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PARADIGM RECEIVES KEY APPROVALS FOR PHASE 2 CLINICAL TRIAL TREATING MPS-VI SUBJECTS WITH PPS IN BRAZIL

KEY HIGHLIGHTS

- Regulatory approval from Brazil's National Health Surveillance Agency (Agência Nacional de Vigilância Sanitária (**ANVISA**)) for a Phase 2 clinical trial evaluating safety and tolerability of injectable (SC) pentosan polysulfate sodium (i**PPS**) versus placebo in subjects with Mucopolysaccharidosis type VI (**MPS VI**).
- Paradigm Biopharmaceuticals Ltd (**Paradigm**) has also received ethics approval from the National Research Ethics Commission (Comissão Nacional de Ética em Pesquisa (**CONEP**)) for the Phase 2 clinical trial.
- The Phase 2 trial will recruit twelve (n=12) MPS-VI participants across two sites in Brazil. Eight (n=8) subjects will receive PPS and four (n=4) subjects will receive placebo.
- Primary objective of the study will be to evaluate the safety and tolerability of PPS in subjects with MPS VI at 6, 12 and 24 weeks.
- Secondary endpoints will include effect of PPS on pain, function and glycosaminoglycan (**GAG**) levels at 6, 12 and 24 weeks.
- Brazil has the highest concentration of MPS-VI sufferers globally. Dr. Roberto Giugliani, MD, PhD, MSc will be the first Principal Investigator for the study.
- This will be the largest clinical trial conducted using PPS in any MPS type subjects. Paradigm's MPS program has received Orphan Drug Designation status in the US and EU for MPS I and MPS VI.

Paradigm Biopharmaceuticals Ltd (ASX: PAR), a clinical stage biopharmaceutical company focussed on repurposing existing molecules for new indications with unmet clinical needs, is pleased to announce it has received regulatory approval from the Brazilian National Health Surveillance Agency, ANVISA, and ethics approval from CONEP, the Brazilian national ethics committee, for its Phase 2 clinical trial evaluating PPS in patients with MPS VI. This will be the largest clinical trial to date using PPS in any MPS type. A successful trial outcome will support partnering discussions for a registrational study to support the use of PPS, in conjunction with enzyme replacement therapy (**ERT**), in this orphan disease population.

The Principal Investigator for the Phase 2 study will be Dr. Roberto Giugliani, MD, PhD, MSc. 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. Giugliani's research interest is the field of inborn errors of metabolism, particularly lysosomal disorders. He has supervised the post-graduate studies of more than 50 MSc/PhD graduates and has more than 220 papers published in international journals.

Trial Design

The phase 2, randomized, double-blind, placebo-controlled study will evaluate the safety and tolerability of PPS in treating subjects with MPS VI who exhibit pain and functional deficiency due to musculoskeletal symptoms associated with the underlying disease. Twelve (n=12) subjects will be recruited into the study and randomised 2:1, with eight (n=8) receiving PPS and four (n=4) receiving placebo. All MPS VI subjects will receive ERT throughout the study. Subjects will receive PPS at a 1.5 mg/kg (≥9 years of age) or 1.0 mg/kg (<9 years of age) dose or placebo by sub-cutaneous injection once weekly for 24 weeks.

Study Endpoints

The primary objective of the Phase 2 study will be to evaluate the safety and tolerability of PPS in subjects with MPS VI at 6, 12, and 24 weeks.

Paradigm will assess a number of key secondary and exploratory endpoints, including effect of PPS on:

- Pain and function (mobility);
- Urinary GAG levels;
- Walking-related pain;
- Quality of Life, activities of daily living, subject/parent global impression of response to therapy; and
- Pulmonary function.

Mr. Paul Rennie, Paradigm's Chief Executive Officer, said:
"We are delighted to achieve this regulatory milestone during a busy period with the IND application process with the US FDA for our lead indication in Osteoarthritis. Paradigm will be monitoring the current COVID situation in Brazil to plan the trial commencement and will update the market once a timeline is determined".

About MPS

The MPS is a family of orphan diseases. The cumulative rate for all types of MPS is around 3.5 in 100,000 live births and generally the patients present in one of three ways:

1. As a dysmorphic syndrome (MPS IH, MPS II, MPS VI) often with early onset middle ear disease, deafness, or upper airways obstruction.
2. With learning difficulties, behavioural disturbance and dementia and mild somatic abnormalities (MPS III).
3. As a severe bone dysplasia (MPS IV).

MPS VI is recognised as 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.

Current treatments for MPS VI patients include ERT which acts to replace the enzyme deficiency. However, MPS VI patients undergoing ERT therapy continue to report ongoing stiffness, pain and inflammation. The current standards of care are not adequate in treating the pain associated with joint inflammation and musculoskeletal issues.

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.

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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