ASX RELEASE **26th March 2021**

PARADIGM SUBMITS INVESTIGATIONAL NEW DRUG (IND) APPLICATION TO US FDA

KEY HIGHLIGHTS

- Paradigm has made the first major submission for its Pivotal study in subjects with pain associated with Knee Osteoarthritis (OA) with the submission of its IND application to the US Food and Drug Administration (FDA).
- The submission of the IND within Q1 keeps the company on track to enroll clinical trial subjects on previously reported timelines.
- Once the IND is "Open" Paradigm may begin recruitment and screening of participants for the pivotal Para_002 study.
- The IND application follows a Pre – IND meeting and Type C meeting with the US FDA where the company received valuable feedback from the regulator.
- Following a Scientific Advice meeting with the European Medicines Agency (EMA) in September 2020, Paradigm received EMA acceptance on the company's proposed clinical trial design.
- Paradigm is confident after seeking this critical feedback from both FDA and EMA, that the company will proceed with simultaneous registration for Zilosul® in multiple key regions, upon execution of a successful clinical trial program.
- 60 of a planned 65 sites have been engaged in preparation for commencement of recruitment upon opening of the IND.

Paradigm Biopharmaceuticals Ltd (ASX: PAR) ("Paradigm" or "the Company") is pleased to announce it has submitted its Investigational New Drug (IND) application to the US Food and Drug Administration (FDA) for the planned Pivotal study (Para_OA_002) and Extension study (Para_OA_006) with PPS (Zilosul®) for the treatment of patients with Knee Osteoarthritis (OA). The submission of the IND application marks a significant milestone for the company as Paradigm is now focused on the Pivotal stage of clinical development of Zilosul® and is the culmination of several informative meetings with global regulators throughout 2020.

In preparation for the IND submission and commencement of the pivotal clinical program, Paradigm's goal was to conduct multiple meetings with key regulatory bodies to ensure the clinical trial design would be acceptable on a global platform and meet all obligations required for registration upon successful trial results. Paradigm attended a Pre-IND meeting[1] in February 2020 where the company met with the FDA to discuss the clinical trial protocol and received feedback from a Type-C meeting[2] in December 2020, where the written response to questions posed by Paradigm was received from the US FDA on the proposed clinical trial design.

Regulatory engagement with the EMA was also achieved via a virtual Scientific Advice meeting[3] in September 2020. This was another major milestone toward the goal of a global harmonised clinical program with feedback from the EMA supporting Paradigm's clinical development to date and registration plans for Zilosul® in Europe. Based on the feedback, applications to commence clinical trials in EU member countries may begin,

with a clear path to product registration.

The key items identified by the EMA and FDA throughout the feedback process that have been addressed prior to the IND application submission were:

- The minimally effective dose to be established.
- The requirement for a second phase 3 confirmatory study.
- Additional Pre-clinical studies to be completed at GLP standard.
- Increased number of patients to satisfy safety requirements for a new dosage form.
- WOMAC® Pain and WOMAC® Function to be key endpoints.

The IND application is an over 30,000-page submission which includes reports on the phase 1 study in healthy volunteers that was completed in Q4 2020 as well as several non-clinical studies that detail the pharmacokinetics and toxicology of PPS. The submission also describes the GMP manufacture of the active substance and the drug product used for the pivotal phase 3 studies. Once the IND is 'open', Paradigm may begin recruitment and screening of participants for the pivotal Para_002 clinical study upon institutional ethics committee approval(s). Site selection is close to being finalised in the US and Australia with 60 of a planned 65 sites already approved to participate in the clinical trial. Paradigm remains on track to have the first subject begin screening in Q2 CY2021.

Dr Donna Skerrett, Paradigm CMO commented, *"This IND submission is the product of several informative meetings with the US FDA and EMA where Paradigm's clinical and regulatory teams received critical feedback on the requirements of the data package for submission and overall clinical trial design to ensure it would meet the regulators needs for registration. This led to adjustments in the OA clinical program to make sure Paradigm would have all necessary data to not only open the IND but also to have a harmonised global clinical trial design.*

We believe the process of gaining this important feedback from multiple regulators has de-risked our overall clinical program giving us confidence that should our Pivotal and Confirmatory studies be successful, the company will have all necessary data required for registration of Zilosul® at a minimum with the FDA, EMA and TGA."

Mr. Paul Rennie, Paradigm Chairman and CEO said: "*It has been incredibly pleasing watching all modules of the IND submission come together and I am very thankful for the highly experienced and skilled Paradigm team for achieving this significant milestone on time for all of our stakeholders. We believe that a harmonised clinical trial program that satisfies the requirements for registration with multiple global regulatory agencies will save Paradigm time and money as we approach registration and commercialisation of Zilosul®.*

We anticipate the IND opening will provide further exposure to global investors and partners with the company already receiving an increase in global interest in our Phase 3 clinical program during our attendance this week at the 2021 BIO-Europe Spring Partnering conference where the company has participated in several partnering meetings. We look forward to providing further detail on the final study design and timing once the IND has been opened following the 30-day review period with the FDA".

About Osteoarthritis

Osteoarthritis (OA) is the most common joint disorder in the United States. Symptomatic knee OA occurs in 10% men and 13% in women aged 60 years or older. The number of people affected with symptomatic OA is likely to increase due to the aging of the

population and the obesity epidemic. Current estimates indicate that there are 14 million U.S. adults with symptomatic knee osteoarthritis[4]. The overall number of U.S. adults affected by OA in any joint has increased during recent decades and is estimated to affect over 30 million U.S. adults today, primarily due to an aging population and an ever-increasing prevalence of obesity[5].

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.

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[1]ASX Announcement 6th April: https://asx.api.markitdigital.com/asx-research/1.0/file/2924-02222594-3A538946?access_token=83ff96335c2d45a094df02a206a39ff4

[2]ASX Announcement 28th Sept: https://asx.api.markitdigital.com/asx-research/1.0/file/2924-02285992-3A551181?access_token=83ff96335c2d45a094df02a206a39ff4

[3]ASX Announcement 18th Dec: https://asx.api.markitdigital.com/asx-research/1.0/file/2924-02324053-3A558426?access_token=83ff96335c2d45a094df02a206a39ff4

[4] Deshpande BR, Katz JN, Solomon DH, et al. Number of persons with symptomatic knee osteoarthritis in the US: impact of race and ethnicity, age, sex, and obesity. *Arthritis Care Res (Hoboken).* 2016;68(12):1743-50.

[5] Centers for Disease Control and Prevention. Osteoarthritis. Available at https://www.cdc.gov/arthritis/basics/osteoarthritis.htm

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

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