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PARA_OA_008 Study Evaluating Zilosul® Mechanism and Disease Modifying Effects Completes Recruitment

KEY HIGHLIGHTS

- The phase 2 clinical trial evaluating clinical and biomarker endpoints has reached 100% recruitment.
- The study will evaluate changes in synovial fluid biomarkers associated with osteoarthritis pain, inflammation, and disease progression.
- 60 subjects have been randomised into either PPS twice weekly, once weekly, or placebo groups.
- Top-line data from day 56 endpoints remain on track for release during Q3 CY22.
- Paradigm expects to also provide data updates as the study population reaches 6-month and 12-month timepoints.
- The canine OA study, also evaluating biomarkers and clinical endpoints is nearing completion of recruitment with initial data expected to be available in Q3 2022.

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 complete recruitment of PARA_OA_008. The phase 2 clinical trial evaluating the treatment effects of pentosan polysulphate sodium (**PPS/Zilosul®**) against placebo on synovial fluid biomarkers in participants with knee osteoarthritis (**OA**) pain, has reached 100% recruitment (n=60).

PARA_OA_008 Study evaluating synovial fluid biomarkers

The clinical trial is being run at two sites in Vic and NSW and aims to gather data on the medium- to long-term structure-modifying and symptom-modifying effects of PPS on Knee OA. Sixty subjects have been randomised to receive either PPS twice weekly, once weekly, or placebo. Participants have been randomised into each treatment group according to a 1:1:1 ratio (i.e. 20 randomised to PPS twice-weekly, 20 randomised to PPS once-weekly, 20 randomised to placebo over a 6 week treatment course).

This phase 2, PARA_OA_008, clinical trial aims to provide evidence that disease specific biomarkers in the synovial fluid of symptomatic OA patients are a potential marker of Zilosul® effects on the joint. The data collected from this phase 2 study will be the first OA clinical trial data reported by Paradigm since the release of the Phase 2B (PARA_OA_005) clinical trial data in 2018. Paradigm expects to release data as the various timepoints are reached, such as day 56 biomarker and clinical endpoints, 6-month MRI and clinical endpoints, and 1 year follow-up clinical effect duration endpoint data.

The Company remains on track for the interim (day 56) data to be released to the market in Q3 2022.

Canine OA Model Evaluating Disease Modification markers

To generate further data establishing the *in vivo* mechanism of action of PPS in disease modification and provide complimentary data in parallel with the PARA_OA_008 human clinical trial, Paradigm is concurrently conducting a trial in dogs with naturally occurring OA at the U-Vet Werribee Animal Hospital.

In the proposed investigation, up to 21 dogs with osteoarthritis of the stifle joint are treated with 3mg/kg PPS (1.7mg/kg human equivalent) or placebo (2:1 randomisation) via a subcutaneous weekly injection for 6-weeks. Clinical outcomes of pain and function will be assessed, together with structural changes from baseline as determined by the global OA score measured by X-ray, and bone marrow lesions and cartilage volume by MRI. In addition, molecular biomarkers associated with inflammation, cartilage degradation, and pain will be assessed in the synovial fluid and serum to ascertain correlations with clinical outcome measures of pain and function as well as structural changes. The longer 20-week follow-up period (equates to approximately 3 years in a human lifespan) from the cessation of treatment in the study will assess the durability of response and structural changes following therapy. The collective analyses of pain, function, joint structure, and biomarker levels following PPS therapy will provide informative data to assess the potential of PPS as a disease-modifying osteoarthritis drug (DMOAD).

Paradigm intends to have data from the canine OA model available for release to the market In Q3 2022.

Dr Donna Skerrett, Paradigm's Chief Medical Officer said:
"We have reached an important milestone with 100% completed recruitment in our PARA_OA_008 clinical trial. We thank all our volunteer trial participants, research physicians and their staff, and our dedicated and enthusiastic clinical staff for their time and commitment to this important study. Paradigm looks forward to sharing early data outcomes in Q3 2022 from this exciting exploratory study as well as our continued progress in the ongoing global Phase 3 clinical trial."

About Para_OA_008

Osteoarthritis (OA) is a heterogenous and chronic progressive disease of the whole joint, where patients experience persistent pain and progressively reduced joint function. The disease pathogenesis in OA is mediated by inflammation, cartilage degradation, and adverse remodelling of the subchondral bone. Pre-clinical and clinical evidence has demonstrated that PPS is active through multiple modes of action including decreasing inflammation by down-regulating inflammatory cytokines, reducing pain by reducing the production of NGF, protecting cartilage as evidenced by the downregulation of cartilage degrading enzymes, and supporting bone repair through improved blood flow. Until now, these effects have been evaluated by measuring serum biomarkers which may not fully describe the changes in the local OA joint environment. Therefore, the PARA_OA_008 study will evaluate molecular biomarkers in the synovial fluid to more directly evaluate the disease modifying potential of PPS on the diseased joint.

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, ageing, 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.

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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