ASX RELEASE

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PARADIGM ACHIEVES 60% REDUCTION IN OSTEOARTHRITIS PAIN

Key Highlights:

- Paradigm is pleased to report that a 60.5% reduction in pain (on average) has been achieved, from an additional 25 patients with osteoarthritis after treatment with the injectable Pentosan Polysulfate Sodium (iPPS)**.** Paradigm has now received data from a total of 100 patients treated by their doctors under the Therapeutic Goods Administration Special Access Scheme (TGA SAS).
- Combining today's results of 25 patients with the previously reported 75 patients increases the average reduction in pain scores to 52.9%.
- 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 100 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 TGS SAS.
- OA is a blockbuster indication, a condition with a significant unmet medical need.

Paradigm Biopharmaceuticals Ltd (ASX: PAR) is pleased to announce a 60.5% 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 4) 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 improved the average pain reduction in the total 100 patients treated under the TGA SAS from 50.3% (n:75) to 52**.**9% (n:100).

In the 100 patients treated, 85.0% responded with both a reduction in joint pain and an improvement in knee function. Patients, self-reported pain scores were reduced over 52.9% and function was

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

improved 67% (on average) from baseline pain scores in 100 patients with knee osteoarthritis (OA) and concurrent Bone Marrow Lesions (BML).

A 52.9% (average) reduction in pain scores, observed with iPPS in a relatively large population (n:100) 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 100 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 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 100 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) and 25 who have been treated and assessed between July and August (Group 4).

The 100 patients [51 males and 49 females, median age of 57.6 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:

- 85 out of 100 - (85.0%) patients showed a reduction in pain;
- Average pain reduction was clinically meaningful at 52.9% 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

- 92 out of 100 - (92.0%) patients showed improvement in knee function;
- The average improvement in knee function was clinically meaningful at 67.0% compared to pre-treatment function.

Mr. Paul Rennie, Paradigm's Chief Executive Officer said: *"We are very pleased to see the fourth group of Real World Evidence patients report results that have outperformed the previous three groups of patients we treated under the program.*

Of great importance to us is that Paradigm now has data on 100 patients being successfully treated with iPPS for OA associated BMELs. 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 greater than 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 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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