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FIRST PATIENT DOSED IN PHASE 2 CLINICAL TRIAL IN BRAZIL INVESTIGATING PPS FOR THE TREATMENT OF MPS-VI

KEY HIGHLIGHTS

- The first MPS-VI participant has been dosed at Hospital de Clinicas de Porto Alegre, Brazil.
- The study is evaluating PPS compared to placebo in up to 12 patients in a 2:1 randomization at two investigator sites in Brazil.
- Primary objective of the study is to evaluate the safety and tolerability of PPS in subjects with MPS-VI at 6, 12 and 24 weeks.
- Secondary endpoints will include reduction in, and glycosaminoglycan (**GAG**) levels and an increased function.
- This will be the largest clinical trial conducted using PPS in any MPS population.
- Paradigm's MPS program has received Orphan Drug Designation status in the US and EU for MPS-I and MPS-VI.
- Interim data from Paradigm's ongoing Australian Phase 2 study in MPS-I will be presented at the International ICIEM meeting In November 2021.

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 randomised and dosed the first MPS-VI participant in its Phase 2 clinical trial, Para_MPSVI_001, evaluating pentosan polysulfate sodium (**PPS**) in patients with MPS-VI (Maroteaux-Lamy syndrome).

MPS-VI (Maroteaux-Lamy syndrome) is an orphan disease, and classified as a rare autosomal recessive, inherited lysosomal storage disorder caused by a deficiency of N-acetyl galactosamine 4–sulfatase, leading to physical manifestations associated with accumulation of GAGs in the lysosomes. The cumulative rate for all types of MPS is approximately 3.5 in 100,000 live births and generally the patients present in one of three ways: as a dysmorphic syndrome (MPS IH, MPS II, MPS-VI) often with early onset middle ear disease, deafness, or upper airways obstruction, with learning difficulties, behavioural disturbance and dementia and mild somatic abnormalities (MPS-III), and as a severe bone dysplasia (MPS-IV).

Pentosan polysulfate sodium (PPS) presents the first possible drug therapy targeted specifically at complications associated with MPS including pain and arthropathy in the MPS-VI patient population. As individuals treated with enzyme replacement therapy (ERT) continue to experience pain and other symptoms that impact quality of life (QOL), PPS is being investigated for use as an adjunctive treatment to ERT to alleviate progressive arthropathy via the multiple actions of PPS on disease modifying pathways (Francis et al. 1993, Ghosh et al. 2010).

The study is designed to enrol patients with MPS-VI who are currently receiving enzyme replacement therapy (**ERT**) and exhibit pain and functional deficiency due to musculoskeletal symptoms associated with the underlying disease (Berger et al., 2013 [1]) (Hack et al., 2016 [2]) (Mitchell et al., 2016 [3]). All MPS-VI subjects will receive ERT throughout the study. Subjects will be administered PPS or placebo at a 1.5 mg/kg (≥9 years of age) or 1.0 mg/kg (<9 years of age) sub-cutaneous injection once weekly for 24 weeks. The primary objective of the Phase 2 study will be to evaluate safety and tolerability. Paradigm will also assess a number of key secondary and exploratory endpoints, including the effect of PPS on pain and function, mobility, urinary GAG levels, mobility, Quality of Life, activities of daily living, subject/parent global impression of response to therapy; and Pulmonary function. The clinical trial is being conducted in Brazil at the Hospital de Clinicas de Porto Alegre and the Hospital Universitário Alcides Carnerio, The Principal Investigator is Dr. Roberto Giugliani, a world-renowned geneticist specialising in inherited metabolic diseases.

Dr. Giugliani is a Professor at the Department of Genetics of the Federal University of Rio Grande do Sul and Chief of the Medical Genetics Service of Hospital de Clinicas de Porto Alegre, Brazil. Dr. Giugliani was past President of the Brazilian Society of Clinical Genetics, President of the Latin American Society of Inborn Errors of Metabolism and Neonatal Screening and President of the Latin American Network of Human Genetics. Currently, Dr. Giugliani is Researcher level IA of the Brazilian Council for Development of Science and Technology and Director of the WHO Collaborating Centre for the Development of Genetic Services in Latin America.

Dr. Gulgliani, commented: "*MPS-VI patients on Enzyme Replacement Therapy continue to experience stiffness, pain, inflammation, and heart and airway soft tissue manifestations. Pentosan polysulfate sodium (PPS) has been shown to reduce urinary GAGs and improve joint mobility and pain that impact Activities of Daily Living (ADL) in MPS-I patients. Likewise, preclinical studies of PPS in Maroteaux-Lamy syndrome (MPS-VI) have demonstrated similar results, which may translate to significant clinical benefit for this patient population. We strongly believe that PPS has the potential to address this unmet medical need in the MPS-VI patient population*."

Dr. Donna Skerrett, Paradigm's Chief Medical Officer, said:
"*Current treatment options for MPS-VI have very limited effects on some organs, in particular the skeletal system. Despite current treatment options, such as enzyme replacement therapy, people with MPS-VI continue to have joint pain and joint dysfunction. Current treatment options have limited effect on the concentrations of glycosaminoglycans (GAGs) in tissues and body fluids however a pilot clinical trial (Hennermann et al) demonstrated MPS-I subjects treated with PPS over 25 weeks, the urinary GAG's returned to the upper level of normal. Paradigm is investigating the role of PPS in patients with MPS-VI to see if our drug is safe, well tolerated and additionally, reduces pain, improves joint function and demonstrates the potential for urinary GAG's reduction to a normal level*".

MPS-I

Preliminary data from Paradigm's ongoing Australian Phase 2 study in MPS-I is very promising and has been accepted for a presentation at the International ICIEM meeting In November 2021. We believe that these early results, coupled with previous clinical and non-clinical data in MPS, provide a foundation for the development of PPS to address the unmet medical need of chronic pain and limited function in MPS-VI patients.

About Paradigm Biopharmaceuticals

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

Paradigm has the intellectual property and exclusivity to commercialise PPS for the treatment of multiple conditions including Lysosomal Storage Diseases (LSD) encompassing MPS (MPS types I, II, III, IV, VI and VII), Gaucher disease and Fabry disease, whether alone or as adjunctive therapy. In addition, Paradigm has an exclusive supply and license agreement with the only FDA approved PPS supplier, bene pharmaChem, extending for 25 years post marketing approval.

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.

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

To learn more please visit: www.paradigmbiopharma.com

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