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MPS I phase 2 clinical trial shows promising results of primary, secondary, and exploratory endpoints.

KEY HIGHLIGHTS

- Primary Endpoint attained: iPPS was well tolerated with no serious adverse events reported out to 73 weeks.
- Secondary Endpoints also attained; meaningful improvements in pain, function, and activities of daily living and an overall improvement in quality of life were observed in all patients.
- Changes in biomarker profiles at 49 and 73 weeks of iPPS treatment suggest that iPPS has the potential to modulate the biomarkers that are associated with joint degeneration and arthralgia in MPS I patients.
- The predominant MPS I GAG fragment decreased from baseline at Week 73.
- Aggregate (paediatric and adult) PROMIS T scores for pain behaviour, pain interference, and fatigue improved in all subjects evaluated at all timepoints (Weeks 49 and 73).

Paradigm Biopharmaceuticals Ltd (ASX:PAR) ("Paradigm" or "the Company"), report a top-line summary of outcomes from the phase 2 open-label, single centre pilot study to evaluate injectable pentosan polysulfate sodium (**iPPS**) treatment in subjects with mucopolysaccharidosis type I (**MPS I**). Four subjects (n=4) were sequentially allocated to Cohort 1 (0.75 mg/kg) or Cohort 2 (1.5 mg/kg) and administered iPPS subcutaneous injections once weekly through to Week 12, then fortnightly to Week 48. Eligible subjects were invited to continue in a study extension for an additional 6 months of treatment (Week 72). The MPS I clinical trial has shown positive outcomes in primary, secondary, and exploratory endpoints, supporting iPPS as an adjunct therapy to treat the residual joint pain and reduced function observed in MPS I sufferers.

The results from this study in MPS I are a significant development in the treatment of this rare disease. This release details the summary of outcomes from the Phase 2 trial only, as Paradigm intends to release the complete data set in a peer reviewed publication.

MPS I is a rare disease caused by reduced levels, or the complete lack of an enzyme responsible for the catabolism (break down) of glycosaminoglycans (**GAGs**). This disruption of normal cellular processes results in the progressive accumulation of GAGs in bodily tissues. The disorder causes problems with neurological, skeletal, and cardiovascular development. There is no cure and children born with the most severe form of MPS I do not typically survive beyond 10 years of age without treatment. Current standard treatments include bone marrow transplant and enzyme replacement therapy to address the underlying cause of the disease.

The primary objective of the study was to evaluate safety and tolerability of iPPS over an initial 48-week treatment period, with a 6-month treatment extension available, in patients treated with the current standard of care. Secondary and exploratory

objectives included examining the effects of iPPS on pain, function, and quality of life, pharmacokinetics, biomarkers of inflammatory processes. The study was conducted at the Adelaide Women's and Children's Hospital with Dr David Ketteridge, the Principal Investigator and Dr Drago Bratkovic (Head of the Metabolic Clinic) leading the clinical trial.

Paradigm Managing Director, Mr Paul Rennie commented: "*The top-line summary of results from this phase 2 trial are a significant outcome not only for Paradigm but also for those with MPS who suffer ongoing pain and joint disfunction. The Company is in the process of developing a manuscript for peer review publication and look forward to sharing the full data and outstanding results with investors and the MPS community. I congratulate the Paradigm MPS team for the completion of this study and the data produced prior to our reported timelines*".

Top-Line Data Summary

The primary endpoint, safety, and tolerability of iPPS in subjects with MPS I, showed positive outcomes in the phase 2 study. Subcutaneous iPPS was well tolerated at doses of 0.75 and 1.5 mg/kg out to 72 weeks of dosing with no serious adverse events reported.

Secondary and exploratory endpoints assessed the efficacy of iPPS in MPS I subjects. A summary of secondary and exploratory outcomes include:

- Improved outcomes in physical tests (e.g., 2-minute and 6-minute walk tests, gait/stairs/Gower's/chair test, 9-hole peg test) demonstrating improved mobility and dexterity.
- Improvements in patient reported outcomes (PRO) of pain, function, fatigue, and quality of life.
- Changes in the profile of biomarkers after 48 and 72 weeks of iPPS treatment suggest that PPS has the potential to modulate bone and cartilage degradation biomarkers that are associated with cartilage loss and arthralgia in MPS I patients.
- Reduction from baseline (standard of care) in urinary MPS I GAG fragments.

Paradigm Global Head of Safety and MPS, Dr Michael Imperiale commented: "*I am very pleased that iPPS has demonstrated a favourable safety profile, along with significant improvements in both biomarkers and clinical outcomes in MPS I patients. Paradigm is encouraged that iPPS may be an important addition to the armamentarium for treating this devastating disease.***"**

About Paradigm Biopharmaceuticals

Paradigm Biopharmaceuticals Ltd. (ASX:PAR) is a late-stage drug development company driven by a purpose to improve patients' health and quality of life by discovering, developing, and delivering pharmaceutical therapies. Paradigm's current focus is developing injectable (subcutaneous) pentosan polysulfate sodium (**iPPS**) for the treatment of diseases where inflammation plays a major pathogenic role, indicating a need for the anti-inflammatory and tissue regenerative properties of iPPS, such as in osteoarthritis (Phase 3) and mucopolysaccharidosis (Phase 2).

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 the Paradigm Board of Directors.

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