ASX RELEASE

Paradigm's PPS as a potential breakthrough in the treatment of viral arthritis and joint pain

Key Highlights:

- In a preclinical study of alphavirus infection pentosan polysulfate sodium (PPS) significantly alleviated the severity of disease and reduced both the inflammatory response and the loss of articular cartilage;
- Preclinical data suggests PPS has the potential to treat both acute and chronic symptoms associated with mosquito transmitted alphavirus infections (Ross River virus (RRV) and chikungunya virus (CHIKV);
- Five patients with RRV-arthralgia (joint pain) already treated with PPS under the TGA Special Access Scheme demonstrating tolerance and potential clinical effects;
- Paradigm establishes strategic partnership with the Institute for Glycomics at Griffith University to embark on a Phase 2 clinical trial to develop PPS for the treatment of RRV-and CHIKV-induced arthritis and arthralgia;
- Paradigm has exclusive world-wide rights to commercialise the patent along with Paradigm's sole right to acquire (assign) from Griffith University the patent after Paradigm commences a Phase 2 clinical trial;
- Apart from some medications providing temporary symptomatic relief, there are no specific therapeutics or vaccines to treat RRV and CHIKV infections so there is a pathway for accelerated approval for the treatment in some countries;
- Potential global market for PPS to treat RRV and CHIKV viral arthritis and joint pain is estimated to be in hundreds of millions of dollars per annum and this represents outstanding big pharma partnering opportunity.

Melbourne 7 September 2016 Paradigm Biopharmaceuticals Ltd (ASX:PAR) announces pentosan polysulfate sodium (PPS) as a potential breakthrough in the treatment for alphavirus induced arthralgia and arthritis.

PRECLINICAL STUDY: Paradigm is pleased to announce a collaborative partnership with the Institute for Glycomics at Griffith University following crucial preclinical data demonstrating efficacy of PPS in the mouse models of RRV and CHIKV infection. In mice, infection resulted in a significant acute inflammatory response and cartilage destruction. The severity of disease was alleviated by PPS therapy as assessed by histological analysis, gene expression and soluble biomarkers. Severe RRV-induced joint pathology, including thinning of articular cartilage and loss of proteoglycans in the cartilage matrix, was diminished with PPS treatment. Leading Research Scientist at the Institute for Glycomics Dr Lara Herrero said "PPS is a promising new agent for RRV-induced arthritis acting to reduce viral-induced inflammation and preserve the cartilage matrix, which is damaged during virus infection.". Dr Herrero also said "our study showed that treatment with PPS also reduced the loss of articular cartilage and protected the level of proteoglycans in the cartilage matrix. Overall we concluded in our study PPS was a safe and effective treatment for both acute and chronic RRV-infection."

TGA Special Access Scheme for Treatment of RRV patients: Publication of Dr Herrero's research has generated significant interest from both treating doctors and patients suffering from RRV infections. Paradigm is further pleased to announce the successful treatment of 5 patients suffering from RRV-induced arthralgia with PPS who have failed current standard of treatment. These patients were treated in a number of Queensland GP clinics under the authority of the TGA special access scheme. While all patients showed no adverse events most patients showed improvement in the quality of life assessments. Paradigm's Chief Scientific Officer, Dr Ravi Krishnan said " We are ecstatic that the scientific validation and independent preclinical research performed by Dr Herrero has provided the basis to treat patients suffering from virally transmitted arthralgia with PPS ". Dr Krishnan further remarked that "There is clearly an unmet medical need for this ailment and Paradigm will be embarking in a Phase 2 clinical trial to consolidate our preliminary clinical findings".

Alphavirus infection: Mosquito-transmitted arthritogenic alphaviruses such as Ross River virus (RRV) and chikungunya virus (CHIKV) cause large epidemics of severe musculoskeletal disease world-wide. They have been progressively expanding their global distribution, regularly emerging in new regions of the world. The hallmark of alphavirus disease is crippling joint pain and arthritis, which often has an extended duration leaving patients bed-ridden and incapacitated. CHIKV has further expanded its global distribution by entering the Americas. As of 26th August 2016, the Pan American Health Organization (PAHO) reported an estimated total of over 1.7 million cases in the region since 2014, with 180,000 reported in 2016 so far. The first report of locally contracted CHIKV transmission in mainland USA was reported in July 2014. Due to the expanding range of alphaviral infections, treating the debilitating arthritic diseases they cause has become increasingly important, especially as there are no specific treatments available. The severe arthralgia/arthritis in the joints caused by alphaviruses can be both acute and chronic. (Ref: Herrero L et al (2015) J. Virol. Doi:10.1128/JVI.00224-15). About 95% of all symptomatic cases report joint pain (arthralgia). Acute onset affects multiple joints including fingers, toes, ankles, wrists, back, knees and elbows. Fatigue occurs in 90% and fever, muscle pain (myalgia) and flu-like symptoms occur in 50–60%. Ref: RACGP http://www.racgp.org.au/afp/200908/200908barber.pdf.

Paradigm's commercial interest in treating alphavirus arthritis and joint pain: PPS has previously been shown to significantly increase the production of anti-inflammatory cytokine (IL-10) and reduce the production of pro-inflammatory cytokines (TNF and IL-1). In vitro studies, PPS has also been shown to inhibit enzymes that degrade the joint cartilage and proteoglycans. [Ref: Troeberg et al (2008) FASEB J http://dx.doi.org/10.1096/fj.08-112680].

In 2014, CHIKV expanded into the Americas with approximately 1.7-million cases reported there. Currently world-wide there are no pharmaceutical agents registered to treat both the inflammatory driven acute phase and the cartilage-damaging chronic phase of alphavirus infections.

Paradigm's CEO, Mr Paul Rennie said "given (i) the safety of PPS in humans is established, (ii) the route of administration and dosage has been confirmed in humans, (iii) the preclinical study has been peer-reviewed and published demonstrating both safety and efficacy and (iv) the scarcity of any registered pharmaceutical agents to treat this disease, Paradigm is hopeful to receive accelerated approval for the treatment in some countries". This clinical program may be a partnering opportunity for big pharma companies developing products for musculoskeletal indications and/or as an addition to the product portfolio of those big pharma companies developing therapies and vaccines for other infectious diseases.

Paradigm's Clinical Development Programs: Paradigm adds a new clinical program to its development plans. Paradigm's CSO, Dr Ravi Krishnan identified Dr Herrero's et al research. Paradigm approached Griffith University and expressed an interest in commercialising the patent covering the use of PPS to treat alphavirus arthritis and joint pain. Mr Rennie also said "I am delighted to announce that Griffith University and Paradigm Biopharmaceuticals Ltd have entered into a license and assignment agreement (the Agreement). The Agreement gives Paradigm the exclusive world-wide rights to commercialise the patent along with Paradigm's sole right to acquire (assign) from Griffith University the patent post a Phase 2 clinical trial. I also want to highlight the proof-of-concept translation of Dr Herrero's preclinical research into humans (n=5) has already occurred. These 5 cases further de-risk this commercial opportunity".

Paradigm's lead clinical programs are and continue to be the use of PPS to treat bone marrow lesions (bone bruising as seen on MRI) and the intra-nasal use to treat allergic rhinitis. The additional clinical program, to use PPS to treat patients with alphavirus arthritis and bone pain, is additive to our clinical development plans.

Paradigm's Phase 2 bone bruising clinical trial continues to recruit patients. Our allergic rhinitis / hay fever bridging toxicology, preclinical (safety and efficacy) and Phase 1 (safety) studies are complete and our Phase 2 randomised, double-blind, placebo-controlled study is on schedule to commence December, 2016.

Now, Paradigm adds the commercial value of a peer-reviewed scientific publication of the preclinical study-outlining the potential role of PPS in treating alphavirus arthritis and joint pain. Additionally, Paradigm adds the value of five patients already treated with PPS demonstrating safety, tolerability and signals of efficacy.

About Griffith University: With five campuses across South-East Queensland, Griffith is a comprehensive, research-intensive university, ranking in the top 3% of universities worldwide. Griffith University's teaching and research activities span all disciplines, while its network of more than 200,000 graduates extends around the world.

About Paradigm Biopharmaceuticals Ltd: (ABN: 94 169 346 963) Paradigm Biopharmaceuticals Ltd (ASX: PAR) is an Australian biopharmaceutical company focused on repurposing the historic drug PPS (Pentosan Polysulfate Sodium) as a potential new treatment for Bone Marrow Edema (BME) lesions following traumatic injury. Paradigm Biopharmaceuticals is also repurposing PPS for respiratory diseases including Allergic Rhinitis (AR) also known as hay fever. Repurposing an existing drug diminishes early developmental risks associated with traditional new drug development and usually means shorter development times, lower development costs and less safety risk.

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Link to Dr Herrero's publication: http://www.paradigmbiopharma.com/investors/media-analyst-reports