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Paradigm Reports Successful Safety Review in MPS VI Phase 2 Clinical Trial and update on timing of PARA_008 top-line data readout.

KEY HIGHLIGHTS

- In Paradigm's mucopolysaccharidosis VI (**MPS-VI)** phase 2 trial based in Brazil, the safety monitoring physician for the MPS-VI study confirmed successful evaluation of subjects aged 9 to 16 years.
- Paradigm may now commence screening in the youngest patient cohort of 5- to 9-year-olds.
- The first patient in this youngest cohort has entered screening in Brazil.
- These additional age groups are highly relevant to future potential therapeutic registration as the disease is detected and can manifest early in children and adolescents.
- Over 50% of the planned number of subjects have been recruited to the 24-week study comparing pentosan polysulfate sodium (**PPS**) to placebo.
- PPS is a non-opioid subcutaneous injectable with the potential to treat residual musculoskeletal symptoms in MPS patients.
- **Business Update**: Paradigm confirms the release of the top-line PARA_OA_008 and preliminary analysis of PPS treated canine's that have completed the day-56 follow-up, during September.

Paradigm Biopharmaceuticals Ltd (ASX: PAR) ("Paradigm" or "the Company"), a late-stage drug development company focused on delivering new therapies to address unmet medical needs, is pleased to provide an update on the ongoing multi-centre double-blind randomised phase 2 study comparing PPS to placebo in mucopolysaccharidosis type VI (**MPS-VI**) patients. The safety monitoring physician for this trial being conducted in Brazil has confirmed a safety review has been completed with no serious adverse events reported in the 9- to 16-year-old cohort. This is another key milestone for the phase 2 study, which now allows the inclusion of subjects aged 5 to 9 years to assess the safety and tolerability of PPS amongst this paediatric population.

The paediatric baseline data demonstrate how these children continue to experience joint pain and stiffness that limits their mobility and function despite ERT therapy. Therefore, early therapeutic intervention is critical in this paediatric population to improve symptoms that remain. PPS is a non-opioid subcutaneous injectable with the potential to treat residual musculoskeletal symptoms in MPS as an adjunct therapy to current standards of care. Previous studies have shown PPS improves pain and function in patients with MPS I, MPS II and MPS VI [1, 2, 3].

Paradigm's Global Head of Safety and Head of the MPS program, Dr. Michael Imperiale, said "We are working closely with our sites to provide comprehensive

monitoring, and pleased to report that patients are tolerating the therapy well as we work to address this important unmet medical need in MPS VI patients."

MPS-VI multi-centre double-blinded phase 2 trial

Brazil has one of the largest populations of MPS-VI patients globally so researchers there are evaluating the use of Paradigm's PPS to treat MPS-VI patients in a phase 2 study. The study is randomised, double-blind, and placebo-controlled to evaluate the safety and tolerability of PPS in patients with MPS-VI. According to the study protocol, approximately 12 patients will be randomised 2:1 to receive PPS or placebo. Participants are dosed weekly for 24 weeks with the primary endpoint being safety. The secondary endpoints are improvements in pain and function. This study is the largest of its kind in the world and has attracted the interest of medical researchers and MPS patient advocacy groups globally.

To date, three adult and three adolescent subjects have been enrolled in the study and ninety weeks of cumulative data across the subjects have been assessed. Paradigm expects to randomise the next participant shortly following the completion of this safety review as per the protocol.

Paradigm's CEO, Marco Polizzi, said "It is pleasing to have reached yet another milestone in this phase 2 MPS study. The ability to include the youngest patient cohort following a positive safety review is important for the commercial potential of PPS to treat the residual symptoms that impact the daily activities of MPS sufferers. Paradigm looks forward to further updates as we progress toward the completion of this study in calendar year 2023."

Business Update

PARA_008 Clinical Study: Paradigm would like to confirm the release of top-line data from the PARA_OA_008 phase 2 clinical trial and preliminary analysis of PPS - treated dogs that have completed follow-up, by September 30.

Day 56 is an early time-point, and the Company is hopeful for positive trends at Day 56 but the data at the 6-month time point will provide further insights to the DMOAD capabilities of the drug along with imaging data (MRI) and clinical effect data (pain and function).

Day 56 data from the PARA_OA_008 trial is currently being analysed by an independent clinical research organisation to then be prepared for market release. The data anticipated to be released to the market will include synovial fluid biomarker trends from baseline for the two PPS treatment groups (once and twice weekly) and placebo group. Paradigm will also report change in WOMAC® pain and function from baseline data for the two PPS treatment groups vs the placebo group.

Canine Study: Early interim observations in osteoarthritic dogs administered PPS subcutaneously at a dose of 3 mg/kg (human equivalent dose of 1.7 mg/kg) weekly for 6 weeks, will also be reported with the PARA_OA_008 human clinical trial data. This will be an early examination of dogs that have completed the day 56 follow up, with further data from the 20-week follow-up (3-year human equivalent) to be reported in CY 2023. The

longer follow up period at week 26 in the study will allow for assessment of the durability of response and structural changes following PPS treatment.

Mucopolysaccharidoses

The mucopolysaccharidoses and related disorders belong to a group of more than 40 inherited lysosomal storage diseases. Lysosomes are the recycling centres of all cells that break down excess or worn-out cell parts with their digestive enzymes. Mucopolysaccharidosis disorders are due to errors with one of the enzymes that break down and recycle glycosaminoglycans (**GAGs**), previously known as mucopolysaccharides. As these waste products cannot be eliminated, they accumulate within the lysosomes of virtually every type of cell in the body, causing cells, tissues, and organs to function abnormally, leading to progressive damage. The heart, bones, joints, respiratory system, and central nervous system, including cognitive function, may eventually be affected. In most cases, symptoms are not apparent at birth, but emerge gradually as a result of defective lysosomal storage and resulting cell damage over time [(4,5)]. Eleven different types of mucopolysaccharidosis have been described, where each is the result of a deficiency in one of the enzymes in the glycosaminoglycan degradation pathway.

Mucopolysaccharidosis type VI, also known as Maroteaux-Lamy syndrome, is an ultra-rare autosomal recessive lysosomal storage disorder that affects between 0.36 and 1.30 of every 100,000 live births[(6)]. It results in the development of multisystem clinical manifestations. Mucopolysaccharidosis type VI disorders range from very slowly to rapidly progressing, depending on the specific disease-causing mutation.

Current treatments for MPS VI patients include enzyme replacement therapy, however MPS-VI patients undergoing this therapy continue to report ongoing stiffness, pain, and inflammation which impacts their activities of daily living. The current standards of care are not adequate in treating the pain associated with joint inflammation and musculoskeletal issues.

With approximately 1900 people living with MPS VI, the global opportunity for an adjunctive treatment for residual musculoskeletal symptoms is in the tens of millions of dollars annually.

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 is currently developing pentosan polysulfate sodium for the treatment of pain associated with musculoskeletal disorders driven by injury, inflammation, ageing, degenerative disease, or genetic predisposition, such as 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.

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