ASX RELEASE

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PARADIGM'S OSTEOARTHRITIS TREATMENT MAINTAINS >50% KNEE PAIN REDUCTION

Key Highlights:

- Paradigm has now received knee OA pain data from a total of 145 patients treated with iPPS by their doctors under the Therapeutic Goods Administration Special Access Scheme (TGA SAS).
- Combining today's results of 20 patients with the previously reported 125 patients brings the on average reduction in pain scores to 51.2% across the 145 patients.
- 145 total patients being successfully treated and reported on without any serious adverse events is a significant number of patients over which to report such meaningful reductions in pain scores.
- 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 patient 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 145 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 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, further compounded by the worsening global Opioid Epidemic.

Paradigm Biopharmaceuticals Ltd (ASX: PAR) is pleased to announce consitent reduction in pain (on average), from an additional 20 patients with osteoarthritis treated with injectable Pentosan Polysulfate Sodium (iPPS) under the Therapeutic Goods Administration Special Access Scheme (TGA SAS).

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

Results from the additional 20 patients have continued to show average knee pain reduction in the total of 145 patients treated under the TGA SAS from 50.3% (n:75); 52.9% (n:100); 51.5% (n:125) and 51.2% (n:145).

Paradigm is pleased to report that of the 145 patients that have been treated and reported on there have been no serious adverse events. This provides further validation of the well established safety profile of iPPS, reassuring the Company that a similar safefty profile is likely to be displayed in the current Phase 2b OA/BMEL trial. Having a very safe pharmaceutical treatment is paramount in modern day drug development.

In the 145 patients treated, 86.8% responded with a reduction in joint pain and 91.0% an improvement in knee function. Patients, self-reported pain scores were reduced over 51.2% and function was improved 64.8% (on average) from baseline pain scores in 145 patients with knee osteoarthritis (OA) and concurrent Bone Marrow Edema Lesions (BMEL).

A 51.2% (average) reduction in pain scores, observed with iPPS in a relatively large population (n:145) 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 145 patients precede the read-out from Paradigm's 110 patient 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 200 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 145 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) and 20 who have been treated and assessed between September and October (Group 6).

The 145 patients [76 males and 69 females, median age of 57.4 years (range 18 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.

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

Patients were administered with two injections of iPPS 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 iPPS treatment were as follows:

- 126 out of 145 - (86.8%) patients showed a reduction in pain;
- Average pain reduction was clinically meaningful at 51.2% compared to pre-treatment pain.

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

- 132 out of 145 - (91.0%) patients showed improvement in knee function;
- The average improvement in knee function was clinically meaningful at 64.8% 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 sixth group of Real World Evidence patients there is a consistent average knee pain reduction of greater than 50% in the 145 patients".*

"Of important relevance to us is that Paradigm now has accumulated data on 145 patients being successfully treated with iPPS for 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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