ASX RELEASE 18 September 2024

Paradigm Receives Positive Response from the US FDA.

FDA Response Provides a Clear Pathway to OA Phase 3 Clinical Trial.

Paradigm Biopharmaceuticals Ltd (ASX:PAR) ("Paradigm" or "the Company"), a late-stage drug development company, is pleased to announce that it has received a detailed response from the U.S. Food and Drug Administration (FDA) following the Type D meeting response submitted to the agency in April 2024. The response from the FDA comprises a detailed set of comments that provides a pathway for progression of the Company's phase 3 clinical program for knee osteoarthritis (OA).

The FDA confirmed Paradigm's phase 2 clinical data (PARA_005 and PARA_OA_008) supported the safety and tolerability of the twice weekly 2 mg/Kg dose, and that the clinical monitoring for adrenal effects will continue. The FDA has provided detailed guidance for the use of the Company's selected dosing regimen of 2mg/kg injectable pentosan polysulfate sodium (iPPS) administered twice weekly. This is a significant outcome for Paradigm, since based on the clinical data generated to date, with a dosing regimen of 2mg/kg iPPS administered twice weekly, the phase 3 clinical trial is best set up for success.

In addition to feedback on the dosing regimen, the FDA provided feedback on amendments to the monitoring and mitigation plan, and statistical guidance. These changes to the monitoring and mitigation were supported by clinical and nonclinical data generated by Paradigm in its clinical development programs to date. Paradigm intends to implement these changes and submit the updated protocol under the open Investigational New Drug (IND) application currently in place with the FDA.

Once the protocol is submitted, Paradigm anticipates a 30-day review period before proceeding with enrolment for the PARA_OA_012 trial.

Paul Rennie, Managing Director of Paradigm, said: "*I understand that many investors are eager to know the dosage that will be used in the pivotal phase 3 clinical trial. I am pleased to announce that the FDA has indicated our clinical data supports the safety and tolerability of the twice-weekly administration of 2 mg/kg, the same dosing regimen Paradigm used in its phase 2 clinical studies (PARA_005 and PARA_OA_008). We would like to extend our gratitude to the US FDA for their valuable guidance on the phase 3 protocol."*

Paradigm Chief Medical Officer, Dr Donna Skerrett, commented: *"I believe the clarity provided by the FDA's response has brought us one step closer to entering the pivotal phase of the program. We now have a clearer and more certain path forward, enabling us to optimize the clinical protocol. We are incredibly proud of the collaborative efforts and hard work that have led us to this point, and we are excited to move forward with a protocol designed to maximise our chances of success. The alignment with the FDA's guidance further strengthens our confidence as we progress towards a successful outcome, bringing us closer to achieving our goal of securing approval for iPPS."*

Next Steps

The Company has commenced to incorporate the FDA comments into its phase 3 PARA_OA_012 trial protocol and, once completed, will submit the updated protocol under the open IND application. Paradigm expects to begin pre-screening and enrolment activities for PARA_OA_012 following the 30-day review period, with preparations already underway at trial sites in both the U.S. and Australia.

Paradigm will continue to keep investors informed as the phase 3 program activity advances and provide further information on the trial design and timelines following the mandatory review period.

-Ends-

About Paradigm Biopharmaceuticals Ltd.

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 injectable (subcutaneous) pentosan polysulfate sodium (**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 iPPS, 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.

To learn more please visit: https://paradigmbiopharma.com

Approved 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