ASX RELEASE

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Paradigm Confirms 50% of Patients Dosed in Phase 3 OA Trial Enabling Progress Toward Interim Analysis

Key Highlights

- 50% of patients now dosed in the global PARA_OA_012 Phase 3 study, which is on track consistent with the company's previously announced time schedule.
- Interim dataset is on schedule to undergo independent statistical analysis, with results expected in August 2026.
- Phase 3 study design closely aligns with the patient population and protocol of the successful PARA_OA_008 trial, while strengthening data quality and managing placebo response.

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 50% enrolment in the global Phase 3 PARA_OA_012 clinical trial has now been achieved, with dosing of the final participants required for inclusion in the interim analysis dataset having commenced.

Participants are followed from first dosing through the Day 112 assessment period in accordance with the study protocol.

Following completion of the Day 112 assessments, the interim dataset will undergo data cleaning and independent data monitoring committee (DMC) statistical analysis, which is expected to take approximately four to six weeks. Based on the current study timeline, Paradigm expects the interim analysis results to be delivered in August 2026.

The PARA_OA_012 study is designed to enrol 466 participants globally, with patients randomised to receive injectable pentosan polysulfate sodium (iPPS) or placebo. The primary endpoint of the study is the change in weekly average of daily pain at Day 112, with secondary endpoints including improvements in physical function, imaging-based structural outcomes, and safety assessments.

Patient recruitment continues across Paradigm's global network of clinical trial sites spanning Australia, the United States, Europe and Asia, as progression toward 100% enrolment is expected in the coming months.

The PARA_OA_012 Phase 3 trial has been designed to closely align with Paradigm's earlier PARA_OA_008 study, which demonstrated clinically meaningful improvements in pain and function. The two studies utilise a comparable patient population, the same dosing regimen of injectable pentosan polysulfate sodium (iPPS), and similar study duration and endpoints. Maintaining this consistency in trial design is intended to reduce development risk and support comparability across the clinical program.

Importantly, the PARA_OA_012 protocol also incorporates key learnings generated across Paradigm's earlier clinical studies, including the PARA_OA_002 dose-ranging study. These

learnings have informed refinements to the trial methodology that were developed in consultation with regulatory agencies and leading scientific advisors.

One of the key enhancements relates to the measurement of pain outcomes. The PARA_OA_012 study utilises weekly average of daily pain recordings as the primary pain endpoint. This approach captures real-time patient pain assessments and reduces recall bias compared with retrospective questionnaires.

The study continues to collect WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) outcomes as secondary endpoints. While WOMAC relies on approximately 48-hour recall of symptoms, the inclusion of daily pain recordings provides an immediate assessment of patient experience and is intended to improve sensitivity in detecting treatment effects.

These refinements reflect learnings from prior clinical studies and align with contemporary regulatory and scientific guidance regarding approaches to mitigate placebo response and improve data reliability in osteoarthritis trials.

Paradigm Managing Director Paul Rennie commented: "*Achieving 50% enrolment in the PARA_OA_012 study represents a significant milestone as we progress toward the interim analysis. The trial design closely mirrors our earlier PARA_OA_008 study in terms of patient population and dosing regimen, while incorporating important refinements developed in consultation with regulatory agencies and leading scientific advisors.*"

"*These improvements, including the use of weekly average of daily pain recordings alongside continued WOMAC assessments, are intended to strengthen the study's ability to detect clinically meaningful treatment effects while managing placebo response, which is a recognised challenge in osteoarthritis clinical trials*."

Paradigm will continue to update the market as patients progress through the Day 112 follow-up period and the study advances toward the planned interim analysis.

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 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).

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.

Authorised for release by the Paradigm Board of Directors.

Investor Q&A

What milestone has Paradigm recently achieved in the Phase 3 study?

Paradigm has now achieved 50% enrolment in the global Phase 3 PARA_OA_012 clinical trial evaluating injectable pentosan polysulfate sodium (iPPS) in knee osteoarthritis. Importantly, the final participants required for the interim analysis dataset have now commenced dosing. These patients will be followed through the Day 112 assessment period, after which the interim dataset will undergo data cleaning and independent statistical analysis. Based on the current study timeline, Paradigm expects the interim analysis results to be delivered in August 2026.

What will the interim analysis evaluate?

The interim analysis will assess efficacy and safety in approximately half of the total planned study population. The primary endpoint of the trial is the change in weekly average of daily pain at Day 112. The interim analysis provides an early look at the treatment effect in the study and represents an important clinical milestone for the program.

How similar is the Phase 3 study to Paradigm's earlier successful trial?

The Phase 3 PARA_OA_012 study closely mirrors the design of Paradigm's earlier PARA_OA_008 study, which demonstrated clinically meaningful improvements in pain and function. Both studies utilise a comparable patient population, the same dosing regimen of injectable pentosan polysulfate sodium, and similar trial duration and endpoints. Maintaining this continuity in study design reduces development risk and supports comparability across the clinical program.

What improvements were made in the Phase 3 trial design?

While maintaining strong continuity with the earlier study, several refinements were incorporated following engagement with regulatory agencies and consultation with key scientific advisors. These refinements incorporate learnings from previous clinical studies, including the PARA_OA_002 dose-ranging trial.

One important improvement relates to the measurement of pain. The Phase 3 study uses weekly average of daily pain recordings as the primary endpoint. This captures real-time patient pain assessments and reduces recall bias compared with retrospective questionnaires.

Why is managing placebo response important in osteoarthritis trials?

Placebo response is a well-recognised challenge in osteoarthritis clinical trials, particularly when relying on retrospective pain assessments. By capturing daily pain scores and averaging them weekly, the study aims to reduce variability and improve the sensitivity of detecting treatment effects.

The trial continues to collect WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) outcomes as secondary endpoints. WOMAC relies on approximately 48-hour recall of symptoms, whereas daily pain recording captures more immediate patient experience.

How large is the osteoarthritis opportunity?

Osteoarthritis affects more than 500 million people globally and remains one of the leading causes of disability. Despite the size of the market, there are currently no widely approved disease-modifying treatments for osteoarthritis, with most therapies focused only on symptom management.

Paradigm's injectable PPS program is being developed with the potential to address both symptoms and underlying disease mechanisms, positioning the therapy in a large and underserved global market.

What are the next major milestones for the study?

The key near-term milestone is the interim analysis expected in August 2026. Between now and then, participants will complete their Day 112 follow-up assessments. After this period, the interim dataset will undergo independent data monitoring committee (DMC) statistical analysis before the results are delivered.

Why is the interim analysis important for investors?

The interim analysis represents the first look at Phase 3 efficacy data from the PARA_OA_012 trial. Given the strong alignment between the Phase 3 study design and Paradigm's earlier clinical trials, the interim readout is expected to be a major inflection point for the program and an important milestone in the development of injectable PPS for osteoarthritis.

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