

ASX RELEASE

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## 50% REDUCTION IN OSTEOARTHRITIS PAIN MAINTAINED

### Key Highlights:

- Paradigm is pleased to report a maintained 50% reduction in pain (on average), from an additional 30 patients with osteoarthritis after treatment with the injectable Pentosan Polysulfate Sodium (PPS).
- Paradigm has now received data from a total of 75 patients treated by their doctors under the Therapeutic Goods Administration Special Access Scheme (TGA SAS).
- In the 75 patients treated, 84.0% responded with both a reduction in joint pain and an improvement in knee function.
- 50% reduction in pain scores observed with PPS is considered superior than the typical 15% pain reduction scores reported for opioid treatments for chronic pain in OA of the knee and hip.<sup>1</sup>
- These patients were treated under a similar dosing regimen as Paradigm's current Phase 2b Osteoarthritis randomised double-blind, placebo-controlled, clinical trial, which is expected to release results in Q4 CY 2018.
- The results from these 75 patients provides important Real-World Evidence data, which can be used in combination with Randomised Controlled Clinical Trials to support product registration for repurposed pharmaceuticals under the 505(b)(2) regulatory pathway.
- Paradigm will continue to report over the coming months on the groups of patients that are currently undergoing treatment from their doctors under the TGS SAS.
- OA is a blockbuster indication, a condition with a significant unmet medical need: therapeutic market size is US\$5bn p.a., whilst the total economic burden in the US alone, is estimated to be US\$128bn<sup>2</sup>.

**Paradigm Biopharmaceuticals Ltd (ASX: PAR)** is pleased to announce that in the 75 patients treated, 84.0% responded with both a reduction in joint pain and an improvement in knee function.

Patients, self-reported pain scores were reduced over 50% (on average) from baseline pain scores in 75 patients with knee osteoarthritis (OA) and concurrent Bone Marrow Lesions (BML). Patients were treated by their doctor with Pentosan Polysulfate Sodium (PPS) under the Therapeutic Goods Administration's (TGA) Special Access Scheme (SAS).

The maintained 50% (average) reduction in pain scores, observed with PPS in 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".<sup>3</sup>

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

<sup>2</sup> National Institute of Health; Emerging drugs for osteoarthritis; Hunter DJ and Matthews G 16(3): 479-491; 2011 September.

<sup>3</sup> Seghal N, Colson J and Smith H; Expert Rev Neurother. 2013;13(11):1201-1220

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The comparative effects of PPS 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"<sup>4</sup>.

These patient-reported outcomes from 75 patients precedes the read-out from Paradigm's Phase 2b randomised, double-blind, placebo-controlled, multicentre, clinical trial, which is expected in Q4 CY 2018. The Phase 2b clinical trial will be supplemented by additional SAS RWE patient groups as and when they are ready to report. The total figure is difficult to estimate due to the ever increasing patient demand to be treated via the TGA Special Access Scheme. Paradigm now envisages that there may potentially be more than 150 patients in total reported on before the Phase 2b clinical trial results.

### **Details of case study patients and outcomes**

These data pool the patient-reported effects of injectable PPS on painful OA. The 75 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) and 30 patients who have been treated and assessed between March 2018 and June 2018 (Group 3).

The 75 patients [38 males and 37 females, median age of 57.8 years (range 31 to 84 years)] had been clinically diagnosed with OA and subchondral BMELs (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.
- 70% of the patients had moderate to severe BMELs 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 PPS per week for three to six weeks depending on the severity of the BMEL (a total of 6 to 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 after the initiation of PPS treatment were as follows:

- 63 out of 75 - (84.0%) patients showed a reduction in pain;
- Average pain reduction was clinically meaningful at 50.3% compared to pre-treatment pain

Clinical knee function outcome measures after the initiation of PPS treatment were as follows:

- 68 out of 75 - (90.6%) patients showed improvement in knee function;
- The average improvement in knee function was clinically meaningful at 67.4% compared to pre-treatment function

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<sup>4</sup> Seghal N, Colson J and Smith H; Expert Rev Neurother. 2013;13(11):1201-1220

Mr. Paul Rennie, Paradigm's Chief Executive Officer said: "We are very pleased to see the third group of Real World Evidence patients report results that are consistent with the first and second groups of patients we treated under the program.

*Of great importance to us is that Paradigm now has data on 75 patients being successfully treated with iPPS for OA associated BMEs. The number of patients seeking treatment via the TGA SAS is accelerating, which we believe is a strong indication that the patients are receiving a clinical benefit from the iPPS treatment.*

*"Furthermore, it is a significant positive outcome that all these patients have on average, a clinically meaningful reduction in pain of 50%. Given these patients have a very similar treatment regimen to subjects being treated under the current Phase 2b Osteoarthritis randomised, double-blind, placebo-controlled, clinical trial and these patients have failed current therapies to treat OA, we feel particularly confident regarding a positive clinical trial outcome, with the expected release of headline results for that trial due in Q4 CY 2018."*

#### **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.

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