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Paradigm's PARA_OA_002 Pivotal Phase 3 Clinical Trial to Proceed Without Modification Following Formal Safety Review

Paradigm Biopharmaceuticals Ltd (ASX:PAR) ("Paradigm" or "the Company"), a late-stage drug development company focused on delivering new therapies to address unmet medical needs, is pleased to advise that the first safety review meeting of the Data Monitoring Committee (**DMC**) for the pivotal PARA_OA_002 clinical trial was conducted on 20 December 2022. The DMC review of trial progress and safety data concluded that the PARA_OA_002 clinical trial should proceed without modification.

The DMC is responsible for assessing safety and efficacy during the conduct of Paradigm's PARA_OA_002 study, as well as ensuring the validity and scientific merit of the trial.

The Phase 3 Pivotal PARA_OA_002 clinical trial is a randomised, double-blind, placebo-controlled, multicentre (US/AU/UK/EU/CA) study that will evaluate the dose and treatment effect of injectable pentosan polysulphate sodium (**iPPS**) in participants with knee osteoarthritis (**kOA**) pain.

Paradigm Managing Director, Mr Paul Rennie commented: *"The DMC is a formal review process, and a written response has been received by the Company. This is a positive outcome for Paradigm that the early safety data from the pivotal PARA_OA_002 clinical trial has been reviewed by the DMC and it was recommended to continue without modification. Injectable PPS has been well tolerated throughout all of Paradigm's clinical programs, including real-world evidence with treatment of over 600 participants via the TGA Special Access Scheme. I look forward to updating our shareholders in calendar year 2023 on the progress of Paradigm's exciting OA clinical program with further PARA_OA_002 updates, as well as 6-month data from our PARA_OA_008 clinical trial exploring the disease modifying potential of iPPS".*

About PARA_OA_002

The purpose of this study is to measure the change in pain and function with subcutaneous injections of iPPS compared with subcutaneous injections of placebo in participants with knee osteoarthritis (kOA) pain. This is a 2-stage, adaptive study that will evaluate the dose and treatment effect of iPPS in participants with kOA pain.

Stage 1 comprises phase 2b dose selection, with approximately 468 participants randomised to receive 1 of 3 iPPS dose regimens or placebo for 6 weeks. The primary objective of stage 1 is to identify the minimal effective dose that will be used in stage 2 and in Paradigm's confirmatory trial. The selected dose is based on an optimal balance of efficacy and safety.

Participants in stage 1 will be randomly allocated to receive one of the following:

- 1.5 mg/kg calculated for ideal body weight (IBW) iPPS twice weekly
- 2 mg/kg IBW iPPS once weekly + placebo once weekly
- Fixed doses
    - 100 mg iPPS for ≤65 kg IBW once weekly + placebo once weekly, or
    - 150 mg iPPS for >65 to ≤90 kg IBW once weekly + placebo once weekly, or
    - 180 mg iPPS for >90 kg IBW once weekly + placebo once weekly
- Placebo twice weekly

In stage 2 (phase 3), approximately 470 participants will be randomised 1:1 to receive the selected iPPS dose regimen or placebo for 6 weeks.

Participants in stage 2 will be randomly allocated to receive:

- One of the 3 stage 1 iPPS dose regimens selected by the DMC, or
- Placebo twice weekly

The primary endpoint in the pivotal study is a change from baseline at day 56 in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain. Secondary outcomes include change from baseline at multiple time points out to day 168 in WOMAC pain and function, Patient Global Impression of Change (PGIC), and Quality of Life (QoL).

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 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 PPS, such as in osteoarthritis (phase 3) and mucopolysaccharidosis (phase 2).

Authorised for release by the Paradigm Board of Directors.

To learn more please visit: www.paradigmbiopharma.com

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