ASX RELEASE **19TH MAY 2021**

PARADIGM ACHIEVES FIRST REVENUE

KEY HIGHLIGHTS

- Paradigm achieves its first revenue via the provision of Zilosul® (injectable Pentosan Polysulfate Sodium (**iPPS**)) under the pay-for-use Special Access Scheme (**SAS**).
- Under the Therapeutic Goods Administration **(TGA)** SAS, Zilosul® has been made available to physicians with SAS approval to treat patients experiencing chronic arthralgia from Ross River Virus **(RRV)** infection, previous SAS participants seeking re-treatment and other subjects that would not qualify for recruitment into the Para_OA_008 or Para_OA_002 clinical trials.
- The Company's efforts and resources remain focused on the pivotal clinical trial program for osteoarthritis (**OA**) and seeking global marketing approval as soon as possible.
- Modest revenues are expected, as limited supply of Zilosul® has been made available for SAS due to stock prioritization for pivotal clinical trial program.
- Under the pay-for-use SAS program, Paradigm has already received 5 prescriptions for Zilosul® from physicians and the five patients will commence Zilosul® treatment in the coming week.
- PARA_OA_008 Synovial Fluid Biomarker study (or Disease Modifying Osteoarthritis Drug (**DMOAD**) study) continues to progress with almost half of the required subjects having commenced screening and many moving to randomisation and treatment.
- At the time of writing, Paradigm has not received any additional questions from the US Federal Drug Administration (**FDA**) regarding its IND submission. The Company and our consultants continue to prepare responses to potential/possible questions from the regulator.
- Paradigm is working on paths to revenue, including the SAS provisional approval registration, and at the same time executing on the global registration of Zilosul®.

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 it has received first revenue through a physician prescription of Zilosul® to patients via the TGA SAS. In Australia, injectable Pentosan Polysulfate Sodium (i**PPS/Zilosul**®) is not currently available for sale. Injectable PPS for human use is only available to patients who qualify for inclusion into a Paradigm Sponsored clinical trial or via a treating physician applying for its use in patients via the TGA's SAS (Category B).

The pay-for-use SAS program

Zilosul® will only be provided to practitioners with SAS approval and who are willing to perform the recommended monitoring of patients who have received Zilosul®.

Previously, the Company provided Zilosul® for no cost to prescribing physicians but the Company requested physicians to collect safety and efficacy data from patients receiving treatment. With the impending commencement of the pivotal clinical trial program in OA, Paradigm has concentrated efforts and resources, including available stock of Zilosul®, on the execution and completion of the pivotal clinical trial program and achieving global marketing approval as soon as possible.

The cost to patients under the pay-for-use program will be at a premium to previously disclosed price estimates for Zilosul® due to significant setup costs, including the platform for safety monitoring and reporting requirements. Revenue generated by the patient pay-for-use SAS program will be used to recoup the expenses incurred by Paradigm to support the provision of Zilosul® via this program. As a result, the Company is expecting modest revenue as only limited stock has been made available for the SAS due to stock being prioritised for the clinical trial program.

Paradigm will make stock available to physicians prescribing Zilosul® under the TGA SAS, who are trained and experienced in the use of Zilosul® and are willing to undertake the testing and monitoring recommended by the Company. All patients accessing Zilosul® via the SAS will undergo monitoring that is similar to participants in our clinical trial programs.

Following receipt of TGA SAS approval, physicians who have been informed by the Company on the use of Zilosul® may now prescribe Zilosul® to patients with persistent pain and loss of joint function due to arthralgia associated with RRV, patients who have previously received, tolerated, and benefited from the Zilosul® treatment under SAS and other patients who do not qualify for recruitment into the Para_OA_008 or Para_OA_002 clinical trials. Currently, physicians have limited therapeutic options when treating the persistent symptoms associated with RRV, as no treatment has shown to shorten the duration or alter the course of RRV. Up to 10 clinics across Australia have registered interest in being able to treat patients with RRV-induced arthralgia. Since recommencing the availability of Zilosul® to treating physicians to prescribe to patients following approval from the TGA, Paradigm has received several requests for Zilosul® under the pay-for-use program. Paradigm has shipped treating physicians five courses of Zilosul® as requested, following the necessary approvals.

Paradigm CEO and Chairman, Paul Rennie, commented: *"To achieve Paradigm's first revenue through the first patient treated with Zilosul® by a physician under the pay-for-use SAS program is very pleasing and an exciting time for Paradigm shareholders. The recommencement of this program gives (i) patients suffering arthralgia as a result of RRV infection and previous patients who have received Zilosul® the ability to be re-treated, and (ii) Paradigm to transition from a pre-revenue to revenue generating company, further increasing Paradigm's institutional investment potential. Paradigm remains focussed on our current OA clinical program as we prepare for anticipated questions from the FDA, to ensure we minimize any further delays.*

Shareholders please note, the revenue from the sale of iPPS under the pay-for-use SAS program will generate modest sales initially but the Paradigm Executive Management Team achieved this milestone as we continue to work on the commencement of the Phase 3 clinical trial. In addition, Paradigm is working on characterizing the disease modifying effects of Zilosul® in the PARA_008 clinical trial. This data will assist Paradigm with the continuation of its Provisional Approval submission to the TGA. Should the Provisional Approval submission be successful, this has the potential to generate significantly more revenue (from the Australian market) well before the product is registered in the USA or Europe. Paradigm is working to find paths to revenue and at the same time execute on the global registration of Zilosul"

IND Update

Paradigm will inform the market on the receipt of the FDA questions as soon as possible following sufficient internal review time. At the time of writing, Paradigm has not received any additional questions from the US FDA regarding its IND submission.

PARA_OA_008 – Synovial Fluid Study or DMOAD study Progress

The PARA_OA_008 synovial fluid study is progressing well with 24 participants having commenced screening and many moving to randomisation and treatment at Sportsmed Biologic in Box hill, Victoria. The Phase 2b study will measure the change in synovial fluid biomarkers associated with pain, inflammation and osteoarthritis disease progression following treatment with subcutaneous injections of PPS compared with subcutaneous injections of placebo in sixty participants (n=60) with knee OA.

The Primary Endpoint for PARA_OA_008 will be change from baseline at day 56 (two weeks post final injection) in one or more synovial fluid biomarkers. The biomarkers evaluated in this study are among the biomarkers most often associated with OA pain, inflammation, and cartilage degradation. Literature suggests that iPPS may be a potential treatment for OA because iPPS has been shown to exert anti-inflammatory activity by:

- blocking the effects of proinflammatory cytokines, such as TNFα and IL-1β, associated with OA (Sunaga et al, 2012[1]).
- inhibit the expression of NGF, a pain mediator, in osteocytes in subchondral bone of OA subjects (Stapledon et al, 2019[2]); and
- inhibit cartilage degrading enzymes known to play a key role in OA disease progression (Troeberg et al, 2012[3]).

In small clinical studies, iPPS has been shown to reduce pain and improve joint function in patients with knee OA (Ghosh et al, 2005[4], Kumagai et al, 2010[5]).

With this study, Paradigm hopes to provide further evidence that certain biomarkers are more prevalent in the synovial fluid of symptomatic OA patients with radiographic evidence of joint damage[6], determine if biomarker concentrations change in the synovial fluid with iPPS treatment, and to assess possible disease modifying effects of iPPS on patients with Knee OA pain.

Positive results from this study will assist Paradigm's data package for submission to the TGA to gain Provisional Approval for Zilosul® in Australia. Data from this study will also further inform the Mechanism of Action and potential Disease Modifying effects of iPPS assisting with the future pricing and reimbursement plans.

About 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 OA[7]. 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[8].

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 guaranteeing nor predicting 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.

References:

[1] Sunaga T, Oh N, Hosoya K, et al. Inhibitory Effects of Pentosan Polysulfate Sodium on MAP-Kinase Pathway and NF-κB Nuclear Translocation in Canine Chondrocytes In Vitro. J Vet Med Sci. 2012
[2] Stapledon CJM, Tsangari H, Solomon LB, et al. Human osteocyte expression of Nerve Growth Factor: The effect of Pentosan Polysulphate Sodium (PPS) and implications for pain associated with knee osteoarthritis. Heymann D, editor. PLOS ONE [Internet]. 2019
[3] Troeberg L, Mulloy B, Ghosh P, et al. Pentosan polysulfate increases affinity between ADAMTS-5 and TIMP-3 through formation of an electrostatically driven trimolecular complex. Biochem J [Internet]. 2012
[4] Ghosh P, Edelman J, March L, et al. Effects of pentosan polysulfate in osteoarthritis of the knee: A randomized, double-blind, placebo-controlled pilot study. Curr Ther Res [Internet]. 2005
[5] Kumagai K, Shirabe S, Miyata N, et al. Sodium pentosan polysulfate resulted in cartilage improvement in knee osteoarthritis - An open clinical trial. BMC Clin Pharmacol [Internet]. 2010
[6]Haraden CA, Huebner JL, Hsueh M-F, et al. Synovial fluid biomarkers associated with osteoarthritis severity reflect macrophage and neutrophil related inflammation. Arthritis Res Ther [Internet]. 2019
[7] 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.
[8]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.

To learn more please visit: www.paradigmbiopharma.com

FOR FURTHER INFORMATION PLEASE CONTACT:

Investors	Clinical Trial & SAS Enquiries
Simon White **Director of Investor Relations** **Tel: +61 (0) 404 216 467** **Paradigm Biopharmaceuticals Ltd** **ABN: 94 169 346 963** **Level 15, 500 Collins St, Melbourne, VIC, 3000, AUSTRALIA** **Email: investorrelations@paradigmbiopharma.com**	Paradigm Biopharmaceuticals Ltd is currently recruiting for clinical trials. All information regarding recruitment activity is published via our ASX announcements and via an appropriate clinical trial registry. **Clinical Trial Registries: https://clinicaltrials.gov/** **http://www.anzctr.org.au/** **Special Access Scheme: SASrequests@paradigmbiopharma.com**