PARADIGM BIOPHARMACEUTICALS LIMITED

ASX RELEASE

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FIRST PATIENT DOSED IN PHASE 2 CLINICAL TRIAL EVALUATING PPS IN MUCOPULYSACCHARIDOSES TYPE-1 (MPS-I)

KEY HIGHLIGHTS

- **MPS-I open label Phase 2 clinical trial has been initiated with the first patient enrolled and treated with their first dose of pentosan polysulfate sodium (iPPS).**
- **The Phase 2 trial will evaluate the safety and tolerability of iPPS in subjects with Mucopolysaccharidosis type I (MPS-I).**
- **Patients in the trial will be sequentially allocated to one of 2 dose cohorts to receive PPS for a 48-week treatment duration.**
- **Phase 2 trial will be Paradigm's first in MPS-I patients and will investigate treatment in a population including pediatric patients. Paradigm previously in-licensed the MPS indication from Icahn School of Medicine at Mount Sinai, New York.**
- **Initiation of study represents the culmination of partnering with global and local key opinion leaders in MPS, to develop a robust study design investigating the role of PPS in the unmet need in the MPS population.**
- **Paradigm's open-label study for MPS-I to be conducted at Adelaide's Women's & Children's hospital with Dr David Ketteridge as the Principal Investigator.**

Paradigm Biopharmaceuticals Ltd ("PAR" or the "Company") is pleased to announce the initiation of a Phase II clinical trial of sub cutaneous injectable Pentosan Polysulphate Sodium (iPPS), in patients with the ultra-rare Orphan disease Mucopolysaccharidosis Type 1 (MPS-1). The study will be conducted at the Adelaide Women's and Children's Hospital (WCH) with Dr David Ketteridge, the Principal Investigator (PI) and Dr Drago Bratkovic (Head of the Metabolic Clinic) leading the clinical trial. The Principal Investigator Dr David Ketteridge, is a Paediatrician and Metabolic Physician at the Adelaide WCH, and has extensive experience in treating Lysosomal Storage Disorders. The first patient to be enrolled in the study has completed screening and has received the first dose of iPPS.

MPS-I Open Label Phase 2 Clinical Trial

Mucopolysaccharidosis type I **(MPS-I)** is a rare inborn metabolic disorder caused by a genetic defect in the catabolism of two glycosaminoglycans (GAGs): heparan sulphate and dermatan sulphate. Disorders in the catabolism of these GAGs interfere with cellular function, resulting in abnormal bone development, growth retardation, cardiac and respiratory problems, and sometimes cognitive impairment (Schroeder et al. 2013). The current treatments Enzyme Replacement Therapy (ERT) and/or Hematopoietic Stem Cell Therapy (HSCT) are available and indicated for people diagnosed with MPS-I to treat the underlying disease by reducing the accumulation of glycosaminoglycans (GAGs).

Paradigm's open-label Phase 2 trial will primarily assess the safety of Pentosan Polysulphate Sodium (PPS) in patients with MPS-I. Secondary objectives of the study will be to evaluate if PPS can successfully alleviate pain and functional symptoms in MPS-I patients who have received ERT and/or HSCT, where these patients continue to have residual musculoskeletal symptoms (joint pain, muscle pain and limited range of motion in various joints). Patients will be dosed for 48 weeks and will be evaluated according to incidence of treatment-emergent adverse events (TEAEs) and changes in clinical laboratory data, pain and function.

The open label study will recruit up to 10 participants (male and female) aged 5 years or greater who meet specific inclusion criteria. Participants enrolled into the study will be sequentially assigned to one of two dosing cohorts (0.75mg/kg and 1.5mg/kg) and study drug will be administered via subcutaneous injection weekly for the first 12 weeks and then every second week until week 48.

Paradigm has previously reported that MPS-1 has been granted Orphan Designation by both the US FDA and EMA.

Paradigm CEO, Paul Rennie on the initiation of the Open Label Phase 2 trial:

"It is personally gratifying to see Paradigm's study successfully progressing in what is an ultra-rare disease state where patients still experience unmet need. The data collected from the Phase 2 trial will be vital to support Paradigm's future regulatory filings and applications for the development of PPS as a potential adjunctive therapy to Enzyme Replacement Therapy (ERT) treatments. Our MPS programs will treat subjects as adjunct to ERT as well as previously bone marrow transplanted patients who may or may not remain on ERT".

"I am pleased to report to our shareholders that Paradigm is making significant progress in the clinical development of PPS in both of our two programs of osteoarthritis (Zilosul®) and the rare disease of MPS. It is important to note both the US FDA and EU EMA have confirmed MPS is an orphan indication and as such the commercial advantage of an orphan drug is the 7-year regulatory exclusivity awarded to orphan drugs".

Adelaide Women's and Children's Hospital – Metabolic Clinic

The Metabolic Clinic at the Women's and Children's hospital in Adelaide aims to make children and adults with metabolic problems as healthy as they can be, treating each person as an individual, but part of a family and society. The clinic works in partnership with families to provide the best possible care.

The Clinic provides a multidisciplinary service caring for children and adults who are born with problems caused by missing enzymes affecting their metabolism, and also with children and adults whose doctors suspect they might have a problem. The Clinic looks after most of the children in South Australia who have problems picked up by the Newborn Screening Test.

The Clinic is headed up by Dr Drago Bratkovic and has a number of skilled specialists including metabolic doctors, dietitians, psychologists, social workers and nurses who have been trained to look after people with metabolic disorders. Dr David Ketteridge is a Staff Specialist Paediatrician and Metabolic Physician at the Women's and Children's Hospital and works alongside Dr Bratkovic in the Metabolic Clinic. Dr Ketteridge will be the Principal Investigator for Paradigm's Pilot Study.

About Paradigm Biopharmaceuticals

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

[1]Aldenhoven, Sakkers, Boelens, de Koning, & Wulffraat, 2009; Beck et al., 2014; Bittar, 2018; Schroeder et al., 2013.

To learn more please visit: www.paradigmbiopharma.com

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