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FIRST SUBJECTS RANDOMISED AND DOSED IN PARA_0A_002 PHASE 3 STUDY IN AUSTRALIA

KEY HIGHLIGHTS

- Subject screening commenced in Q4 CY 2021 with subjects completing screening and being randomised into the PARA_OA_002 study in Australia.
- Paradigm has received confirmation that the first two subjects have now commenced dosing at one of the eight sites that have been selected in Australia.
- All eight sites in Australia are on schedule to be activated for screening subjects in January.
- Paradigm expects to report on first participant dosing in the United States (US) during the current quarter.
- Approximately 65 sites have been identified throughout the US and AUS, with additional sites being added in Europe and the United Kingdom to accelerate recruitment.
- Dose selection will commence following completion of Day 84 of stage 1 participants, which is expected in 1H CY2023. The company expects to begin filing regulatory applications with the EMA and EU member countries for the confirmatory study, PARA_OA_003, soon after confirmation of the selected dose.

Paradigm Biopharmaceuticals Ltd (ASX: PAR) ("Paradigm" or "the Company"), a clinical stage biopharmaceutical company focussed on repurposing existing molecules for new indications with unmet clinical needs, is pleased to report that the first subjects have been randomised and dosed in the pivotal PARA_OA_002 clinical trial, evaluating injectable pentosan polysulfate sodium (**iPPS/Zilosul®)** for the treatment of pain associated with knee osteoarthritis (**kOA**). The first subjects were enrolled by Dr. Arya, Australian Clinical Research Network, NSW. Of the eight sites that have been qualified in Australia, four sites are currently screening and dosing subjects, with the remaining four scheduled to begin screening activities during January.

Dr. Donna Skerrett, Paradigm Chief Medical Officer and interim CEO, said: "*Dosing the first participants in our PARA_OA_002 Phase 3 clinical program is an important achievement for Paradigm and for the development of Zilosul® to treat the millions of people globally suffering from kOA. We now look forward to ramping up recruitment and enrolment throughout Australia and look forward to updating shareholders on first participant dosing in the US shortly*."

About Para_OA_002

The purpose of this study is to measure the change in pain and function with subcutaneous injections of PPS compared with subcutaneous injections of placebo in

participants with kOA pain. This is a 2-stage, adaptive, randomised, double-blind, placebo-controlled, multicentre (US/AUS/UK/EU) study that will evaluate the dose and treatment effect of iPPS in participants with kOA pain.

Stage 1 comprises a phase 2b dose selection, with participants randomised receiving 1 of 3 iPPS dose regimens or placebo for 6 weeks. The primary objective of stage 1 is to select the dose for use in stage 2 and Paradigm's confirmatory trial (PARA_OA_003), the selected dose will be based on an optimal balance of efficacy and safety.

Participants in stage 1 will be randomly allocated to receive:

- 1.5 mg/kg calculated for ideal body weight (**IBW**) PPS twice weekly
- 2 mg/kg IBW PPS once weekly + placebo once weekly
- Fixed dose (100/150mg/180mg PPS ≤65/≥65 to ≤90/>90 kg IBW) once weekly + placebo once weekly
- placebo twice weekly

In stage 2, participants will be randomised 1:1 to receive the selected PPS dose regimen or placebo for 6 weeks.

The primary endpoint in the pivotal study is a change from baseline at Day 56 in WOMAC® pain with secondary outcomes including change from baseline at multiple time points out to day 168 in WOMAC® Pain and Function, Patient Global Impression of Change and Quality of Life.

Lead Investigator

The Australian lead Investigator for the pivotal study Para_OA_002 will be A/Prof Andrew Östör MD, MA, MB BS, FRACP, FRCP, FRCP (Edin). Prof Östör is a Consultant Rheumatologist at Cabrini Medical Centre and Principal Investigator at Emeritus Research, Melbourne. He is an Associate Professor in the Department of Medicine at Monash University. He was formally Director of the Rheumatology Clinical Research Unit at Addenbrooke's Hospital, Cambridge, UK. His research interests include early inflammatory arthritis, osteoarthritis, biologic and novel treatments for rheumatic diseases, clinical trials, RA associated lung disease, rheumatic manifestations of checkpoint inhibitors and disorders of the shoulder joint. Prof Östör was the lead investigator for Paradigm's Phase 2b clinical study.

Market Potential in Osteoarthritis

Osteoarthritis (**OA**) is the most prevalent form of joint disease, affecting up to 16% of the population in the developed world, with more than 72 million people in the US, EU5, Canada and Australia suffering from OA.[1]

OA has a significant impact on day-to-day functioning and, although the levels of pain and disability may fluctuate, it has no known cure or spontaneous remission and is associated with irreversible structural damage and progression over time. Presently, there are no drugs approved that can prevent, stop, or even restrain progression of OA. Moreover, the available medications that claim to mitigate the pain of OA have numerous risk/benefit considerations and market research indicates that only 19% of kOA patients are satisfied with currently available treatments. [2,3]

The prevalence of OA is increasing in line with the aging population and increasing rates of obesity. By 2030, the number of people suffering from OA in the US alone is predicted

to increase by 86% to 67 million.[2] If we assume a similar increase across the other markets defined above, even allowing for lower rates of obesity in non-US markets, it is plausible that more than 120 million people will be suffering from osteoarthritis by 2030.

About injectable PPS

Injectable PPS is not currently registered in Australia. Injectable PPS for human use is currently only available by inclusion into a Paradigm sponsored clinical trial or via the Therapeutic Goods Administration Special Access Scheme under limited and specific circumstances.

About Paradigm Biopharmaceuticals

Paradigm Biopharmaceuticals Ltd (ASX: PAR) is a late-stage drug development company with the mission to develop and commercialise PPS for the treatment of pain associated with musculoskeletal disorders driven by injury, inflammation, ageing, degenerative disease, infection, or genetic predisposition. Paradigm is also investigating proof-of-concept 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.

References

[1] Global Health Data Exchange, Institute for Health and Metrics Evaluation, University of Washington. Accessed June 2021 http://ghdx.healthdata.org/gbd-results-tool.
[2] OARSI. Osteoarthritis: A Serious Disease, Submitted to the U.S. Food and Drug Administration December 1, 2016.
[3] Matthews GL, Hunter DJ. Emerging drugs for osteoarthritis. Expert Opin Emerg Drugs. 2011;16(3):479-491. doi:10.1517/14728214.2011.576670.

Authorised for release by the Paradigm Board of Directors.

Zilosul® is a registered Trademark of Paradigm Biopharmaceuticals Ltd (ASX: PAR).

To learn more please visit: www.paradigmbiopharma.com

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