipates receiving centralised ethics approval for its phase 3 clinical trial in Australia. This approval streamlines the activation of clinical sites across the country, enabling faster initiation of site activities and participant recruitment**.**
- **Commencement of Phase 3 Patient Enrolment Activities** (Q1 2025): Paradigm is targeting the start of patient enrolment activities for the phase 3 clinical trial in Q1 2025 with the first patient dosed expected in Q2 CY2025. 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	31 December 2024

Consolidated statement of cash flows		**Current quarter $A'000**	**Year to date (6 months) $A'000**
1.	**Cash flows from operating activities**		
1.1	Receipts from customers	-	41
1.2	Payments for		
	(a) research and development	(2,415)	(6,209)
	(b) product manufacturing and operating costs	-	-
	(c) advertising and marketing	(46)	(51)
	(d) leased assets	(33)	(48)
	(e) staff costs	(484)	(1,052)
	(f) administration and corporate costs	(634)	(985)
1.3	Dividends received (see note 3)	-	-
1.4	Interest received	36	88
1.5	Interest and other costs of finance paid	(2)	(4)
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**	**(3,578)**	**(8,220)**

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 (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)	-	-
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	16,000
3.2	Proceeds from issue of convertible debt securities	-	-
3.3	Proceeds from exercise of options	1	1
3.4	Transaction costs related to issues of equity securities or convertible debt securities	(825)	(825)
3.5	Proceeds from borrowings	-	-
3.6	Repayment of borrowings (lease liabilities)	(24)	(58)
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**	**15,152**	**15,118**

4.	**Net increase / (decrease) in cash and cash equivalents for the period**		
4.1	Cash and cash equivalents at beginning of period	**13,147**	**17,867**
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(3,578)	(8,220)
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 (6 months) $A'000
4.4	Net cash from / (used in) financing activities (item 3.10 above)	15,152	15,118
4.5	Effect of movement in exchange rates on cash held	57	13
4.6	**Cash and cash equivalents at end of period**	**24,778**	**24,778**

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	24,778	13,147
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)**	**24,778**	**13,147**

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	42
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)	(3,578)
8.2	Cash and cash equivalents at quarter end (item 4.6)	24,778
8.3	Unused finance facilities available at quarter end (item 7.5)	-
8.4	Total available funding (item 8.2 + item 8.3)	24,778
8.5	**Estimated quarters of funding available (item 8.4 divided by item 8.1)**	6.92

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: ..30 January 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.