PARADIGM BIOPHARMACEUTICALS LIMITED

ASX RELEASE

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PARADIGM'S CLEAR PATH TOWARDS ZILOSUL'S OA PHASE 3 CLINICAL TRIAL AND PRODUCT REGISTRATION IN EUROPE.

KEY HIGHLIGHTS FROM SCIENTIFIC ADVICE MEETING WITH EMA

- Positive feedback received from European Medicines Agency (EMA) after Paradigm's recent Scientific Advice meeting.
- This is a key regulatory milestone for Paradigm, which supports and validates our clinical development to date and our commercialisation plans for Zilosul® in Europe.
- Based on this feedback applications to commence clinical trials in EU member countries can now begin, with a clear path to product registration.
- EMA agreed with the primary endpoint to evaluate WOMAC pain and WOMAC function.
- EMA confirmed no active comparator required and Zilosul® will be evaluated against a saline placebo arm.
- Paradigm is in the process of seeking advice on the phase 3 clinical trial design through the Type C meeting process with the FDA. This meeting provides an opportunity for formal written response to clarify and agree on the clinical trial design and other supporting components for the IND submission and subsequent NDA submission, thus providing clarification for the product registration pathway in the US.
- Paradigm's Type C briefing book will be submitted, to the US FDA, in the coming weeks and will include the phase 3 protocol as agreed upon with the EMA.

Paradigm Biopharmaceuticals Ltd (ASX: PAR) is pleased to announce that the company has received positive feedback from an EMA scientific advice meeting which provides Paradigm with a clear path forward to registration for Zilosul® in Europe. Paradigm submitted its Scientific Advice briefing pack for the lead indication, knee osteoarthritis (OA) in May 2020, with the virtual meeting taking place between Paradigm and EMA representatives on September 1st.

The regulatory engagement conducted with the EMA covered key elements of the Phase 3 clinical studies and associated pre-clinical and manufacturing processes for Zilosul® that will support the submission of a Marketing Authorisation Application (MAA) in Europe for the targeted knee osteoarthritis indication.

The EMA agreed on key aspects of the proposed adaptive clinical trial design, including the conduct of two global, multicentre and randomised studies that will assess pain reduction from baseline and improved function in OA patients.

What is a scientific advice meeting with the EMA?

EMA provides scientific advice to support the timely and sound development of high-quality, effective and safe medicines, for the benefit of patients. Scientific advice helps to ensure that developers perform the **appropriate tests and studies**, so that no major objections regarding the design of the tests are likely to be raised during the evaluation of the marketing authorisation application. This also helps avoid patients taking part in studies that will not produce useful evidence. The process also provides guidance on the path to registration.

At any stage of a medicine's development, a developer can ask guidance and direction from EMA on the best methods and study designs to generate robust information on how well a medicine works and how safe it is. This is done by submitting a briefing pack to the EMA for evaluation. The data provided in the Paradigm briefing book covered the following areas; safety, preclinical, clinical, toxicology, manufacturing, statistical analysis and proposed clinical trial design. The primary purpose of the scientific advice request was to obtain advice and feedback from the EMA on the Sponsor's clinical trial designs and on a path towards registration.

Paradigm received positive feedback from an EMA scientific advice which provides Paradigm with a clear path forward for registration of Zilosul in Europe. Specific areas on which agreement was reached with the EMA include the adaptive trial design, the overall statistical approach, the patient population – moderate to severe osteoarthritis who have failed to respond to NSAIDS and paracetamol, the primary endpoint to evaluate WOMAC pain and WOMAC function, and the use of a placebo arm.

Paradigm confirms it will use a non-active placebo (saline) and the trial is not required to include an active comparator arm.

Paradigm can commence clinical trials in Europe

Paradigm now has an agreed upon regulatory path forward for the development of Zilosul® for the treatment of OA based on detailed review, discussion and written feedback from the EMA concerning our product characterization, nonclinical, phase 2 clinical data and phase 3 clinical trial designs. Based on this feedback applications to commence clinical trials in EU member countries can now begin. Paradigm intends to submit the same phase 3 clinical trial protocol to the US FDA in its upcoming Type C briefing book in order to receive similar detailed feedback on the sufficiency of the planned phase3 trials and supporting documents for the regulatory pathway in the US.

Paradigm's Chief Medical Officer, Dr Donna Skerrett, said:

"Paradigm is very pleased with the valuable guidance received from the EMA which provides clear direction as we advance our Phase 3 registration program toward bringing Zilosul® to market. The company remains focused on further demonstrating, via our Phase 3 clinical trials, the potential for Zilosul® to be a treatment for the huge population of people suffering with chronic knee pain as a result of OA. This is another step toward our aim to have the pivotal protocol acceptable in all major jurisdictions providing Paradigm with a clarified path to global approval of Zilosul® should our clinical trials be successful. We look forward to updating the market on the FDA Type C meeting progress in the coming weeks".

About Paradigm Biopharmaceuticals

Paradigm Biopharmaceuticals Limited (PAR) is a late stage drug development company with the mission to develop and commercialise pentosan polysulphate sodium (PPS) for the treatment of pain associated with musculoskeletal disorders driven by injury, inflammation, aging, degenerative disease, infection or genetic predisposition.

Authorised for release by Paul Rennie, CEO & Interim Executive Chairman.

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