

ASX RELEASE

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First UK Subject Randomised and Dosed for the Pivotal Phase 3 Trial for the Treatment of Pain Associated with Knee OA

KEY HIGHLIGHTS

- The first UK subject has now been randomised and has commenced dosing in the global PARA_OA_002 phase 3 study.
 - This pivotal two-stage, adaptive, randomised, double-blinded, placebo-controlled, multicentre (US/CAN/AUS/UK/EU) trial will evaluate the dose and treatment effect of injectable pentosan polysulfate sodium (iPPS) in participants with knee osteoarthritis (OA) pain.
 - To date, over 50 sites across three jurisdictions are actively screening and recruiting candidates.
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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 announce that the first subject in the United Kingdom (UK) has 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 (**OA**). The first subject was randomised at Leeds University, by lead investigator, Professor Hemant Pandit. Paradigm aims to activate a total of seven sites across the UK for this phase 3 study.

This PARA_OA_002 global phase 3 trial has activated 8 sites across Australia, and 58 sites in the US. From the start of the calendar year, clinical trial site activation has been a key focus for Paradigm, to enable the largest pool of potential candidates to be identified and processed for participation. Site selection, initiation, and activation for Europe and Canadian is in progress with Paradigm to update investors as milestones are reached.

Dr. Donna Skerrett, Paradigm’s Chief Medical Officer said: *“To have our first participant randomised outside of the US and Australia is another important milestone in our global phase 3 program. Dr Pandit and his team at Leeds University have demonstrated strong interest the Paradigm OA clinical program and we look forward to many more participants joining the study throughout the UK”.*

About PARA_OA_002

The purpose of this pivotal phase 3 study is to establish the efficacy of subcutaneous injections of PPS (iPPS) participants with knee OA pain. This is a two-stage, adaptive, randomised, double-blinded, placebo-controlled, multicentre (US/CAN/AUS/UK/EU) study that will evaluate both the dose and treatment effect of iPPS in participants with knee OA pain.

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

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

The primary endpoints in this pivotal study are changes from baseline at day 56 (two weeks after the final dose) in Western Ontario and McMaster Universities Osteoarthritis Index (**WOMAC**) pain. Secondary outcomes include change from baseline at multiple time points out to day 168 (24 weeks from the start of the study, and 18 weeks after the last treatment) in WOMAC pain and function, Patient Global Impression of Change (**PGIC**), and Quality of Life (**QoL**) assessments.

Additional information on Paradigm's clinical trials can be found at ClinicalTrials.gov (002 - NCT04809376, 006 - NCT04814719) or via the Paradigm website under the Investor tab www.paradigmbiopharma.com.

In April this year, Paradigm's OA program investigating PPS received **Fast Track Designation** from the US FDA.

UK Lead Investigator

The UK lead investigator for the PARA_OA_002 phase 3 clinical study is Professor Hemant Pandit. Prof. Pandit has pursued a career in translational research in orthopaedics, having previously worked in Oxford for 16 years, and is particularly interested in hip and knee arthroplasty. He completed his DPhil (PhD) in knee kinematics and was first to describe the problems associated with metal-on-metal hips (pseudotumours). Prof. Pandit's contributions in the fields of arthroplasty, enhanced peri-operative recovery, teaching and training medics and paramedics are well recognised. He has also made a significant contribution towards teaching and capacity building in the low/middle-income countries of Asia and Africa. He has published more than 250 scientific articles and book chapters.

Professor Pandit also holds the title of Professor of Orthopaedic Surgery with the University of Oxford. He collaborates with various colleagues both nationally as well as internationally and is a member of various National Joint Registry (NJR) subcommittees.

Market Potential in Osteoarthritis

Osteoarthritis 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 knee OA 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 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 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).

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 the registered trademark of Paradigm Biopharmaceuticals Ltd. for injectable pentosan polysulfate sodium in the treatment of osteoarthritis.

To learn more please visit: www.paradigmbiopharma.com

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