ASX RELEASE **28th July 2022**

JUNE QUARTERLY ACTIVITIES REPORT

KEY HIGHLIGHTS

- **FDA Fast Track Designation:** Paradigm reported in April it had received US FDA Fast Track Designation for its osteoarthritis (**OA**) clinical program. The FDA Fast Track Designation for pentosan polysulphate sodium (**PPS/Zilosul®**) offers an expedited pathway for development of Paradigm's osteoarthritis clinical program. The designation has been granted for Paradigm's broad OA program and not specific to OA of the knee. It allows Paradigm the opportunity to interact and collaborate with the FDA more frequently during program development, enabling a stronger overall program in line with the FDA's expectations and provides opportunity for shorter review timelines.
- **First UK subject dosed in phase 3 trial:** Regulatory and ethics approval was received on 16th March from the Medicines & Healthcare products Regulatory Agency (**MHRA**) in the UK. The confirmation from the MHRA means that all required approvals are in place to commence clinical trial activities in the UK for the global Phase 3 PARA_OA_002 clinical trial.
- **R&D Tax Incentive:** The Company reported during the June quarter it had received the R&D tax incentive refund of $8,212,492 as part of Australia's R&D Tax Incentive Scheme.
- **100% Enrolment in Synovial Fluid Biomarker Trial:** The phase 2 clinical trial evaluating the treatment effects of Zilosul® against placebo on synovial fluid biomarkers in participants with knee OA pain, completed recruitment (n=60) during the June quarter. Paradigm confirmed its expected timing of top-line data to be reported to the market during Q3 of CY2022.
- **CEO Appointment:** Paradigm welcomed experienced US based pharmaceutical executive, Marco Polizzi, as its new CEO. Mr. Polizzi joins Paradigm with over 30 years of experience in the pharmaceutical industry in various commercially focused roles, including the creation of new divisions within branded and generic pharmaceutical businesses. Mr Polizzi commented on his appointment: "*With my pharmaceutical experience, I strongly believe that I will be able to make a significant contribution to the Paradigm business in the short and long term. I have had the opportunity to meet the Paradigm Board and key management personnel and I can say that Paradigm's potential to help millions of people, excites me*".
- **Peer Reviewed Publication:** A peer reviewed article titled "*Pentosan Polysulfate inhibits attachment and infection by SARS-CoV-2 in vitro: Insight into structural requirements for binding*" was published in the online journal Thrombosis and Haemostasis in April 2022. The publication is a result of work on the effectiveness of PPS performed by the Ronzoni Institute as part of the bene pharmaChem and Paradigm research collaboration agreement (ASX release 31/03/21). The *in vitro* study demonstrated that PPS inhibited the uptake of SARS-CoV2 in the established Vero cells that are used as an industry model. Mechanistically, PPS demonstrated binding to the S1 receptor binding domain (**RBD**) on SARS-CoV2 which led to the inhibition of viral uptake and viral propagation by Vero cells. These observations suggest that PPS is a potential novel inhibitor of SARS-CoV2 infection and transmission.

  The peer reviewed publication can be viewed at: https://www.thieme-connect.com/products/ejournals/html/10.1055/a-1807-0168

- **Intellectual Property:** During the quarter, Paradigm received official acceptance of the Australian patent application "Treatment of bone marrow pathologies with polysulfated polysaccharides (Australian application number (2021201198)". The patent acceptance adds strength to Paradigm's portfolio of patents that continues to expand through prosecution of additional patents in multiple jurisdictions.
- **BIO International Partnering Conference:** Dr Donna Skerrett (Chief Medical Officer) and Dr Michael Imperiale (Global Head of Safety) attended the BIO International partnering conference that was held in June in San Diego. During the conference, Dr Skerrett delivered a presentation on Paradigm's clinical development program and with Dr Imperiale undertook many 1 on 1 meetings with potential partner companies.

Paradigm Biopharmaceuticals Ltd (ASX: PAR) ("Paradigm" or "the Company") is pleased to provide its quarterly update for the three months ended 30th June 2022 to accompany its Appendix 4C cash flow report for the period.

- Cash balance as of 30th June 2022 was $39.72m (on 31st March 2022 was $39.89m) with a net cash outflow during the quarter of $0.28m. The June quarter saw a receipt of R&D tax incentive refund of $8.21m.
- Research & development expenditure for the quarter was $7.5m compared to the previous quarter of $14.03m. The difference in spend on Q3 is related to the milestone payment of US$5m to Paradigm's CRO during the March quarter. Spend during Q4 is associated with PARA_OA_008 complete enrolment of participants in the study and PARA_OA_002 continuing trial activities. The quarter also saw spend related to continuation of MPS I and MPS VI phase 2 studies, 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 30th June 2022 were fees of $124k, which included Chairman fees and Director fee payments to Non-Executive Directors.

OUTLOOK

Paradigm is pleased to provide an update on achievements and upcoming events for the 2H 2022.

PARA_OA_002 Phase 3 Clinical Trial

- On 6 July, Paradigm reported it had activated the first UK site in the global phase 3 clinical trial. This first site is located at the University of Leeds under lead investigator Prof. Hemant Pandit, with participant screening and enrollment commencing during Q3. Paradigm aims to activate a total of seven sites across the UK for the phase 3 study.

- Regulatory approval from Health Canada for the phase 3 study was also reported in July. Paradigm can also confirm it has since achieved ethics approval from the research ethics board in Canada. The Company may now commence clinical trial site activation in Canada where it plans to activate up to 10 sites. First participant enrolled into the PARA_OA_002 study will be reported once achieved.

- The first formal review by the Data Safety Management Board (**DSMB**) for stage 1 of the PARA_OA_002 phase 3 trial is expected to occur in Q4 CY2022. Paradigm expects to provide an update on the progress for the phase 3 clinical program following this review.

Synovial Fluid Biomarker Study (PARA_OA_008)

- Paradigm expects to report top-line data in Q3 CY2022 from the phase 2 study exploring change in synovial fluid biomarkers associated with joint destruction in knee OA patients. Data reported will include the change in baseline of synovial fluid biomarkers following treatment once and twice weekly with Zilosul® versus placebo. Clinical endpoints of improvements in WOMAC® pain and function following Zilosul® treatment versus placebo at day 56 will also be reported. The data collected from this phase 2 study will be the first OA clinical trial data reported by Paradigm since the release of the Phase 2B (PARA_OA_005) clinical trial data in 2018. The collective analyses of pain, function, joint structure, and biomarker levels following PPS therapy will provide informative data to assess the potential of PPS as a disease-modifying osteoarthritis drug (**DMOAD**).

Mucopolysaccharidosis (MPS I and VI)

- The Open-Label MPS I trial includes 1 active subject and 3 completed subjects. PPS is well tolerated in this population with no Serious Adverse Events reported to date. Additionally, to date, there appears to be an overall trend toward meaningful improvements in pain, function, ADLs, and overall improvement in quality of life. Further data will be reported on this study following the final patient completing PPS treatment.
- The Double-Blinded, Multi-Centre, MPS VI trial is actively recruiting. To date, a total of 50% of subjects have been enrolled. Fifty-two weeks of cumulative data across the 3 adult subjects (all data through Week 4 of subject 3) have been assessed as required by the protocol. No significant safety signals were noted. Enrollment has now begun in subjects between 9 and 16 years of age to assess the safety and tolerability of PPS among pediatric populations.

Canine OA Model Evaluating Disease Modification by PPS

- To generate further data establishing the *in vivo* mechanism of action of PPS in disease modification and provide complementary data in parallel with the PARA_OA_008 human clinical trial, Paradigm is concurrently conducting a trial in dogs with naturally occurring OA at the U-Vet Werribee Animal Hospital. The longer 20-week follow-up period (equates to approximately 3 years in a human lifespan) from the cessation of treatment in the study is designed to assess the durability of response and structural changes following therapy. Paradigm intends to have data from the canine OA model available for release to the market along with the interim analysis data from PARA_OA_008 in Q3 CY2022.

NFL Alumni Health Research Partnership

- Paradigm reported on July 13 that it entered into a research partnership with the NFL Alumni Health to inform its members about OA and potential clinical trial participation. Paradigm is working closely with the NFL Alumni Health team and Alumni members to

inform them of the onset and progression of OA and Paradigm's clinical progress through phase 3 as we strive to bring Zilosul® to commercialisation for the millions suffering from the debilitating effects of OA. Updates on the progress of the research partnership are expected throughout the remainder of CY2022.

R&D Tax Incentive

- Paradigm is finalising its application for the FY22 R&D tax incentive for lodgment. The Company expects to receive the R&D tax incentive refund in the coming months.

Investor Webinar

- On the 21st of July, Paradigm conducted an investor webinar with its new CEO, Marco Polizzi, and Dr Donna Skerrett, CMO, who provided a clinical program update for all shareholders. Mr Polizzi, Dr Skerrett and Chairman, Paul Rennie, also answered several investor questions at the conclusion of the presentation. We would like to thank all investors for participating and submitting questions during the webinar.
  The investor webinar is available to view via the link:
  https://us02web.zoom.us/webinar/register/WN_W_Zh6750RaiC2Oda0t32SQ

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	30 June 2022

Consolidated statement of cash flows		**Current quarter $A'000**	**Year to date (12 months) $A'000**
1.	**Cash flows from operating activities**		
1.1	Receipts from customers	13	81
1.2	Payments for		
	(a) research and development	(7,563)	(36,367)
	(b) product manufacturing and operating costs	-	-
	(c) advertising and marketing	(121)	(845)
	(d) leased assets	(39)	(86)
	(e) staff costs	(441)	(2,459)
	(f) administration and corporate costs	(337)	(2,074)
1.3	Dividends received (see note 3)	-	-
1.4	Interest received	2	48
1.5	Interest and other costs of finance paid	(7)	(29)
1.6	Income taxes paid	-	-
1.7	Government grants and tax incentives	8,212	9,526
1.8	Other (provide details if material)		
1.9	**Net cash from / (used in) operating activities**	**(281)**	**(32,205)**

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 (12 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)	(35)	(135)
3.7	Transaction costs related to loans and borrowings	-	-
3.8	Dividends paid	-	-
3.9	Other (Limited recourse loan repaid under ESP)	126	205
3.10	**Net cash from / (used in) financing activities**	**91**	**70**

4.	**Net increase / (decrease) in cash and cash equivalents for the period**		
4.1	Cash and cash equivalents at beginning of period	39,894	71,081
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(281)	(32,205)

Consolidated statement of cash flows		Current quarter $A'000	Year to date (12 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)	91	70
4.5	Effect of movement in exchange rates on cash held	17	775
4.6	**Cash and cash equivalents at end of period**	**39,721**	**39,721**

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	39,721	39,894
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)**	**39,721**	**39,894**

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	124
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)	(8,493)*
8.2	Cash and cash equivalents at quarter end (item 4.6)	39,721
8.3	Unused finance facilities available at quarter end (item 7.5)	-
8.4	Total available funding (item 8.2 + item 8.3)	39,721
8.5	**Estimated quarters of funding available (item 8.4 divided by item 8.1)**	4.68*

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.

** Our quarterly cash expenditure was $281k which was distorted by the cash refund received under the Australian R&D tax incentive scheme of $8,212k. To use $281k would distort the Estimated Quarters of Funding Available, so we took out the $8,212k to leave the quarterly cash expenditure of $8,493k which we used in Note 8.1 for the calculation in Note 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: ..28 July 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.