PARADIGM BIOPHARMACEUTICALS LIMITED

ASX RELEASE

30th July, 2020

PARADIGM (ASX: PAR) REPORTS: 65% PAIN REDUCTION IN OA PATIENTS TREATED UNDER THE US FDA EXPANDED ACCESS PROGRAM

KEY HIGHLIGHTS

- **65% mean reduction in WOMAC pain from baseline across total patient population (n=10) using WOMAC Pain Subscale.**
- **WOMAC pain results were reported at week 12 (day 81-83).**
- **All patients in the program reported meaningful improvements in WOMAC Pain, Function and NRS pain (77.79% reduction).**
- **The WOMAC pain score which is a composite of 5 pain subgroups demonstrated pain reductions across patients in; pain walking on flat surface (61.6%), pain on stairs (57.6%), night pain (69.7%), pain sitting (61.6%) and pain standing (68.3%).**
- **Patients in the EAP treated with Paradigm's Phase 3 product was well tolerated with no serious Adverse Events (AE's) reported.**
- **Expanded Access Program Results Presentation released.**
- **Paradigm has also released a Results Video which include testimonials from patients who participated in this program.**

Paradigm Biopharmaceuticals Ltd (ASX: PAR) is pleased to announce a mean pain reduction of 65% at week 12 (Day 81-83), across the ten patients treated with Zilosul® under the FDA approved Expanded Access Program (EAP) in the US.

65% Reduction (from baseline) in WOMAC Pain

"Oral NSAID treatment and potent oral opioids (such as oxycodone) reduced pain with similar effect ie of around a 30% reduction in the patients' pain. In short, each of these medications helped reduce pain, with similar reported effects. The finding on average of 30% reduction in pain is very consistent with studies of many treatments for chronic pain[1]".

A review of many clinical studies (meta-analysis) using the WOMAC pain scale conclude "NSAIDs and opioids offer similar pain relief in OA patients of roughly 30% reduction from baseline[2]".

[1] We estimate each of these medications achieved around a 30% reduction in patients' pain. In short, each of these medications helped reduce pain, with similar reported effects. The finding of a roughly 30% reduction in pain is very consistent with studies of many treatments for chronic pain. While we are fairly good at acute pain management, many chronic pain conditions such as OA, low back pain, and others are harder to treat effectively. (ref: https://www.health.harvard.edu/blog/is-there-a-best-pain-reliever-for-osteoarthritis-201604049398).

[2] NSAIDs and opioids offer similar pain relief in OA patients. Smith S.R. Comparative pain reduction of oral non-steroidal anti-inflammatory drugs and opioids for knee osteoarthritis: systematic analytic review. Osteoarthritis and Cartilage 24 (2016) 962-972.

Paradigm's Zilosul® in the FDA EAP demonstrated a 65% reduction in pain (from baseline) 12 weeks following initiation of treatment. We believe these FDA EAP results, if replicated in a confirmatory Phase 3 clinical study, would provide a compelling product alternative to the use of current treatments of moderate to severe OA pain (NSAIDs and Opioids) as Zilosul® has demonstrated a significant improvement in pain reducing effects over current therapies **(65% vs 30%),** plus both NSAID and Opioids have undesirable side-effects.

So, what does a 65% reduction in pain (from baseline) 12 weeks from the initiation of the treatment mean for further development and commercialization?
Paradigm believes the combined pain reducing effects and tolerance of Zilosul® would allow it to become front-line OA therapy for patients with moderate to severe OA pain that have not responded to initial oral pain therapy.

Paradigm submitted an Expanded Access Investigational new drug application (IND) for pentosan polysulfate sodium (PPS) for the treatment of approximately 10 patients with pain associated with knee osteoarthritis (KOA) with concurrent bone marrow lesions where patients have failed to respond to current standard of care. The US FDA provided clearance for this program to proceed in September 2019.

The US FDA Expanded Access Program

Each Patient enrolled in the program was screened to measure their baseline pain scores under the WOMAC osteoarthritis index and evaluated with MRI scans to determine the presence of Bone Marrow Edema Lesions (BMEL) within the Knee joint.

The EAP commenced on the 18th February with the treatment of the first patient and the last patient completing treatment on the 30th April (refer ASX Announcement). All patients taking part in the study completed regular evaluations with the treating physician (Dr East). Follow up scan and pain measurements were then recorded at 6 weeks post treatment completion (day 81/83).

FDA Expanded Access Protocol Design

Intermediate-size Patient Population Expanded Access (Compassionate Use) Protocol Using Pentosan Polysulfate Sodium (Zilosul®) in patients with Osteoarthritis (OA) of the Knee with Bone Marrow Lesions (BML).

Efficacy Measures	**WOMAC® Osteoarthritis Index (NRS) and NRS Pain (24 hour recall) at week 12**
Safety Measures	Adverse Events, Lab changes, Vital signs
No. Participants	10
Active : Placebo	Open Label
Dosing	2mg/kg Pentosan Polysulfate Sodium (100mg/ml injectable solution), administered by subcutaneous injection, twice weekly for 6 weeks.
Recruitment Sites	1 Site (Texas, USA)

Figure 1: PPS treatment demonstrated reduction in WOMAC Pain Scores at 12 weeks after the initiation of treatment

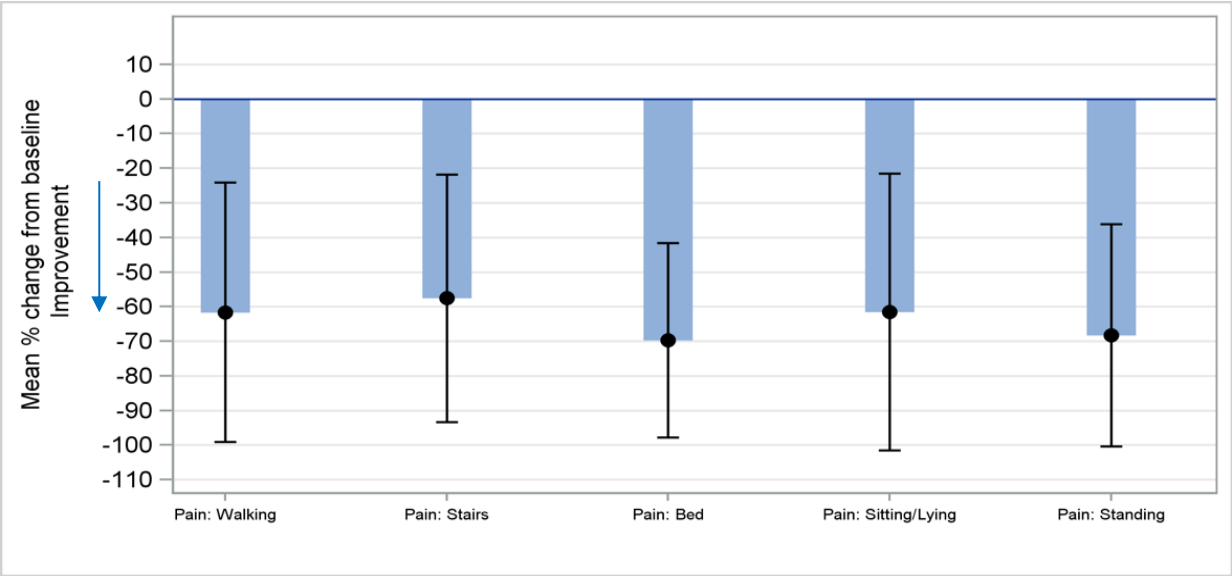
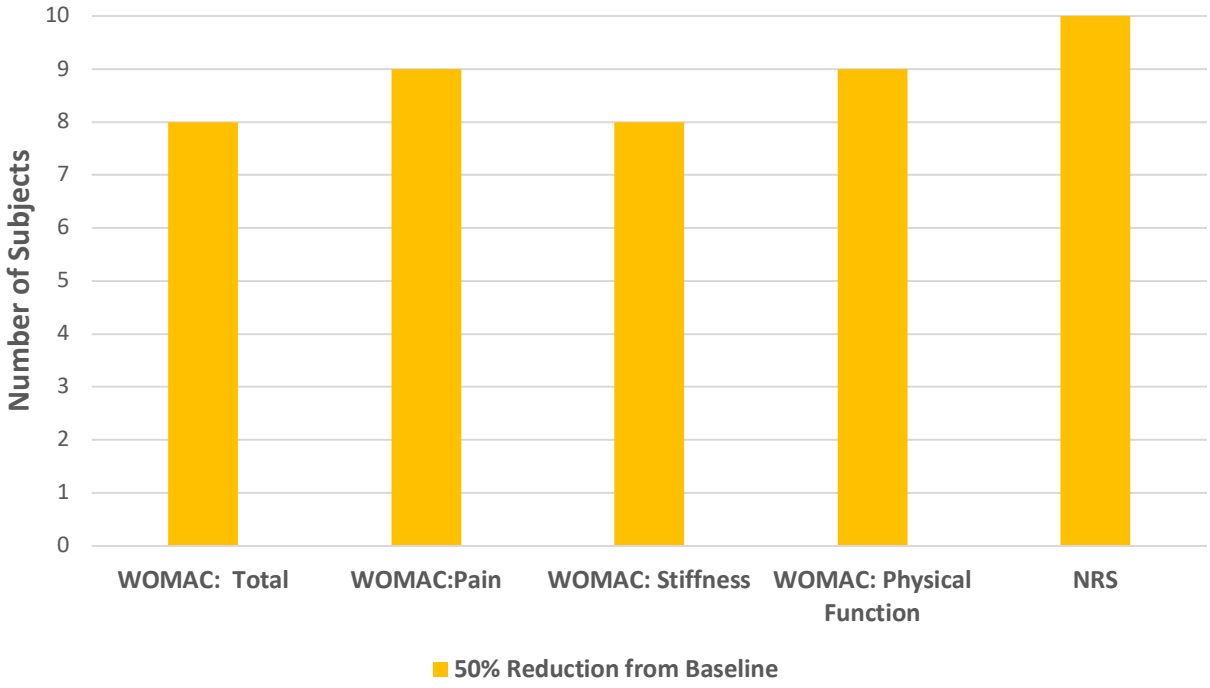


Table 1: Shows the average WOMAC pain reduction (5 items) for 10 patients treated with PPS under the FDA EAP.

WOMAC Pain Questionnaire	Mean Baseline value (95% Confidence interval)	Mean Post-treatment value at 12 weeks (95% Confidence interval)	Mean Reduction in Pain(percentage) (N=10 patients)
1. Pain Walking on flat surface	5.5 (3.8, 7.2)	1.8 (0.3, 3.3)	**61.64 (99.10, 24.18)**
2. Pain Going up/downstairs	7.5 (5.9, 9.1)	2.8 (1.3, 4.3)	**57.59 (93.39, 21.79)**
3. Pain At night	4.5 (2.7, 6.3)	1.1 (-0.1, 2.3)	**69.67 (97.76, 41.58)**
4.Pain Sitting/lying	4.9 (3.0, 6.8)	1.3 (-0.2, 2.8)	**61.57 (101.59, 21.55)**
5. Pain Standing upright	5.8 (4.1, 7.5)	1.7 (0.4, 3.0)	**68.27 (100.31, 36.23)**
WOMAC Pain Subscale	28.2 (20.3, 36.1)	8.7 (2.2, 15.2)	**65.73 (97.08, 34.38)**

These data are well defined within 95% confidence intervals. This means these data have tight standard deviation around the mean with no overlap of intervals between the baseline results and the post PPS treatment results.

Figure 2: Clinically meaningful reduction in WOMAC and NRS Pain Scores after PPS treatment – Number of responders showing greater than 50% reduction in Pain, Stiffness, Physical function and NRS pain from baseline to 12 weeks after the initiation of PPS treatment



Expanded Access Program Results

Paradigm has released a results presentation to accompany this announcement detailing the EAP protocol and subsequent results achieved across the patient population. The company has also produced a video detailing the patients under the EAP and their experiences with OA caused by joint issues sustained during the professional NFL careers. The video presenters are Dr Donna Skerrett (Paradigm CMO), Dr John East (Regenerative Medicine Specialist and treating Physian) and Dr Ravi Krishnan (Paradigm CSO). Results are presented through outcomes data. Patient testimonials of their experiences with Zilosul® treatment are also included in the video.

The Results Presentation and Results Video can be viewed on the Paradigm website www.paradigmbiopharma.com via the below link:

Paradigm's Expanded Access Program Results Presentation and Video

https://paradigmbiopharma.com/investors/presentations/

Mr. Paul Rennie, Paradigm's CEO and Interim Executive Chairman said:

"This is a fantastic outcome not only for Paradigm as our first treatment of a cohort of patients in the US under an FDA approved program, but also for all patients that have participated in the program. Paradigm has previously reported on its completed Phase 2 double blinded placebo controlled study multicentred osteoarthritis clinical trial (AUS), Real World Evidence via the TGA Special Access Scheme (AUS) and now a single arm study via the US Expanded Access Program, with all studies demonstrating Zilosul® has a consistent and durable pain reducing effect on those suffering from Knee Osteoarthritis. We are very encouraged with the EAP results which were reported, at 12 weeks, with the same pain scoring system Paradigm will use in its Phase 3 clinical trial (ie WOMAC)".

"Paradigm would like to thank Dr East and all his staff in Dallas, for all their work and assistance with this program. We would also like to thank the 10 participants in the program and wish them all the best in returning to many activities that had previously been limited by the pain associated with OA".

What is The FDA Expanded Access Program?

"Expanded access" (also called "compassionate use") provides a pathway for doctors and patients to gain access to investigational drugs, biologics, and medical devices used to diagnose, monitor or treat patients with serious diseases or conditions for which there are no comparable or satisfactory therapy options available outside of clinical trials[3].

FDA recognizes that osteoarthritis (OA) can be a serious disease with an unmet medical need for therapies that modify the underlying pathophysiology of the disease and potentially change its natural course to prevent long-term disability.

Through this Expanded Access Program, Paradigm provided Zilosul® (iPPS) to a limited number of patients who have failed other conservative therapies (standard of care), and for whom access was requested by the treating physician.

Early Onset Osteoarthritis in retired NFL Players.

In under the age of males 60, arthritis is over 3 times more prevalent in retired NFL players than in the general U.S. population. This excess of early-onset arthritis may be due to the high incidence of injury in football[4].

About Injectable PPS (iPPS).

Injectable PPS (iPPS) is not currently registered in Australia, but it is registered in four of the seven major global pharmaceutical markets. In those European markets, iPPS is registered as an antithrombotic agent. In Australia, iPPS for human use is not currently available for sale.

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

Authorised for release by Paul Rennie, CEO and Interim Executive Chairman.

[3] https://www.fda.gov/news-events/public-health-focus/expanded-access

[4] Golightly E. et al Journal of Physical Activity and Health, 2009, 6, 638-643

To learn more please visit: www.paradigmbiopharma.com

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