PARADIGM BIOPHARMACEUTICALS LIMITED

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PARADIGM REPORTS GREATER THAN 50% PAIN REDUCTION ACROSS 205 PATIENTS WITH KNEE OSTEOARTHRITIS

KEY HIGHLIGHTS

- Paradigm reports greater than 50% reduction in pain across 205 patients with knee osteoarthritis.
- Combining the results of the 22 patients with the previously reported 183 patients brings the average reduction in pain scores to 51.3% across a total of 205 patients.
- These results show consistent safety and efficacy across 205 patients.
- The results from these 205 patients provides important Real-World Evidence (RWE).
- RWE provides important safety and efficacy data of the drug when used in everyday clinical practice and will support Paradigm's Phase 3 clinical trial.
- As previously reported, Paradigm has completed the production of its Phase 3 Clinical trial product.
- From Q3 CY2019 doctors will treat patients with the Phase 3 Clinical Trial product under the TGA SAS.

Paradigm Biopharmaceuticals Ltd (ASX: PAR) Paradigm is pleased to report a greater than 50% reduction in pain across 205 patients with knee osteoarthritis (OA). Doctors treated their OA patients with injectable pentosan polysulfate (iPPS) under the Therapeutic Goods Administration Special Access Scheme (TGA SAS).

Combining the results of the 22 patients with the previously reported 183 patients brings the average reduction in pain scores to 51.3% across the 205 patients.

Results from the additional 22 patients have continued to show average knee pain reduction in the total of 205 patients treated under the TGA SAS from 50.3% (n:75); 52.9% (n:100); 51.5% (n:125); 51.2% (n:145); 51.4% (n:183) and 51.3% (n:205).

In the 205 patients treated, 89.7% responded with a reduction in joint pain and 91.2% an improvement in knee function. Patients pain scores were reduced over 51.3% and function was improved 58.4% (on average) from baseline pain scores in 205 patients with knee osteoarthritis (OA) and concurrent Bone Marrow Lesions (BML).

A 51.3% (average) reduction in pain scores, observed with iPPS in a relatively large population (n:205) with knee OA, continues to demonstrate superiority over the "15% pain reduction scores reported for opioid treatments for chronic pain in OA of the knee and hip".[1]

1 Seghal N, Colson J and Smith H; Expert Rev Neurother. 2013;13(11):1201-1220

The comparative effects of iPPS therapy against opioid treatments implies that the patient-reported data have provided evidence of clinically meaningful improvements in chronic pain. **"Clinically meaningful reduction of chronic pain has been defined to be between 25-30% pain reduction"[2]**.

What is Real World Evidence?

When the pharmaceutical agent is used in patients outside a randomised clinical trial it is referred to as Real World Data (RWD) and that RWD provides important clinical evidence (safety and efficacy) on how the agent works in people outside the confines of a clinical trial population and is known as Real World Evidence (RWE).

The results from these 205 patients provides important Real-World Evidence (RWE) which has the potential to be used in combination with data from the Company's Randomised Controlled Clinical Trials to support regulatory filings with the Agencies like the US Food and Drug Administration.

"By supplementing and complementing safety and efficacy data obtained in a narrowly defined (and often optimized) patient population in the clinical trial setting, real world evidence (RWE) may provide stakeholders with valuable information about the safety and effectiveness of a medication in large, heterogeneous populations" [3].

Real World Evidence is also onsidered to be useful in discussing label expansion claims with the Regulatory Agencies and also beneficial in discussions with reimbursement bodies.

The TGA SAS data is collected by the Doctor on a patient-by-patient basis known as Real World Evidence. This is not a clinical trial and the safety and efficacy data is acquired when the drug is used in everyday clinical practice. For a doctor to treat a patient with iPPS under the TGA SAS the patient needs to have failed current standard of care (non-steroidal anti-inflammatories, cortisone, and analgesics). The RWE across 205 patients with knee osteoarthritis (who have failed standard of care) have responded with an average reduction in pain of over 50%.

Paradigm has also received RWE from doctors treating their patients with osteoarthritis of other joints such as the hip, ankle and hands. These data will be released in Q4 CY2019.

Details of case study patients and outcomes

These data pool the patient-reported effects of injectable iPPS on painful OA. The 205 patients are a pool of the results from 24 patients, which were reported in October 2017 (Group 1); 21 patients between November 2017 and February 2018 (Group 2); 30 patients March 2018 and June 2018 (Group 3); 25 patients July and August 2018 (Group 4); 25 patients August and September 2018 (Group 5); 20 patients September and October 2018 (Group 6); 38 patients October and November 2018 (Group 7) and 22 who have been treated and assessed between November 2018 and May 2019 (Group 8).

The 205 patients [118 males and 87 females, median age of 56.5 years (range 18 to 84 years)] had been clinically diagnosed with OA and subchondral BMLs (as determined by multiple MRI). At the onset of PPS treatment:

- All patients were symptomatic with OA pain for at least six months and had failed current standard of care, which involved treatment with analgesics, NSAIDs (non-steroidal anti-inflammatory drugs) or corticosteroids.

[2] Seghal N, Colson J and Smith H; Expert Rev Neurother. 2013;13(11):1201-1220

[3] Katkade V et al "Real world data: an opportunity to supplement existing evidence for the use of long-established medicines in health care decision making" Journal of Multidisciplinary Healthcare 2018:11 295–304

- 70% of the patients had moderate to severe BMLs with a size ranging from five millimetres to more than 20 millimetres in diameter.
- 30% had lesions less than five millimetres in diameter.

Patients were administered with two injections of iPPS per week for three, four or six weeks (a total of 6, 8 or 12 injections). Patients were followed up at four to six weeks following the last treatment. During the course of PPS treatment, patients did not receive NSAIDs or corticosteroid treatment.

Clinical knee pain outcome measures (NRS pain score 0-10) after the initiation of iPPS treatment were as follows:

- 184 out of 205 - (89.7%) patients showed a reduction in pain;
- Average pain reduction was clinically meaningful at 51.3% compared to pre-treatment pain.

Clinical knee function outcome measures (Lysholm Knee Score 0-100) after the initiation of iPPS treatment were as follows:

- 187 out of 205 - (91.2%) patients showed improvement in knee function;
- The average improvement in knee function was clinically meaningful at 58.4% compared to pre-treatment function.

Mr. Paul Rennie, Paradigm's Chief Executive Officer said: *"We are very pleased to see that since October 2017 and after the report of the eighth group of SAS patients there is a consistent average knee pain reduction of greater than 50% across 205 patients".*

"Of important relevance to us is that Paradigm now has accumulated data on 205 patients being successfully treated with iPPS for OA associated BMLs. The number of patients seeking treatment via the TGA SAS is a strong feedback that the patients are receiving a clinically meaningful benefit from the iPPS treatment".

"Our strategy of obtaining real world evidence as we prepare our FDA IND submission for our Phase 3 OA trial will provide valuable data on our newly manufactured Phase 3 trial product and will assist in fine tuning our Phase 3 Trial design."

About injectable PPS

Injectable PPS is not currently registered in Australia, but it is registered in four of the seven major global pharmaceutical markets. In those European markets, injectable PPS is registered as an antithrombotic agent. In Australia, injectable PPS for human use is not currently available for sale. Injectable PPS for human use is only available by inclusion into a Paradigm Sponsored clinical trial or via a treating physician applying for its use in patients via the TGA's SAS - Category B.

To learn more please visit: www.paradigmbiopharma.com

For more information, please contact

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