ASX RELEASE **18th March 2021**

PEER-REVIEWED PUBLICATION SUPPORTS PPS AS A POTENTIAL DISEASE MODIFYING THERAPY FOR RRV-INDUCED ARTHRALGIA

KEY HIGHLIGHTS

- Paradigm's successful Phase 2A Ross River Virus clinical trial results have been peer-reviewed and published online in the journal, BMC Musculoskeletal Disorders.
- The data show that iPPS is well tolerated and showed improvements in joint symptoms and the objective measures of hand grip strength and disease biomarkers in subjects with Ross River Virus-induced arthritis.
- The potential for disease modification is demonstrated by statistically significant reductions in cartilage destruction enzymes in the iPPS group compared to the placebo group as measured by novel biomarkers, including COMP and CTX-II.
- Findings support continued evaluation of PPS as a disease modifying therapy for the improvement of RRV-induced arthralgia and other viral arthralgias.
- Currently no vaccine is available to protect against RRV infection nor is there specific treatment to reduce the duration of symptoms or alter the course of the disease[1].
- Australian infectious disease physicians will be able to provide iPPS through the TGA Special Access Scheme (SAS) for patients with chronic RRV-induced arthritis where there are no other treatment options. Access will be available in Q2 CY 2021 as a pay-for-use program, providing a path to first revenues for Paradigm.

Paradigm Biopharmaceuticals Ltd (ASX: PAR) ("Paradigm" or "the Company") is pleased to announce the publication of "Pentosan Polysulfate Sodium for Ross River Virus (RRV)-Induced Arthralgia: A Phase 2A, Randomised, Double-Blind, Placebo-Controlled Study" in the peer-review scientific journal, BMC Musculoskeletal Disorders, which was published online on 12 March 2021 (see link to article- https://bmcmusculoskeletdisord.biomedcentral.com/track/pdf/10.1186/s12891-021-04123-w.pdf). The data produced in the Pilot Study are provide clinical evidence that PPS may offer patients a treatment option for a disease that has little or no therapeutic options for chronic RRV infection.

Paradigm's successful Phase 2A trial results, previously announced to the ASX on 4th June 2019, have been subject to a scientific peer review process and the data have now been published. The published study demonstrated that iPPS is a safe and effective treatment in participants with chronic and sustained symptoms (arthralgia) associated with RRV. The publication describes the details of the Phase 2A study, its background, design, treatment interventions and the outcomes for the per protocol population (18 subjects, 11 iPPS and 7 Placebo) who completed the full course of treatment and final follow-up.

Paradigm's published Phase 2A clinical trial data demonstrated PPS administered at a dose of 2mg/kg twice weekly for 6 weeks has the potential to improve pain and function in subjects suffering RRV-induced arthralgia.

Efficacy outcomes in participants with RRV-induced arthralgia involved assessment of disease symptoms at Day 15, 29, 39 and 81. The outcomes measured were:

- change from baseline in hand grip strength scores (objective data);
- assessment of joint symptoms by RAPID 3 scores;
- changes from baseline of SF-35 scores a measurement of Quality of Life (QoL); and
- Change from baseline in 6 Biomarkers associated with Inflammation and cartilage degradation.

Results of the Phase 2 Study:

Safety

The primary endpoint of the trial was the evaluation of the safety and tolerability of subcutaneous PPS in subjects with RRV-induced arthralgia.

PPS was well tolerated, with a similar treatment-emergent adverse event (TEAE) profile in the treatment and placebo groups. No serious adverse events occurred in the study.

PPS demonstrates improvement in the objective assessment of Hand Grip Strength

Hand grip test measured the maximum isometric strength of the hand and forearm muscles using a handgrip dynamometer. Hand grip strength is a clinically important measure of function as it provides objective data on strength improvements of patients treated with iPPS versus Placebo. Data from the Pilot study demonstrated following PPS treatment patients had improvements in hand grip strength at all time points (day 15, 29, 39 and 81). Hand grip strength improvement of 6.99kh ($p=0.0189$) was observed in patients treated with PPS versus placebo at day 15.

PPS demonstrates reduction in disease severity and progression

At baseline 90.9% (10/11) participants in the iPPS group and 100% (7/7) in the placebo group were categorised with clinical disease severity (Rapid-3) ranging from low, moderate and high severity. At Day 81, 61.5% of participants in the iPPS group showed near remission in comparison to 14.3% in the placebo group.

PPS demonstrates reduction in the levels of biomarkers involved in joint inflammation

Changes in inflammatory cytokines, chemokines and biomarkers associated with bone and cartilage remodelling showed that PPS treatment produced statistically significant changes compared to placebo in six novel biomarkers COMP, CTX-II, CCL1, CXCL12, CXCL16 and CCL17. The reduction of the serum biomarkers, COMP and CTX-II suggests that the degenerative process in the joints of RRV subjects are inhibited by PPS in a similar manner that was reported for osteoarthritis[2]. The biomarkers involved in the synovial recruitment of inflammatory cells, CCL1, CXCL12 and CXCL17 were also reduced in iPPS subjects compared to placebo. Importantly the biomarker CCL16, involved in bone integrity by recruiting osteoblasts, was increased following PPS treatment versus placebo.

Dr Ravi Krishnan, Paradigm Chief Science Officer, commented: *"We are very pleased that the data from this double-blind, placebo-controlled pilot study has provided compelling clinical and scientific evidence to suggest that PPS can be safely administered to subjects with RRV induced arthralgia and demonstrate improved clinical outcomes in pain and function. In addition, the data are supportive of the anti-inflammatory and chondroprotective (cartilage) actions of PPS which showed reduction in inflammatory biomarkers. The findings in RRV induced arthralgia complement the actions of PPS in other musculoskeletal indications in osteoarthritis and MPS which involve pain and dysfunction."*

Please refer to the following link for the full article: https://rdcu.be/cgGQA

RRV Special Access Scheme

In the last 12-months Paradigm has commenced preparations to make iPPS available via the TGA Special Access Scheme (SAS), to physicians treating patients with persistent pain and loss of joint function due to arthralgia associated with RRV. 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. Analgesics (paracetamol and aspirin) and NSAIDS are recommended, although, there is limited relief of symptoms by most patients. Corticosteroids can improve outcomes but are generally not recommended due to risks outweighing any benefit[1]. The findings from the Phase 2 study have now been validated through the peer review process. This will inform infectious disease physicians regarding the potential use of PPS for RRV induced arthralgia where there are no other treatment options.

The TGA SAS for RRV will be a patient pay-for-use program and will be available in Q2 CY2021 at up to 10 clinics across Australia. Clinic selection will be dependent on adherence to strict patient safety monitoring protocols during the treatment cycle. Paradigm will update the market further on participating clinics and pricing once they have been finalised.

Dr Paul Griffin, Principal Investigator and Infectious Disease Physician, commented: *"Recently, we have observed a significant spike in cases of Ross River virus fever in NSW, Victoria and Queensland. Following the acute phase of RRV fever many patients will experience in the coming weeks persistent debilitating joint pain and there are currently no satisfactory treatments available. As the Principal Investigator on Paradigm's Phase 2A RRV clinical trial, I am very pleased that the data have been acknowledged by robust scientific peer-review and the work is now published. Most importantly, the data supports the use of PPS as a potentially effective treatment for the disease symptoms of RRV-induced arthralgia and may alter the course of the illness".*

About Ross River Virus[1]

Ross River Virus (RRV) is a mosquito transmitted alphavirus that causes epidemic polyarthritis and arthralgias, that may lead to significant muscle and joint damage. It is Australia's most common arbovirus effecting 4000-5000 people per year. RRV most commonly occurs in adults aged 25-44 years with males and females equally affected. The incubation period is 7-9 days, with a range of 7-21 days. In the acute phase, functional ability can be significantly impaired, with about 50% of patients requiring time off work. Joint pain is present in 95% of patients, most commonly affecting fingers, toes, wrist, ankles, elbows and knees. The disease is associated with significant morbidities during the first few months following diagnosis, with arthralgias have a prolonged effect more than 3 months after diagnosis in over two-thirds of RRV patients.

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] https://www.racgp.org.au/download/Documents/AFP/2009/August/200908barber.pdf

[2] ASX Announcement: Paradigm discovers Zilosul® (iPPS)) protects cartilage in Knee OA (29th Aug 2019)

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