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Paradigm to Proceed with Phase 3 Knee OA Trial

Key Highlights

- Successful conclusion of 30-day FDA review period enabling Paradigm to proceed with the pivotal phase 3 clinical trial (PARA_OA_012).
- Optimal 2mg/kg twice weekly iPPS dosing regimen reflecting multiple successful phase 2 trials.
- Preparations for the pivotal phase 3 clinical trial well advanced.
- On track to commence patient enrolment in Q1 CY2025.

Paradigm Biopharmaceuticals Ltd (ASX:PAR) ("Paradigm" or "the Company"), a late-stage drug development company, is pleased to announce the successful conclusion of the U.S. Food and Drug Administration's (FDA) 30-day review period for its phase 3 pivotal clinical trial protocol (PARA_OA_012). The 30-calendar day review period officially commenced on 28 October 2024 and concluded on 27 November 2024 (US time). With no substantive questions or concerns raised by the FDA, Paradigm can proceed with its pivotal phase 3 clinical trial, utilising the 2mg/kg twice weekly iPPS dosing regimen.

Preparations for the pivotal phase 3 clinical trial are well advanced, and Paradigm remains on track to commence patient enrolment in Q1 CY2025, with up to an initial 10 clinical sites in Australia, with sites in the United States anticipated to follow.

The primary endpoint of the pivotal phase 3 clinical trial is a change from baseline in pain, while key secondary endpoints include pain and functional assessments at multiple timepoints up to Day 404, the Patient Global Impression of Change (PGIC), and structural changes as measured by MRI and X-ray.

The FDA's feedback has been fully integrated into the pivotal phase 3 clinical trial design, clinical endpoints, and statistical methodology, with structural changes now upgraded to secondary endpoints to enhance their importance in regulatory submissions and potential label claims.

PARA_OA_012 is designed to enrol approximately 466 participants in a 1:1 randomisation design, with an interim analysis planned when 50% of subjects reach the Day 112 follow-up. The interim analysis will assess potential early efficacy.

Commencement of Paradigm's pivotal phase 3 clinical trial represents a major milestone for the Company. This milestone enables both progress of the clinical program and enables active engagement with key potential partners who may wish to support and/or co-fund the pivotal phase 3 clinical trial and future commercialisation efforts.

Paul Rennie, Managing Director of Paradigm, commented: "*Today I am pleased to report that Paradigm is now a Phase 3 Company. I would like to thank all our staff and consultants for their persistence and hard work during this year to make multiple submissions to the FDA. We are confident that, based on the clinical and other data generated to date and the enhancements to our trial design, informed by FDA guidance and commercial input, Zilosul® is positioned as a leading therapeutic candidate for the large poorly met need of pain associated with knee osteoarthritis. I am excited by the various strategic options available to the Company now we have progressed through this critical milestone.*"

Next Steps

Paradigm is now focussing on start-up and other preparatory activities to ensure timely initiation of patient enrolment. The Company anticipates conducting a webinar to provide a complete overview of the pivotal phase 3 clinical trial in the coming weeks.

The FDA has the authority to engage with clinical trial sponsors throughout the conduct of a trial, ensuring compliance with regulatory standards and addressing potential concerns. Paradigm will provide updates as appropriate, ensuring stakeholders remain informed of any developments relevant to the phase 3 pivotal clinical trial.

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About Paradigm Biopharmaceuticals Ltd.

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 iPPS, 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.

To learn more please visit: https://paradigmbiopharma.com

Approved for release by the Paradigm Board of Directors.

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