PARADIGM BIOPHARMA

ASX RELEASE **31st January 2022**

DECEMBER QUARTERLY ACTIVITIES REPORT

KEY HIGHLIGHTS

- **Investigational New Drug (IND) Application:** Paradigm reported that the US Food and Drug Administration (**FDA**) has cleared the Company's Investigational New Drug (**IND**) application to proceed with Paradigm's phase 3 study, evaluating injectable pentosan polysulfate sodium (**PPS/Zilosul®)** for the treatment of pain associated with knee osteoarthritis (**kOA**). This was a major milestone for Paradigm. Pain associated with kOA is a potential blockbuster opportunity and the clearance through the FDA was the culmination of many months of dialogue with the FDA.

- **CEO Transition:** The Company reported in November, CEO, Paul Rennie, was transitioning from his executive role (Managing Director) to a non-executive role (Chairman). Mr Rennie stated "In the non-executive role, I will be focussed on the strategic direction of the Company and work to enhance the strategic relationships which are so important to our Company. I will continue to manage the strategic relationship with bene pharmaChem and forge new commercial partnerships". Dr Donna Skerrett, CMO, has been appointed interim CEO as the company completes a global search for the new CEO.

- **Positive Top-line Results in ARDS Preclinical Study:** PPS at the post-acute phase of viral infection (21-days post infection) demonstrated a statistically significant reduction in pulmonary collagen compared to vehicle treated groups based on histological staining of collagen. PPS administered subcutaneously at Day 0 at 3mg/kg resulted in a statistically significant reduction in inflammatory cell infiltrates in the lungs at 8 days post infection.

- **PARA_OA_008:** The Australian Human Research Ethics Committee approved an amendment to the Phase 2 study to evaluate the treatment effect of pentosan polysulfate sodium (PPS) (Zilosul®) compared with placebo on synovial fluid biomarkers in participants with kOA pain. The approval was sought to add a once weekly dosing regimen to the trial design with the remaining 30 subjects to be enrolled using a randomisation scheme which will provide a balanced number of patients to each treatment group according to 1:1:1 ratio by the end of the trial. Once weekly dosing is also being assessed in Paradigm's Phase 3, PARA_OA_002 clinical program. An additional follow-up period to 12-months was also accepted by the ethics committee to assist Paradigm in gathering additional data on the medium-long term combined structure-modifying and symptom-modifying effects of PPS on Knee OA. The recently completed market access research with key physicians and funding bodies (payers) in the US and Europe found that longer follow-up is preferred to support safety and efficacy claims for products that manage the symptoms and potentially attenuate disease progression in OA. With the extension of follow-up out to 12-months in PARA_OA_008, the Company aims to acquire data for mechanism of action and the medium-long term combined structure-modifying in addition to symptom modifying effects of PPS on KOA.

- **Global Market Research:** Global market research to better understand willingness-to-pay and willingness-to prescribe Zilosul® for osteoarthritis was conducted throughout CY2021 and reported During the December Quarter. Research indicated projected price of US$2-3K

p.a likely for Zilosul® as a therapy to reduce pain and improve function. The research also reported, with a disease modifying indication, physicians would consider Zilosul® much earlier in the therapeutic algorithm and if approved by the FDA with a disease modifying label, the price per year of therapy in the US could increase to US$6,000 and potentially higher.

- **Mucopolysaccharidosis type I (MPS I) Interim Phase 2 Data:** Preliminary MPS-I phase 2 data presented at the 14th International Congress of Inborn Errors of Metabolism in Sydney. PPS was well tolerated with no serious adverse events reported over a 24-week period. Meaningful improvements in pain, function, and activities of daily living and an overall improvement in quality of life was observed in this initial cohort of patients.

Paradigm Biopharmaceuticals Ltd (ASX: PAR) ("Paradigm" or "the Company") is pleased to provide its quarterly update for the three months ended 31st December 2021 to accompany its Appendix 4C cash flow report for the period.

- Cash balance as of 31st December 2021 was $55.03m (on 30th September 2021: $64.8) with a net cash outflow during the quarter of $10.41m.
- Research & development expenditure for the quarter was $8.59m compared to the previous quarter of $6.18m. The research and development expenditure are attributed to, PARA_OA_002 site initiations and commencement of participant dosing, PARA_OA_008 resumption of randomising subjects following updated clinical trial protocols and establishment of second site for the study, continuation of MPS I and MPS VI phase II studies, including activating a second site in Brazil, as well as continuing activities described in the outlook below.
- 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 September 2021 were $70k. Fees of $66k were Director fee payments to Non-Executive Directors. The additional $4k payment relates to routine legal services for the clinical programs performed by BioMeltzer, of which Amos Meltzer is a director.

OUTLOOK

- Paradigm expects to complete 100% recruitment in the PARA_OA_008 during 1H 2022. The program is recruiting and treating at two sites across Australia with top-line data expected Q3 CY2022.
- Paradigm will present at the WORLD*Symposium* in San Diego, California, the annual research conference focused on new therapies for lysosomal storage diseases such as MPS VI. The presentation will be conducted by leading geneticist and principal investigator Dr Roberto Giugliani on Paradigm's phase 2 trial for mucopolysaccharidosis type-VI (MPS VI). The Company during the conference will release a MPS VI patient focus group study. The study is the largest of its kind in the world and has attracted the interest of medical researchers and MPS patient advocacy groups globally.
- Paradigm recently reported the first participant dosing in Australia in the PARA_OA_002 clinical trial. Eight sites have been initiated in Australia and are currently screening subjects. Initiation of sites in the US continues to ramp up with 65 sites identified in the

US and AUS to participate in the clinical program. The Company expects to report first participant dosing in the US during Q1 CY 2022.

- The Company expects to continue initiation activities for the PARA_OA_002 clinical study sites in the UK and Europe and will update shareholders on key activities as they are achieved.
- The Paradigm Remuneration and Nominations Committee continues its consultation with a global executive search firm and meetings with shortlisted candidates with the identified experience in the global pharma industry. The market will be notified on Identification of the CEO.
- The peer review publication of the company's Phase 2b study (PARA_005) in knee OA is planned to coincide with publication of ongoing PARA_008. Topline data of PARA-005 have been previously announced in company presentations.
- An Expanded Access Program protocol (EAP) in the US for re-treatment of Zilosul® is being designed following discussions with the participants and their physician who have expressed strong interest in a follow-up retreatment program approximately 18 months following their initial treatment.

About Paradigm Biopharmaceuticals

Paradigm Biopharmaceuticals Ltd (ASX: PAR) is a late-stage drug development company with the mission to develop and commercialise pentosan polysulfate sodium for the treatment of pain associated with musculoskeletal disorders driven by injury, inflammation, ageing, degenerative disease, infection, or genetic predisposition. Paradigm is also exploring proof-of-concept studies for the use of PPS in respiratory and heart failure indications.

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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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 2021

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	26	55
1.2	Payments for		
	(a) research and development	(8,588)	(14,769)
	(b) product manufacturing and operating costs	-	-
	(c) advertising and marketing	(511)	(511)
	(d) leased assets	(23)	(43)
	(e) staff costs	(676)	(1,569)
	(f) administration and corporate costs	(659)	(1,225)
1.3	Dividends received (see note 3)	-	-
1.4	Interest received	22	34
1.5	Interest and other costs of finance paid	(6)	(14)
1.6	Income taxes paid	-	-
1.7	Government grants and tax incentives	-	1,314
1.8	Other (provide details if material)		
1.9	**Net cash from / (used in) operating activities**	**(10,415)**	**(16,728)**

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)	-	-
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)	(33)	(66)
3.7	Transaction costs related to loans and borrowings	-	-
3.8	Dividends paid	-	-
3.9	Other (Limited recourse loan repaid under ESP)	46	79
3.10	**Net cash from / (used in) financing activities**	**13**	**13**

4.	**Net increase / (decrease) in cash and cash equivalents for the period**		
4.1	Cash and cash equivalents at beginning of period	64,768	71,081
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(10,415)	(16,728)

Consolidated statement of cash flows		Current quarter $A'000	Year to date (6 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)	13	13
4.5	Effect of movement in exchange rates on cash held	664	664
4.6	**Cash and cash equivalents at end of period**	**55,030**	**55,030**

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	55,030	64,768
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)**	**55,030**	**64,768**

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	70
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)	(10,415)
8.2	Cash and cash equivalents at quarter end (item 4.6)	55,030
8.3	Unused finance facilities available at quarter end (item 7.5)	-
8.4	Total available funding (item 8.2 + item 8.3)	55,030
8.5	**Estimated quarters of funding available (item 8.4 divided by item 8.1)**	5.28

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 January 2022.....

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.