ASX RELEASE 12th April 2022

US FDA Grants Fast Track Designation

for Paradigm's Phase 3 Osteoarthritis Program

KEY HIGHLIGHTS

- FDA Fast Track Designation for Pentosan Polysulfate Sodium (**Zilosul™/PPS**) offers pathways to expedite development of Paradigm's osteoarthritis clinical program.
- FDA Fast Track acknowledges osteoarthritis as a serious disease with unmet need and the potential for PPS to offer a treatment for OA.
- Fast Track designation allows Paradigm the opportunity to interact and collaborate with FDA more frequently during program development. This enables a stronger overall program in line with the FDA's expectations and provides opportunity for shorter review timelines.
- In February, Paradigm submitted a request for Fast Track Designation, which has now been approved, following the 60-day FDA review process.

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 announce that the U.S. Food and Drug Administration (**FDA**) has granted Fast Track Designation for the company's phase 3 program investigating Pentosan Polysulfate Sodium (**PPS**) for the treatment of osteoarthritis (**OA**).

The FDA Fast Track program offers a number of benefits to help advance development and expedite the review of novel therapies for serious conditions for which there is an unmet medical need, with the aim of getting important new therapies to patients more quickly. This Fast Track Designation from the FDA acknowledges that OA can be a serious disease with an unmet medical need and that preliminary data demonstrate that Zilosul™ has the potential to address this unmet need.

Features of Fast Track Designation

1. **Actions to Expedite Development and NDA Review**

   a. Opportunity to interact and collaborate with FDA more frequently during program development, for example, to discuss study design, extent of safety data required to support approval, dose-response concerns, and use of biomarkers.

b. Other meetings may be scheduled as appropriate (e.g., to discuss potential for accelerated approval request, the structure and content of a New Drug Application (**NDA**), and other critical issues).
c. In addition, such a product could be eligible for priority review request at the time of NDA submission. Priority review reduces the review time from 10 months to 6 months.

2. Submission of Portions of an Application (Rolling Review).

a. the FDA may determine, after preliminary evaluation of clinical data submitted by Paradigm, that that completed sections of the NDA may be submitted for FDA review. This means Paradigm can submit modules of the registration dossier in a staggered manner as opposed to submitting the entire dossier upfront, allowing for a faster review process.

Demonstrating the Potential of Zilosul™ to Address an Unmet Medical Need

Paradigm's submission to the FDA for Fast Track Designation needed to demonstrate the potential of Zilosul™ to address an unmet medical need. An unmet medical need is a condition the treatment or diagnosis of which is not adequately addressed by current therapies. This includes an immediate need for a therapy for a defined population (to treat a serious condition with no or limited treatments).

Paradigm's submission included descriptions of:

- Results from Paradigm's extensive nonclinical portfolio
- Multiple Mechanisms of Action of PPS
- Potential disease modifying properties (biomarker results including BME size and volume and serum biomarker changes observed in Phase 2B clinical trial.)
- Clinical results (001, 004, 005, EAP) with the main emphasis on Paradigm's phase 2b 005 clinical trial
- Supportive Peer Reviewed publications (Ghosh 2005 and Kumagai 2010)
- Summary of Safety
- Intended clinical development for PPS in OA:
    - Phase 3 Pivotal study - Para_OA_002
    - Extension Study – Para_OA_006
    - Phase 3 Confirmatory Study – Para_OA_003
    - Confirmatory Follow-up – Para_OA_007.

Dr Donna Skerrett, Paradigm Chief Medical Officer and Interim CEO commented:

" *This is welcome news from the US FDA as the company continues to gain momentum in site activation and participant screening across the 56 selected sites in the US. Given the need to improve therapeutic options for patients suffering from pain and loss of functionality associated with OA, we are excited to have this Fast Track Designation granted for Zilosul™ and the regulatory support it provides in expediting the phase 3*

development program to advance this promising treatment to patients sooner. Paradigm believes Zilosul™ would represent an important medical advance in the treatment of debilitating osteoarthritis pain for patients who do not experience adequate pain relief or cannot tolerate currently available pain medications."

OA is a chronic degenerative disease characterised by a progressive loss of cartilage, leading to pain, loss of joint function and disability. It 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] 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 listed above, even allowing for lower rates of obesity in non-US markets, it is estimated that more than 120 million people will be suffering from OA by 2030.

About the Phase 3 Trial (PARA_OA_002)

The purpose of the trial is to measure the change in pain and function after subcutaneous injections of PPS compared with subcutaneous injections of placebo in participants with knee OA 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 PPS in participants with pain associated with knee OA.

The primary endpoint in the trial will be change from baseline at Day 56 in WOMAC® pain score, with secondary outcomes to 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**).

The global PARA_OA_002 phase 3 clinical trial is currently screening and enrolling participants in both Australia and the US, with sites in Europe, UK, and Canada to be initiated.

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

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, aging, degenerative disease, infection or genetic predisposition.

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

Authorised for release by Paradigm Chairman, Mr Paul Rennie.

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