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March 2024 Quarterly Activities Report & Appendix 4C

Key Highlights

- **Type D Meeting with US FDA**: Paradigm met with US FDA on the 10th of January 2024 to discuss outstanding requirements for the next stage of the Phase 3 clinical program in Osteoarthritis. Paradigm has completed the response documents to this meeting and filed with the US FDA for review and comment.
- **Board Addition**: Paradigm welcomed Mr Matthew Fry as a Non-Executive Director.
- **OARSI World Congress on OA**: An abstract detailing data from the successful phase 2 PARA_OA_008 clinical trial was selected by the OARSI panel for a podium presentation during the 2024 conference.
- **Primary Endpoint Met**: The phase 2 MPS VI study met the primary endpoint of safety and tolerance and achieved promising clinical improvements in pain and functional assessments following iPPS administration compared to placebo.
- **R&D Tax Incentive**: $7.3m refund from the R&D Tax Incentive refund claim for FY23.

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

- Cash balance as of 31 March 2024 was $26.2m (on 31 December 2023 it was $33.5m).
- Research and development expenditure for the quarter of $13.1m was significantly reduced compared to the previous quarter of $27.06m. This spend in Q3 FY24 was related to continued study close-out costs, Clinical Research Organisation costs as well as FDA meeting fees and consultant costs for the Type D meeting and subsequent response to the US FDA. Paradigm also incurred spend relating to clinical trial product manufacturing in preparation of the next stage of the phase 3 OA program.
- The March quarter saw an increase in spend on patent and IP related cost due to annual renewals and fees for Paradigm's extensive patent portfolio.
- During the period Paradigm received a $7.3m refund from the R&D Tax Incentive refund claim for FY23.
- Net cash outflow for the quarter was $6.8m (inclusive of the $7.3m refund) which is less than the guided $8-11m. Anticipated invoices of $1-1.5m for the March quarter have been received post 31st March and will be paid during the June quarter. Revised guidance for the June quarter is expected to be $7-10m cash outflow.
- Encouragingly, corporate and administration costs continued to reduce in the quarter through Paradigm's cost containment initiatives that were implemented in Q3 CY23. Paradigms spend remains focused on clinical and nonclinical activities that build value in the osteoarthritis clinical program.

- 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 March 2023 were fees of $37K for payment of Director fees.
- 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 US FDA on the 10th of January 2024 to discuss outstanding requirements for the next stage of 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 containing updated nonclinical and clinical data to the Agency as well as the proposed clinical trial protocol utilising 2mg/kg twice weekly for the next stage of the phase 3 OA program. The response package to the US FDA was submitted as directed by the Agency, through a request for review pathway.

The request for review pathway does not have strict Prescription Drug User Fee Act (**PDUFA**) Agency response timelines. Paradigm OA clinical program has FDA granted Fast-track designation and the feedback through this review pathway is typically received within three months.

Paradigm Board Changes

During the December quarter Paradigm welcomed Mr Matthew Fry to the Paradigm Board as a Non-Executive Director. Matthew joins the Paradigm board with more than 25 years in business creation, strategy, and expansion in healthcare and medical diagnostics globally. He is currently the CEO, Managing Director and Founder of AM Diagnostics Pty Ltd, a manufacturer and distributor of world class medical diagnostic products.

Matthew has significant experience with global regulatory agencies, in particular the Australian TGA and US FDA. Through his role as Founder and CEO of AM Diagnostics, Matthew drove the company's expansion into the United States in 2009 and is a leading biotechnology device supplier with a deep understanding of sales channels in both the US medical wholesale market and retail market, and how to negotiate with private health providers.

Paradigm Non-Executive Director, Helen Fisher, notified the Paradigm Board during the quarter that she would step down from her position to focus on other endeavours.

Mucopolysaccharidosis (MPS) VI

During the quarter, Paradigm reported the top-line data from the PARA_MPSVI_001 phase 2 trial. The multi-centre randomised trial conducted in Brazil successfully met the primary endpoint and achieved positive results in several of the secondary outcome.

The primary endpoint of the study was 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 demonstrates that iPPS is a safe adjunctive therapy to enzyme replacement therapy for the continual joint pain, stiffness and functional disability associated with MPS VI.

Multiple clinical endpoints were explored during the phase 2 clinical trial demonstrating positive responses following iPPS compared to placebo. These included:

- **Pain Assessment**: An improvement in PROMIS (Patient-Reported Outcomes Measurement Information System) pain interference is indicated by a lower score. An improvement in PROMIS pain interference was greater in the iPPS-treated group compared to placebo at 25 weeks.
- **Functional Assessment**: Participants receiving iPPS in the phase 2 clinical trial demonstrated greater improvement than placebo in the 9-hole peg test from baseline to week 25 on at least one hand.

Dr Roberto Giugliani, MD, PhD, MSc, the Principal Investigator for the phase 2 clinical trial presented the clinical data at the 17th International Symposium on MPS and Related Diseases in Würzburg Germany on 4-7th April. The presentation titled "*Update on clinical trials with PPS*" was delivered by Dr Giugliani during the "New study approaches" session of the conference.

Paradigm has now completed clinical studies for MPS I and VI with strong data sets and meaningful endpoints identified to progress the clinical development of iPPS as an adjunctive therapy with a commercial partner.

Global Conferences

Managing Director Paul Rennie and Dr Mukesh Ahuja, Paradigm's Global Head of Osteoarthritis attended the Annual Osteoarthritis Research Society International World Congress in Vienna and presented data from the phase 2, randomised, double-blinded PARA_OA_008 clinical trial exploring the disease modifying potential of iPPS in subjects with knee OA.

Paradigm submitted a late breaking abstract to the OARSI panel following the release of the phase 2 data late last year which was reviewed and selected for a podium presentation during the conference. The podium presentation material delivered by Dr Ahuja to over 300 attendees during the conference is available on the Paradigm website (OARSI Podium Presentation).

Paradigm management also conducted a sponsored theatre presentation during the conference detailing Paradigm's clinical development with iPPS for osteoarthritis and a comparison between iPPS and currently available therapies for OA. The theatre presentation can be view here, OARSI Theatre Presentation.

Company Outlook

Phase 3 OA Clinical Program

Subject to FDA clearance, Paradigm intends to promptly move forward with subject enrolment into the phase 3 clinical trial (PARA_OA_012) in 2H CY2024. Clinical trial sites in Australia and the US are planned to commence preparation activities during this quarter (Q2 CY2024) to move the phase 3 program forward as quickly and efficiently as possible.

Once agreement is reached with the US FDA, Paradigm anticipates providing an overview of the next stage of the phase 3 OA program including an overview of the clinical trial design, dose justification and proposed participant numbers for the trial.

TGA Provisional Approval Application

Paradigm is finalising the TGA provisional approval determination application for submission following the response to the US FDA Type D meeting. The determination application will include 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. Should the determination application decision be positive, Paradigm will prepare a full dossier submission for TGA provisional approval marketing authorisation.

Provisional approval offers significant benefits to both patients and manufacturers. Patients gain access to potential life-saving treatments for life-threatening and seriously debilitating conditions sooner, particularly for those lacking satisfactory alternatives. For manufacturers, it provides an opportunity to bring innovative therapies to market faster, while gathering additional clinical data to support full approval. TGA provisional marketing approval for iPPS in Australia would expedite the pathway to revenues. Paradigm expects to receive a decision from the TGA on whether the determination application has met the criteria to move to a full dossier submission during Q2 CY2024.

Other Activities

The PARA_OA_008 phase 2 clinical trial results manuscript has been completed and is expected to be submitted for peer review and publication. Paradigm has also completed a comparison manuscript detailing the clinical trial results from the PARA_OA_008 phase 2 trial compared to currently available and pipeline OA therapies. Both manuscripts are expected to be published during CY2024.

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

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 2024

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	-	30
1.2	Payments for		
	(a) research and development	(13,141)	(62,145)
	(b) product manufacturing and operating costs	-	-
	(c) advertising and marketing	(147)	(284)
	(d) leased assets	(24)	(61)
	(e) staff costs	(480)	(1,684)
	(f) administration and corporate costs	(507)	(1,807)
1.3	Dividends received (see note 3)	-	-
1.4	Interest received	133	768
1.5	Interest and other costs of finance paid	(3)	(9)
1.6	Income taxes paid	-	-
1.7	Government grants and tax incentives	7,327	7,327
1.8	Other (provide details if material)	-	-
1.9	**Net cash from / (used in) operating activities**	**(6,842)**	**(57,865)**

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)	-	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	- -	(1,763) -
3.5	Proceeds from borrowings	-	-
3.6	Repayment of borrowings (lease liabilities)	(27)	(78)
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**	**(27)**	**28,276**

4.	**Net increase / (decrease) in cash and cash equivalents for the period**		
4.1	Cash and cash equivalents at beginning of period	**33,551**	**56,379**
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(6,842)	(57,865)

Consolidated statement of cash flows		Current quarter $A'000	Year to date (9 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)	(27)	28,276
4.5	Effect of movement in exchange rates on cash held	(461)	(569)
4.6	**Cash and cash equivalents at end of period**	**26,221**	**26,221**

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	26,221	33,551
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)**	**26,221**	**33,551**

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	37
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)	(6,842)
8.2	Cash and cash equivalents at quarter end (item 4.6)	26,221
8.3	Unused finance facilities available at quarter end (item 7.5)	-
8.4	Total available funding (item 8.2 + item 8.3)	26,221
8.5	**Estimated quarters of funding available (item 8.4 divided by item 8.1)**	3.83

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: ..30 April 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.