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Patients under the TGA SAS program with OA knee pain continue to experience consistent pain reduction and improvement in function.

KEY HIGHLIGHTS

- Pain reduction in 89 SAS patients (13 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 49.6%.
- After 89 SAS treated patients, the pain reducing effects of Zilosul®, in subjects with knee OA as measured using the WOMAC pain score, shows a very consistent reduction in pain of nearly 50%.
- The cumulative patient data collected includes new data on 13 patients and previously reported data on 76 patients.
- The upcoming Phase 3 clinical trial (PARA-002) primary endpoint will assess change in WOMAC pain and WOMAC function from baseline.
- Paradigm previously reported data on the first 76 patients of this cohort, with the mean reduction being 47.3% (Refer announcement 1st October 2020).
- The WOMAC pain score which is a composite of 5 pain subgroups demonstrated pain reductions across patients in; night-time pain (64.6%); sitting (57.6%), standing (52%), walking on flat surface (48%) and pain on stairs (41.5%).
- WOMAC reduction from baseline scores were observed at day 84 or week 12 after the first Zilosul® injection.
- PPS remains well tolerated across SAS and Paradigm's other development programs.
- SAS program is expected to commence in Q3 CY2021 under pay-for-use program, once the first pivotal study has completed recruitment in Australia.

Paradigm Biopharmaceuticals Ltd (ASX: PAR) is pleased to report this ongoing data update on patients who received Zilosul® under the Therapeutic Goods Administration (TGA) Special Access Scheme (SAS). Paradigm released its first set of data using the WOMAC pain scoring index on April 6th (refer ASX announcement) after receiving feedback from the US FDA (Food and Drug Administration) 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 in WOMAC pain being 44.9%. Data from a further 42 patients was released on 1st of October (refer ASX announcement), updating the mean reduction in WOMAC pain across 76 patients to 47.3%.

Paradigm has received additional data on 13 patients bringing the cumulative **average WOMAC reduction in pain from baseline for the 89-patient cohort to 49.6%** (Table 2). In the 89 patients treated with Zilosul®, 75.3% reported at least a 25% reduction in WOMAC pain with 56.2% of patients reporting a greater than 50% reduction in WOMAC Pain.

Patients under the SAS program treated across multiple sites have either failed standard of care and /or 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 [1].

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 [2]:

- **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 endpoints 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 89 patients treated with Zilosul® under the TGA SAS.

Table 1: WOMAC Pain Reduction at week 12 (N = 89).

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)	5.6 (5.2, 6.1)	3.0 (2.5, 3.4)	48.0 (56.2, 39.8)
2. Pain Going up/downstairs (0-10)	7.1 (6.7, 7.5)	4.2 (3.6, 4.7)	41.5 (50.5, 32.5)
3. Pain At night (0-10)	4.6 (4.0, 5.2)	1.8 (1.3, 2.3)	64.6 (73.3, 56.0)
4.Pain Sitting/lying (0-10)	4.1 (3.6, 4.6)	1.8 (1.3, 2.2)	57.6 (69.8, 45.4)
5. Pain Standing upright (0-10)	5.2 (4.7, 5.6)	2.4 (2.0, 2.9)	52.0 (62.2, 41.9)
WOMAC Pain Subscale (0-50)	**26.5 (24.3, 28.7)**	**13.1 (10.9, 15.3)**	**49.6 (60.4, 38.8)**

Figure 1: Relative (%) Change from Baseline in WOMAC Pain Scores

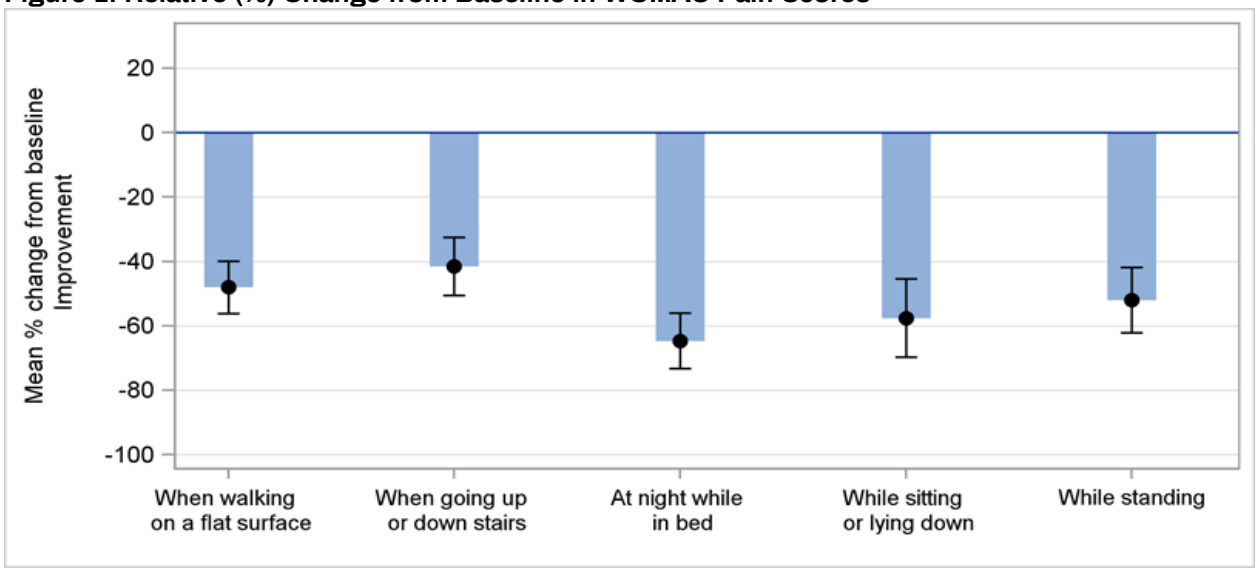

Table 2: Summary of WOMAC Index (n=89)

Scale	Mean Baseline value (95% CI)	Mean Post-treatment value (95% CI)	Mean % Reduction (95% CI)
WOMAC Pain Subscale (0-50)	26.5 (24.3, 28.7)	13.1 (10.9, 15.3)	49.6 (60.4, 38.8)
WOMAC Function Subscale (0-170)	86.1 (77.7, 94.5)	48.3 (41.2, 55.3)	38.4 (51.8, 25.10)
WOMAC Stiffness Subscale (0-20)	12.1 (11.2, 13.0)	6.7 (5.8, 7.7)	34.5 (56.0, 13.0)
WOMAC Total Score (0-240)	**124.1 (112.8-135.5)**	**68.9 (58.8, 79.1)**	**40.1 (54.1, 26.2)**

Patient Global Impression of Change

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 89 patients under the TGA SAS.

Table 3: PGIC Score (Subjects with WOMAC scores)

Visit PGIC Scores	WOMAC Subjects (N = 89)
Post-Baseline	
No Change (or condition has gotten worse)	3 (3.4%)
Almost the same, hardly any change at all	5 (5.6%)
A little better, but no noticeable change	7 (7.9%)
Somewhat better, but the change has not made any real difference	5 (5.6%)
Moderately better, and a slight but noticeable change	22 (24.7%)
Better and a definite improvement that has made a real and worthwhile difference	29 (32.6%)
A great deal better and a considerable improvement that has made all the difference	17 (19.1%)
Missing	1 (1.1%)

76.4% (68 out of 89) of SAS patients had reported Patient global impression of Change (PGIC) ranging from moderately to definite and considerable improvement in their OA condition with iPPS (Zilosul®) treatment.

Special Access Scheme – Pay-for-Use Program

This recent data from 89 patients, updates the current patient cohort under the SAS program for patients with Osteoarthritis. Paradigm treated its first patient under the TGA Special Access Scheme in December 2015, with the program having treated over 480 patients to date with Osteoarthritis. Paradigm's focus will now shift to the initiation and recruitment of Australian patients with Knee OA for, PARA-008 which will evaluate biomarkers in PPS treated subjects, and the Pivotal Phase 3 clinical trials for drug registration. After phase 3 trial recruitment has completed, Paradigm plans to resume participation in the SAS program for patients with OA. The market will be updated when pricing for Zilosul® under the Pay-for-Use program has been confirmed.

Mr. Paul Rennie, Paradigm's Chief Executive Officer said:

"It has been pleasing that as we have had additional patient data reported, we have seen consistent reduction in WOMAC pain with each group of patients with average WOMAC pain reduction across the 89-patient cohort being just under 50%. 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. The focus for Paradigm is firmly on the IND submission this quarter and the initiation and recruitment of our PARA-008 and Pivotal Phase 3 trials. It is very important as Paradigm moves into its Pivotal Phase 3 clinical trial (PARA-002) that we are seeing real world evidence in subjects with knee OA responding in such a positive manner."

Details of case study patients and outcomes

The 89 patients [50 males, 38 females and 1 unknown with median age of 57.7 years (range 29 to 80 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 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.

About Paradigm Biopharmaceuticals

Paradigm Biopharmaceuticals LTD (ASX: PAR) is a late-stage drug development company with the mission to develop and commercialise Pentosan Polysulfate Sodium for the treatment of pain associated with musculoskeletal disorders driven by injury, inflammation, aging, degenerative disease, infection or genetic predisposition.

Forward Looking Statements

This Company announcement contains forward-looking statements, including statements regarding anticipated commencement dates or completions dates of preclinical or clinical trials, regulatory developments and regulatory approval. These forward-looking statements are not guarantees or predictions of future performance, and involve known and unknown risks, uncertainties and other factors, many of which are beyond our control, and which may cause actual results to differ materially from those expressed in the statements contained in this presentation. Readers are cautioned not to put undue reliance on forward-looking statements.

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

[2] https://www.physio-pedia.com/WOMAC_Osteoarthritis_Index

Authorised for release by Paul Rennie, CEO & Interim Chairman.

Zilosul® is a registered Trademark of Paradigm Biopharmaceuticals Ltd (ASX: PAR).

To learn more please visit: www.paradigmbiopharma.com

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