PARADIGM BIOPHARMACEUTICALS LIMITED

ASX RELEASE

1st October 2020

ZILOSUL® REDUCES PAIN IN PATIENTS WITH KNEE OSTEOARTHRITIS

KEY HIGHLIGHTS

- Pain reduction in 76 SAS patients (42 new patient data) being treated using the Phase 3 product (Zilosul®) are consistent with prior reports under TGA SAS. The chronic pain response as measured by the WOMAC pain score demonstrated a mean reduction of 47.3%.
- The cumulative patient data collected includes new data on 42 patients and previously reported data on 34 patients.
- Phase 3 clinical trial primary endpoint will assess change in WOMAC pain and WOMAC function from baseline.
- Paradigm previously reported data on the first 34 patients of this cohort, with the mean reduction being 44.9% (Refer ASX Announcement 6th April 2020)
- The WOMAC pain score which is a composite of 5 pain subgroups demonstrated pain reductions across patients in; night-time pain (63.7%); sitting (56.1%), standing (49.8%), walking on flat surface (45.6%) and pain on stairs (39.1%).
- PPS remains well tolerated across SAS and Paradigm's other development programs
- WOMAC reduction from baseline scores were observed at day 84 or week 12.
- Paradigm expects to report on further patients receiving Zilosul® treatment under the SAS program in Q4, 2020

Paradigm Biopharmaceuticals Ltd (ASX: PAR) is pleased to report additional data on patients who received Zilosul® under the Therapeutic Goods Administration (TGA) Special Access Scheme (SAS). Paradigm has received additional data on 42 patients bringing the cumulative average WOMAC reduction in pain from baseline for the 76-patient cohort to 47.3%. In the 76 patients treated, 73.7% reported at least a 25% reduction in WOMAC pain with 52.6% of patients reporting a greater than 50% reduction in WOMAC Pain.

Paradigm released its first set of data using the WOMAC pain scoring index on April 6th (refer ASX announcement) after receiving feedback from the FDA during its pre-IND meeting that reduced WOMAC pain from baseline would be an acceptable endpoint for the company's upcoming Phase 3 trials. Paradigm reported data on the first 34 patients of this cohort, with the mean reduction being 44.9%.

Patients under the SAS program treated across multiple sites have failed alternative therapies. Baseline WOMAC pain scores are recorded prior to commencing the 6-week treatment program where each patient receives 2mg/kg of Zilosul® twice weekly.

SAS data has provided consistent 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]".

About WOMAC Scores

The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)™ is a widely used, proprietary set of standardized questionnaires used by health professionals to evaluate the condition of patients with osteoarthritis of the knee and hip, including pain, stiffness, and physical functioning of the joints. The WOMAC has also been used to assess back pain, rheumatoid arthritis, juvenile rheumatoid arthritis, systemic lupus erythematosus, and fibromyalgia. It consists of 24 items divided into 3 subscales[1]:

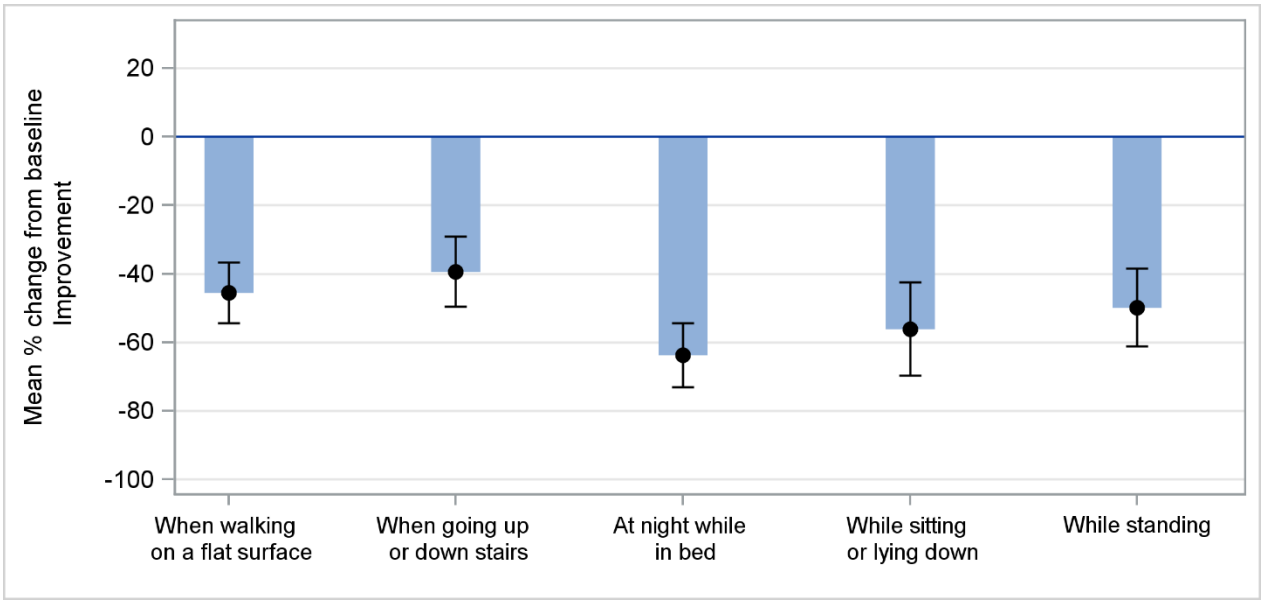
- Pain (5 items): during walking, using stairs, in bed, sitting or lying, and standing upright
- Stiffness (2 items): after first waking and later in the day
- Physical Function (17 items): using stairs, rising from sitting, standing, bending, walking, getting in / out of a car, shopping, putting on / taking off socks, rising from bed, lying in bed, getting in / out of bath, sitting, getting on / off toilet, heavy domestic duties, light domestic duties.

Paradigm's primary endpoint in the forthcoming Phase 3 trial design will be a reduction in pain and function from baseline using the WOMAC osteoarthritis index. **Table 1** below shows the average WOMAC pain reduction (5 items) for 76 patients treated with iPPS under the TGA SAS.

Table 1: Womac Pain Reduction at week 12 (N = 76).

WOMAC Pain Questionnaire	Mean Baseline value (95% CI)	Mean Post-treatment value (95% CI)	Mean % Reduction in Pain (95% CI)
1. Pain Walking on flat surface (0-10)	5.8 (5.3, 6.2)	3.1 (2.6, 3.6)	45.57 (54.4, 36.8)
2. Pain Going up/downstairs (0-10)	7.1 (6.7, 7.6)	4.3 (3.7, 4.9)	39.1 (49.6, 29.2)
3. Pain At night (0-10)	4.8 (4.1, 5.4)	1.9 (1.4, 2.3)	63.75 (73.2, 54.4)
4.Pain Sitting/lying (0-10)	4.2 (3.7, 4.7)	1.9 (1.4, 2.3)	56.12 (69.8, 42.5)
5. Pain Standing upright (0-10)	5.3 (4.8, 5.8)	2.5 (2.1, 3.0)	49.83 (61.1, 38.5)
WOMAC Pain Subscale (0-50)	**27.1 (25.0, 29.3)**	**13.6 (11.3, 15.9)**	**47.30 (59.7, 34.9)**

Table 2: Relative (%) Change from Baseline in WOMAC Pain Scores



Patient Global impression of Change (PGIC) is a self-reported measure that reflects the patient's belief about the overall efficacy of the treatment. Patient's rate their change from No Change (or condition worsened) through to considerable improvement that has made all the difference. Paradigm's Phase 3 trial will include an improved PGIC as an endpoint. Table 3 below shows the PGIC Scores for 76 patients under the TGA SAS.

Table 3: PGIC Score (Subjects with WOMAC scores)

Visit PGIC Scores	WOMAC Subjects (N = 76)
Post-Baseline	
No Change (or condition has got worse)	3 (3.9%)
Almost the same, hardly any change at all	4 (5.3%)
A little better, but no noticeable change	5 (6.6%)
Somewhat better, but the change has not made any real difference	5 (6.6%)
Moderately better, and a slight but noticeable change	19 (25.0%)
Better and a definite improvement that has made a real and worthwhile difference	25 (32.9%)
A great deal better and a considerable improvement that has made all the difference	14 (18.4%)
Missing	1 (1.3%)

76% (58 out of 76) of SAS patients had reported Patient global impression of Change (PGIC) of moderately to definite and considerable improvement in their OA condition with iPPS (Zilosul®) treatment.

Mr. Paul Rennie, Paradigm's Chief Executive Officer said:
"As we progress toward regulatory submissions for Paradigm's proposed Phase 3 global study, its pleasing to receive consistent patient WOMAC pain reduction outcomes through the TGA Special Access Scheme. Consistency is key here. We are seeing consistent clinically meaningful reduction in pain and improvement in joint function in OA patients who have failed to respond to other medications. Paradigm remains primarily focussed on our upcoming submissions to the multiple regulatory agencies as we continue to progress toward commercialisation. Again, I would like to thank all the Doctors who have aided Paradigm in collecting the important patient data from the Special Access Scheme.

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[1] https://www.physio-pedia.com/WOMAC_Osteoarthritis_Index
[2]Seghal N, Colson J and Smith H; Expert Rev Neurother. 2013;13(11):1201-1220

Details of case study patients and outcomes

The 76 patients [43 males, 32 females and 1 unknown with median age of 57.7 years (range 29 to 76 years)] had been clinically diagnosed with OA and subchondral BMLs. At the onset of PPS treatment 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.

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

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

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