ASX RELEASE

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# PARADIGM CONSISTENTLY SHOWS GREATER THAN 50% KNEE PAIN REDUCTION

**Key Highlights:**

- Paradigm has now received data from a total of 125 patients treated by their doctors under the Therapeutic Goods Administration Special Access Scheme.
- Combining today's results of 25 patients with the previously reported 100 patients brings the on average reduction in pain scores of 51.5%.
- The pain reducing effects of iPPS are considered significantly superior than the typical 15% pain reduction scores reported for opioid treatments for chronic pain in OA of the knee and hip.[1]
- These patients were treated under a similar dosing regimen as Paradigm's current 110 participant Phase 2b osteoarthritis randomised double-blind, placebo-controlled, clinical trial, which has completed recruitment and is expected to release results in late Q4 CY2018.
- The results from these 125 patients provides important Real-World Evidence (RWE) data, which can be used in combination with Randomised Controlled Clinical Trials to support product registration for repurposed pharmaceuticals under the US FDA 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 TGA SAS.
- OA is a blockbuster indication, a condition with a significant unmet medical need.

**Paradigm Biopharmaceuticals Ltd (ASX: PAR)** is pleased to announce consitent reduction in pain (on average), from an additional 25 patients with osteoarthritis treated with injectable Pentosan Polysulfate Sodium (iPPS) under the Therapeutic Goods Administration Special Access Scheme (TGA SAS).

Paradigm believes these strong results can be attributed to a vast proportion of the patients (Group 5) undergoing a six week treatment period (replicating the same dosing regimen of the Phase 2b OA clinical trial), suggesting a greater response compared to a three or four week treatment period.

Results from the additional 25 patients have continued to show average knee pain reduction in the total of 125 patients treated under the TGA SAS from 50.3% (n:75); 52.9% (n:100) and 51.5% (n:125).

In the 125 patients treated, 85.6% responded with a reduction in joint pain and 91.2% an improvement in knee function. Patients, self-reported pain scores were reduced over 51.5% and function was

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

improved 69.1% (on average) from baseline pain scores in 125 patients with knee osteoarthritis (OA) and concurrent Bone Marrow Lesions (BML).

A 51.5% (average) reduction in pain scores, observed with iPPS in a relatively large population (n:125) 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".[2]

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"[3]**.

These patient-reported outcomes from 125 patients precede the read-out from Paradigm's 110 participant Phase 2b randomised, double-blind, placebo-controlled, multicentre, clinical trial, which is expected at the end of Q4 CY2018. 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 iPPS on painful OA. The 125 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) and 25 who have been treated and assessed between August and September (Group 5) .

The 125 patients [65 males and 60 females, median age of 57.9 years (range 27 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.
- 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 to six weeks depending on the severity of the BML (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 iPPS treatment were as follows:

- 107 out of 125 - (85.6%) patients showed a reduction in pain;
- Average pain reduction was clinically meaningful at 51.5% compared to pre-treatment pain.

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

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

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

- 114 out of 125 - (91.2%) patients showed improvement in knee function;
- The average improvement in knee function was clinically meaningful at 69.2% 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 fifth group of Real World Evidence patients there is a consistent average knee pain reduction of greater than 50% in the 125 patients".*

*"Of important relevance to us is that Paradigm now has accumulated data on 125 patients being successfully treated with iPPS for knee OA associated BMELs. 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".*

*"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 at the end of Q4 CY2018."*

**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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