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14 November 2023

Successful OrthoATI™ clinical trial

- **Study demonstrates that the tendon cell therapy (OrthoATI™) is as effective, and potentially better than surgery for severe, chronic treatment-resistant lateral epicondylitis (tennis elbow)**
- **OrthoATI™ patients experienced almost complete resolution of pain by 1-month post-treatment compared to 6 months after treatment in the surgery group**
- **Notably, participants in the OrthoATI™ group demonstrated a statistically significant improvement of return of function in half the time than the surgery group**
- **Participants in the OrthoATI™ group returned to work on average one month (32 days) earlier than the surgery group**
- **Study indicated that OrthoATI™ may be a better alternative to surgery, as it is minimally invasive and cost effective**
- **Study results to be presented by lead study investigator and Clinical Professor Eugene Ek at the 83rd Australian Orthopaedic Association Annual Scientific Meeting**
- **Based on the successful study outcomes, Orthocell will look to appoint a US based corporate adviser to assist the Company in securing a strategic partner to progress OrthoATI™**

Orthocell Managing Director, Paul Anderson, said: *"These significant clinical results display once again the continued success of the Orthocell team, its scientific capabilities, and its potential to provide global therapeutic products. Our decision to appoint a US based corporate adviser will enhance progress of the tendon cell therapy and allow us to continue our focus on FDA approval for our leading nerve repair product, Remplir™."*

Orthocell Limited (ASX:OCC, "Orthocell" or the "Company") is pleased to announce final results from its clinical study comparing OrthoATI™ to surgery for the treatment of severe, chronic, treatment-resistant lateral epicondylitis ('LE Study'). The data confirmed that the study met its primary endpoint, demonstrating that OrthoATI™ is as effective as surgery in the treatment of lateral epicondylitis.

Lateral epicondylitis, (also known as tennis elbow), results in considerable pain and disability and affects millions of people every year. Conservative treatment options, such as rest, nonsteroidal anti-inflammatory drugs (NSAIDs) or physiotherapy are usually effective and the symptoms resolve within 6 months. If symptoms persist, patients may be offered steroid injections to manage the pain and inflammation. However, approximately 10% of patients fail to respond to conservative treatment and steroid injections. For patients with severe, chronic lateral epicondylitis that fails to respond to conservative treatment, recovery without further intervention is unlikely and the only option remaining is surgery. Surgery is invasive, costly, not always successful, and requires strict rehabilitation protocols. OrthoATI™ represents a potential breakthrough non-surgical treatment option to resolve pain and return functional mobility for this debilitating condition.

The LE Study was a statistically powered, randomised, multicenter, open-label, non-inferiority study designed to compare OrthoATI™ to the "gold standard" of surgery for patients with severe, chronic, treatment-resistant LE. The study was led by Clinical Professor Eugene Ek (Monash University), Dr Jason Harvey, Clinical Professor Allan Wang (University of Western Australia), and Professor Ming Hao Zheng (University of Western Australia and co-founder of Orthocell). The LE Study participants suffered from pain and loss of elbow function for over 6 months and had previously received and failed conservative therapy including injectables (corticosteroid/PRP), prior to enrolment in the study.

Following treatment, assessment of pain and function showed that OrthoATI™ was as effective as surgery in treating the symptoms of severe, chronic lateral epicondylitis. Importantly, treatment with OrthoATI™

resulted in reduction of pain and improvement in function sooner than treatment with surgery. Participants in the OrthoATI™ group were also able to return to work on average 1 month sooner than patients treated using surgery.

Orthocell Chief Scientific Officer, Professor Minghao Zheng, said: *"Returning patients to pain free function sooner than surgical repair for severe lateral epicondylitis, is a further validation and significant milestone for the commercial development of OrthoATI™. We are absolutely delighted with the study results and the potential to deliver the first injectable cell therapy in orthopaedics, that truly addresses the cause of injury and returns patients to full use of their chronically damaged tendons without the need for surgery."*

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Summary of results

A summary of the study results are presented below. Please refer to the Detailed Study Description and Results section for more information.

- The study met its primary endpoint, demonstrating that OrthoATI™ is at least as effective, if not better than surgery (the gold standard treatment for severe chronic lateral epicondylitis or tennis elbow);
- Improvement in function (mean QuickDASH scores) in the OrthoATI™ group was demonstrated as early as 3 months post treatment, compared to 6 months in the surgery group. Additionally, the OrthoATI™ group's function scores were on average 15.8 points better than the surgery group at 12 months post-treatment (p=0.0028);
- Improvement in pain scores were observed in the OrthoATI™ group as early as 1 month post-treatment, which continued to improve until 12 months, consistent with previous clinical studies of OrthoATI™;
- Participants in the OrthoATI™ group returned to work on average ~1 month (32 days) earlier compared to the surgery group (19 days OrthoATI™ vs 51 days surgery);
- Improvements in grip strength to levels that were equal to the opposite (healthy) side were observed in the OrthoATI™ group within 6 months post-treatment, compared to 12 months post-treatment in the surgery group;
- Both study treatments were well tolerated, and no safety concerns for OrthoATI™ were identified;
- OrthoATI™ offers other advantages over surgery that may be attractive to patients. It is minimally invasive and does not require strict rehabilitation protocols.

US addressable market

Initial market sizing undertaken by Orthocell suggests that OrthoATI™ could be applicable to >350,000 tennis elbow patients per year in the US alone, which equates to a multi-billion market opportunity[1]. Ongoing work by Orthocell aims to assess the savings to the health system that may be delivered by OrthoATI™ when accounting for more effective pain relief and return of function, return to work and avoidance of surgical costs. OrthoATI™ can be used in both pre-surgical and post-surgical applications, not only in treating tennis elbow, but many other tendon injuries and is at the forefront of a significant and increasing market opportunity.

Special Access Scheme

OrthoATI™ is currently not listed on the Australian Register of Therapeutic Goods (ARTG). Patients are treated with OrthoATI™ in Australia via the TGA's Special Access Scheme (SAS).

[1] Internal Orthocell modelling based on published epidemiology data and assuming target pricing for lateral epicondylitis injury segment.

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Next steps and strategic review

With this successful study in lateral epicondylitis completed, Orthocell is now well positioned to engage partners to explore the next stage of development of the product for US FDA registration. The Company will be reviewing its options to progress OrthoATI™ without the need for significant investment in the near term.

Detailed Study Description and Results

Detailed study description

The LE Study was a statistically powered, randomised, multicenter, open-label, non-inferiority study designed to assess OrthoATI™ compared to surgery (standard of care) to treat patients with severe, chronic, treatment-resistant lateral epicondylitis (tennis elbow). The aim of non-inferiority studies is to determine whether the investigative treatment is as good as (i.e. not inferior) to the standard treatment. Non-inferiority study designs are commonly used to compare markedly different treatment methods.

A total of 48 participants were enrolled in the study. All patients had MRI-verified lateral epicondylitis with >6 months of symptoms and had previously failed conservative therapy. Participants were randomised to receive an ultrasound guided injection of the patient's own tendon-derived cells (OrthoATI™; 24 participants), or the gold standard surgical treatment (surgery; 24 participants).

The primary endpoint for the study was the QuickDASH score (a validated measure of upper limb disability) at 12 months post-treatment. **The study would be considered successful if the OrthoATI™ group had a mean QuickDASH score no more than 15 points worse (i.e. not worse by a clinically important amount) than the surgery group (non-inferiority).** Secondary assessments included pain, grip strength, quality of life, and MRI and were performed before treatment, and for up to 12 months post-treatment. Participant ability and time to return to work was also assessed.

Study outcomes:

Patient characteristics

Both groups were comparable with respect to age, gender, duration and severity of symptoms. Participants had experienced symptoms for an average of 25.7 months prior to study participation, and 90% had failed at least one, sometimes multiple, corticosteroid injections.

Primary outcome:

QuickDASH (quick Disabilities of the Arm, Shoulder and Hand) score

The QuickDASH questionnaire measures symptoms and disability in upper limbs. Eleven items are scored on a scale of 1 (no difficulty) to 5 (unable to perform a task). A higher total score represents greater disability. A reduction in score of 15 points or more is considered to be clinically important.

By the end of the study, participants receiving OrthoATI™ experienced a significant and sustained reduction in symptoms and disability that was as good, if not better than, participants undergoing surgery. At 12 months post-treatment, the OrthoATI™ group had a mean QuickDASH score 15.7 points better than the surgery group (p= 0.0028) (Figure 1).

Secondary outcomes:

Pain Assessment

The Visual Analogue Scale (VAS) pain score rates pain from 0 (no pain) to 10 (worst pain). Participants were asked to rate their pain at its worst, at rest, lifting a heavy object, performing a repetitive task, and at night. A change in VAS pain score of 1.4 points (from pre-treatment score) represents the smallest change that patients

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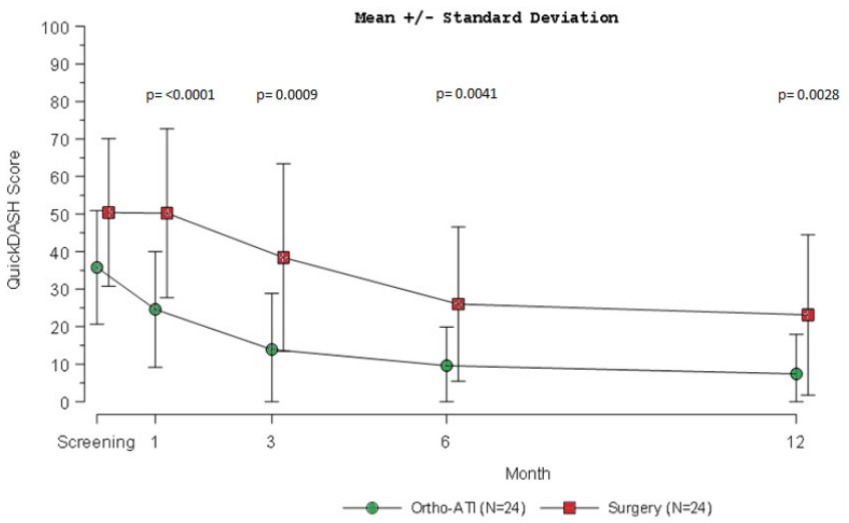
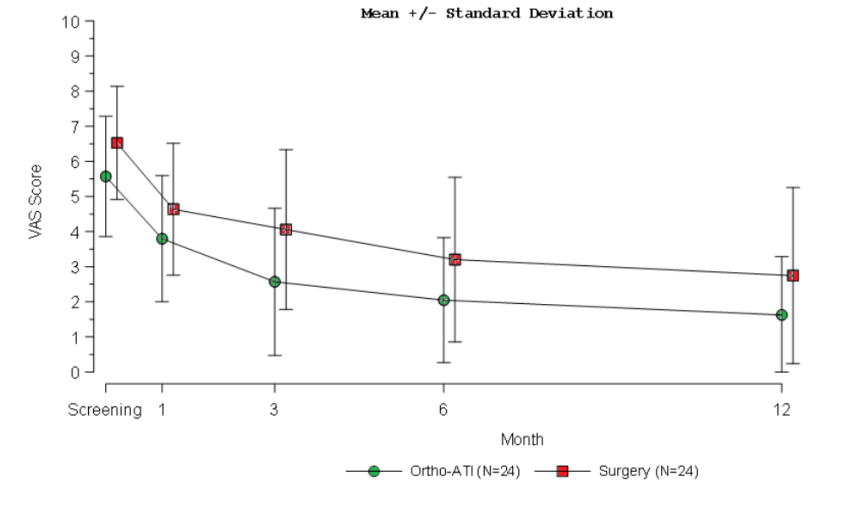
would perceive as improvement. A VAS pain score of 3 or less is considered by patients to be a "successful outcome".

Participants receiving OrthoATI™ experienced a significant and sustained reduction in pain as early as one month after treatments, following a similar pattern to previous clinical studies. Patients treated surgically also experienced a significant reduction in pain over time. The reduction in pain between 1 month and 12 months post-treatment was similar between OrthoATI™ and surgery groups (Figure 2).



- OrthoATI™ group showed meaningful improvements in function as early as 3 months compared to 6 months in the surgery group.
- Significant improvements in QuickDASH scores were observed in both OrthoATI™ and surgery groups from 6 months post-treatment.
- The OrthoATI™ group had significantly better QuickDASH scores than the surgery group at 1 (p= <0.0001), 3 (p= 0.0009), 6 (p=0.0041) and 12 (p= 0.0028) months post-treatment.

Figure 1 – QuickDASH Score Mean QuickDASH score at screening (pre-treatment) and at 1,3, 6 and 12 months post-treatment with ATI or surgery. p values indicate statistically significant differences between treatment groups.



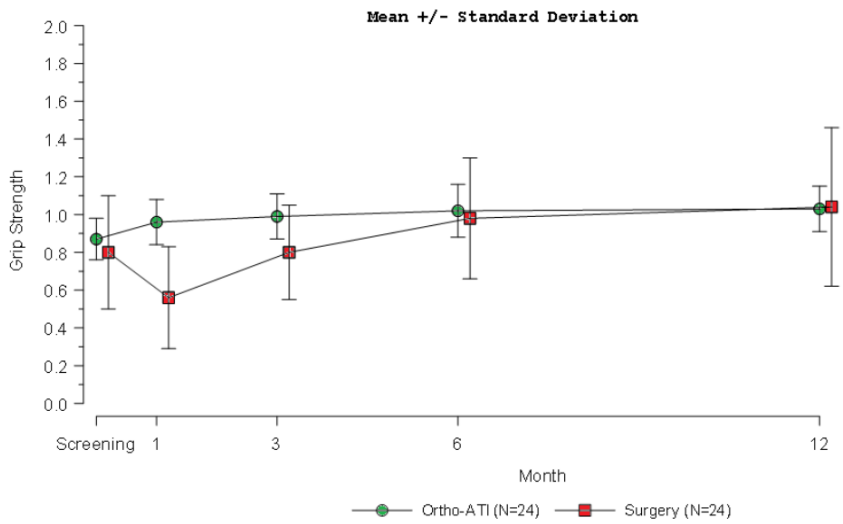
- Both OrthoATI™ and surgery groups showed meaningful reductions in pain as early as 1 month post treatment.
- OrthoATI™ group: VAS score improved from 5.6 (pre-treatment), to 3.8 at 1 month, 2.6 at 3 months, 2.0 at 6 months and 1.6 at 12 months post-treatment.
- Surgery group: VAS score improved from 6.5 (pre-treatment) to 4.6 at 1 month, 4.1 at 3 months, 3.2 at 6 months and 2.7 at 12 months post-treatment.

Figure 2 – VAS pain Mean VAS pain score at screening (pre-treatment) and at 1,3, 6 and 12 months post-treatment with OrthoATI™ or surgery.

Grip strength

Reduced grip strength is a common symptom of lateral epicondylitis (tennis elbow). Grip strength measurements were taken on both hands (affected and unaffected). A score of 1.0 indicates that grip strength

on the side of their injury is the same as the uninjured side. Participants receiving OrthoATI™ had grip strength measurements return to levels equal to their unaffected (healthy) side from 6 months after treatment, compared to 12 months in the surgery group. (Figure 3)



- OrthoATI™ group: Mean grip strength ratio improved from 0.87 (pre-treatment), to 0.96 at 1 month, 0.99 at 3 months, 1.02 at 6 months, and 1.03 at 12 months post-treatment.
- Surgery group: Mean grip strength ratio decreased from 0.80 pre-treatment to 0.56 at 1 month after surgery, as would be expected. Grip strength then improved to 0.80 at 3 months, 0.98 at 6 months, and 1.04 at 12 months post treatment.

Figure 3 – Grip strength Mean grip strength (ratio of injured side to healthy side) at screening (pre-treatment) and at 1, 3, 6 and 12 months post-treatment with OrthoATI™ or surgery.

Return to work

Participants receiving OrthoATI™ returned to work on average 32 days faster than the surgery group. In particular:

- 100% of participants in the OrthoATI™ group returned to work, at an average of 19.3 days after treatment; and
- 80% of participants in the surgery group returned to work, at an average of 51.1 days after treatment.

MRI data

Both treatment groups had improvements in MRI at 12 months, as assessed by a blinded musculoskeletal radiologist. However, MRI is not normally used in clinical practice to assess the effectiveness of treatment. QuickDASH remains the gold standard assessment of treatment efficacy.

About OrthoATI™

OrthoATI™ is an autologous cell therapy comprising tendon derived cells for the repair and relief of chronic tendon injuries. In studies conducted by Orthocell to date, OrthoATI™ has been shown to be a cost effective long-term, non-surgical solution for difficult to treat tendons in the shoulder, elbow, hip, knee and ankle. Treating physicians and insurers are constantly seeking advances in new treatments that are safe, effective and cost efficient. OrthoATI™ addresses these demands by enabling regeneration of injured tendons, directly addressing the underlying cause of injury, replenishing diseased tendon with healthy mature tendon tissue. The treatment has been shown to support patients in their return to recreational activities, the workplace and competitive sports. OrthoATI™ has extensive clinical validation with published clinical data up to 4.5 years post-treatment in leading peer-reviewed journals (e.g. American Journal Sports Medicine), clearly demonstrating durability and efficacy as the leading tendon regeneration treatment.

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Release authorised by Orthocell Ltd Managing Director, Paul Anderson.

For more information, please contact:

General & Investor enquiries

Paul Anderson
Orthocell Limited
Managing Director
P: +61 8 9360 2888
E: paulanderson@orthocell.com.au

Media enquiries

Haley Chartres
H^CK Director

P: +61 423 139 163
E: haley@hck.digital

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About Orthocell Limited

ACN 118 879 135
Registered Office – Building 191 Murdoch University, 90 South Street, Murdoch WA 6150 Australia

Orthocell is a regenerative medicine company focused on regenerating mobility for patients by developing products for the repair of a variety of bone and soft tissue injuries. Orthocell's portfolio of products include CelGro™ platform of collagen medical devices which facilitate tissue reconstruction and healing in a variety of dental and orthopaedic reconstructive applications. Striate+™ was the first product approved for dental GBR applications, is cleared for use in US FDA (510k), Australia (ARTG) and Europe (CE Mark) and is distributed globally by BioHorizons Implant Systems Inc. Remplir™, for peripheral nerve reconstruction, recently received approval and reimbursement in Australia and is distributed exclusively by Device Technologies in the Australian market. SmrtGraft™, for tendon repair, is available in Australia under Special Access Scheme or participation in a clinical trial. The Company's other major products are autologous cell therapies which aim to regenerate damaged tendon and cartilage tissue. Orthocell is accelerating the development of its tendon cell therapy in the US with technology transfer, manufacturing scale up and FDA engagement in advance of a randomised controlled study under FDA supervision.

For more information on Orthocell, please visit www.orthocell.com or follow us on Twitter **@Orthocellltd** and LinkedIn www.linkedin.com/company/orthocell-ltd

Forward Looking Statement

Any statements in this press release about future expectations, plans and prospects for the Company, the Company's strategy, future operations, and other statements containing the words "anticipate," "believe," "estimate, "expect," "intend," "may," "plan," "predict," "project," "target, "potential," "will," "would," "could," "should," "continue," and similar expressions, constitute forward-looking statements. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: the Company's ability to successfully develop its product candidates and timely complete its planned clinical programs and the Company's ability to obtain marketing approvals for is product candidates. In addition, the forward-looking statements included in this press release represent the Company's views as of the date hereof. The Company anticipates that subsequent events and developments will cause the Company's views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, the Company specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing the Company's views as of any date subsequent to the date hereof.