OrthoATI™ rotator cuff clinical study success with cross-over patients

- Previously released results from the successful rotator cuff clinical study showed that **OrthoATI™ was more effective than corticosteroid injection for treatment of rotator cuff tendinopathy** with intrasubstance tendon tear
- **Patients randomised to receive a corticosteroid injection had the option to "crossover" to the OrthoATI™ treatment if there was** a lack of response in the corticosteroid arm of the study
- **82% of participants in the corticosteroid arm elected to crossover to OrthoATI™ and experienced almost complete resolution of pain 6 months post-treatment, which was sustained at 12 months**
- **All crossover participants post OrthoATI™ treatment reported a level of function of the treated shoulder consistent with a successful outcome at 12 months,** after having received an average of 5 failed conservative treatments including physiotherapy and at least 2 steroid injections
- **No participants in the crossover group required additional treatment** for their shoulder injury (e.g. injection/surgery) in the 12 month follow-up period
- **Results in the crossover group mirrored those of the original OrthoATI™ group**, which showed clinically and statistically significant improvements in shoulder pain and function
- There are currently **no proven long-term non-surgical solutions to treat chronic shoulder tendon injuries**
- **OrthoATI™** is well positioned to become **the first FDA-approved injectable cell therapy in orthopaedics** for the treatment of chronic tendon injuries.

Perth, Australia; 29 September 2022: Regenerative medicine company Orthocell Limited (ASX:OCC, "Orthocell" or the "Company") is pleased to announce positive results from the crossover patient extension arm of its randomised, multicentre, controlled rotator cuff tendon clinical study ('RC Study'). This additional data supports the original randomised controlled RC Study results, which demonstrated that OrthoATI™ is a safe and effective treatment for patients suffering from rotator cuff tendinopathy with intrasubstance tendon tear compared directly to the standard of care (steroid injections).

Orthocell Managing Director, Paul Anderson, said: *"*We are delighted with the crossover patient study results clearly demonstrating that OrthoATI™ is more effective than steroid injection for treatment of rotator cuff tendinopathy with intrasubstance tendon tear. This is an important validation for OrthoATI™ and the Company.

We are now in a very strong position to progress our US commercialisation strategy to deliver the first injectable cell therapy in orthopaedics that truly addresses the cause of degeneration and returns patients to full use of their chronically damaged tendons."

Rotator cuff tears lead to considerable pain and disability, and conservative treatment options (such as steroid injections and pain medications which may provide short-term pain relief), do not address the chronic underlying pathology of tendon degeneration. OrthoATI™ represents a potential breakthrough treatment option to resolve pain and return functional mobility for this debilitating condition. **Watch video here.**

To be eligible for the RC Study, participants had to have suffered from pain and loss of shoulder function for at least 6 months (average of 23.5), and had received an average of 4 failed treatments (including physiotherapy, corticosteroid or Platelet Rich Plasma or 'PRP' injections), prior to enrolment. Following treatment, assessment of pain and shoulder function showed that the OrthoATI™ group had significantly better results compared to the steroid group at all post-treatment time points.

Participants in the observational extension study had received at least two corticosteroid injections and had an average symptom duration of 33.1 months, indicating a chronic condition that was unlikely to resolve itself without further treatment.

Leading Australian orthopaedic surgeon and clinical trial lead, clinical professor Allan Wang of UWA, commented: "Patients who received steroid injection in the original study were still experiencing pain and loss of function in their affected shoulder at the end of the study, and the majority requested treatment with OrthoATI™. In the year after their OrthoATI™ treatment, none of the patients required additional medical treatment for their shoulder injury and their symptoms were largely resolved, similar to the patients who received OrthoATI™ in the original trial. These positive outcomes are encouraging and support the results from the original trial."

Summary of results

- Nine of eleven (82%) participants who received corticosteroid treatment in the RC trial requested subsequent crossover treatment with OrthoATI™ due to lack of improvement in their shoulder pain and/or function;
- On average, participants in the crossover group experienced almost complete resolution of pain (VAS score less than 3) by month 6 following treatment with OrthoATI™;
- The crossover group also experienced clinically important improvements in shoulder function (ASES score) at 6 months following OrthoATI™ treatment;
- Results in the crossover group mirror those seen in the OrthoATI™ group in the original RC trial;
- No participants in the crossover group required additional treatment for their shoulder injury within the 12 month follow-up period; and
- No safety concerns for OrthoATI™ were identified.

Clinical trial patient, Paul Speering commented: *"The steroid treatment didn't work and since the OrthoATI™ treatment, as a drug free and fully drug tested athlete, I have become both a Masters National Powerlifting Champion and the Oceanias Masters Powerlifting Champion, and hold all four State Records in my age and weight category. I was so fortunate to be involved in this study, and I wish that more people would be able to take advantage of the treatment. It truly has been life changing for me."*

US addressable market

Initial market sizing undertaken by Orthocell suggests that Ortho-ATI™ could be applicable to >480,000 rotator cuff patients per year in the US alone, which equates to a market opportunity of approximately US$4-5 billion[1]. Ongoing work by Orthocell aims to also 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. Ortho-ATI™ can be used in both pre-surgical and post-surgical applications, not only in treating rotator cuff injuries, but many other tendon injuries and is at the forefront of a significant and increasing market opportunity.

Next Steps

The Orthocell team was responsible for the initial development of a similar cell therapy product for the regeneration of cartilage (known as MACI) which is now being commercialised by US company Vericel, which currently generates more than $120 million in sales and is only used to treat one target joint in the body. Vericel currently has a market capitalisation of approximately $1.2 billion.

[1] Internal Orthocell modelling based on published epidemiology data and assuming target pricing for a subset of the rotator cuff injury segment.

Orthocell is in a strong position to advance its US commercialisation strategy to deliver the first injectable cell therapy in orthopaedics for the treatment of chronic tendon injuries.[2] The results of this study demonstrate that OrthoATI™ is more effective than steroid injections for treatment of rotator cuff tendinopathy with intrasubstance tendon tear. The Company continues to progress its US plans with the evaluation of technology transfer options, FDA engagement and commercial preparation activities to prepare OrthoATI™ for a randomised controlled study under FDA supervision.

Clinical trial investigators

The observational extension study has been led by Clinical Professor Allan Wang (former President of the Australian Elbow and Shoulder Society, Associate Professor and specialist sports and exercise medicine physician Jane Fitzpatrick, and Professor Ming Hao Zheng (University of Western Australia and co-founder of Orthocell). Dr Jeff Hughes (current President of the Australian Elbow and Shoulder Society) was an investigator in the full RC study.

Detailed study description

The RC Study was a randomised, multicenter, open-label study designed to assess OrthoATI™, in comparison to steroids (standard of care), as an emerging treatment for patients with rotator cuff tendinopathy with intrasubstance tendon tear. A total of 30 participants verified by MRI with symptom duration >6 months, and who had previously received physiotherapy AND one or more corticosteroid injections were treated. Participants were randomised to receive an ultrasound guided injection of tendon derived cells that had been cultured from a sample drawn from each patient (OrthoATI™; 19 patients), or an ultrasound guided injection into the subacromial space of Celestone Chronodose (steroid; 11 patients).

Assessment results

Assessments of shoulder function, pain, and quality of life were performed using validated outcome measures before treatment, and for up to 12 months post-treatment.

Visual Analogue Scale Pain Assessment

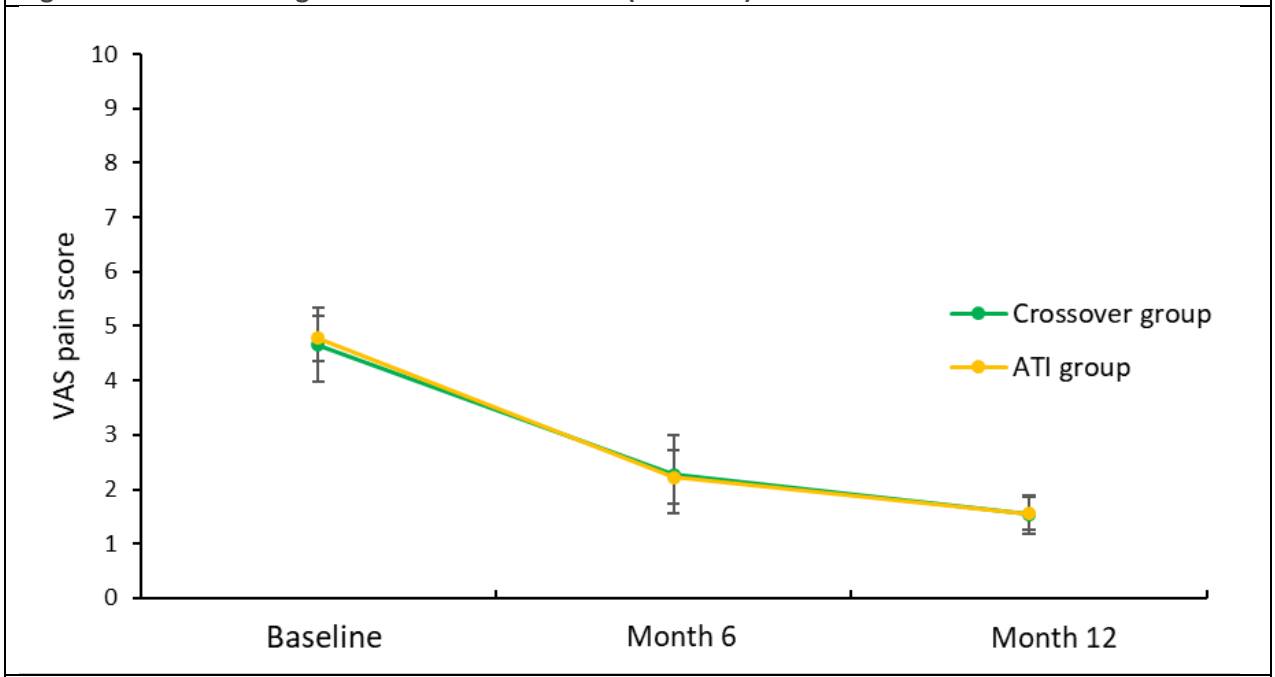
The Visual Analogue Scale (VAS) pain score rates pain from 0 (no pain) to 10 (worst pain). Participants were asked to rate their pain at its worst, at rest, lifting a heavy object, performing a repetitive task, and at night. An overall pain score for each participant visit was calculated by taking the mean of reported scores for individual ratings. **A change in VAS pain score of 1.4 points represents the smallest change in score that patients would perceive as a meaningful improvement**. **A VAS pain score of 3 or less is considered by patients as a "successful outcome".**

After OrthoATI™ treatment, participants experienced a meaningful and sustained reduction in pain.

- **The average VAS pain score reduced by 3.2 points**, from 4.7 pre-treatment to 1.5 at 12 months post-treatment (Figure 1). The reduction in VAS pain score was sustained over the assessment period;
- **At 6 months post-treatment, 67% (6 of 9) of participants reported a VAS pain score of 3 or less ("successful outcome"), improving to 89% (8 of 9) of participants at 12 months post-treatment;**
- Participants in the crossover group had similar improvements in pain to those seen in the original OrthoATI™ group (Figure 1).

[2] A thorough search, conducted by the Company, of published literature and key international (US, EU & UK, AU & WHO) clinical trial registries confirmed there are no completed unpublished or published RCT's assessing the effectiveness of an autologous cell therapy for the treatment of chronic tendon injuries in the shoulder.

Figure 1 – Visual Analogue Scale Pain Assessment (VAS Pain)



Mean overall VAS pain score at baseline (pre-treatment) and at 6 and 12 months post-treatment with ATI.

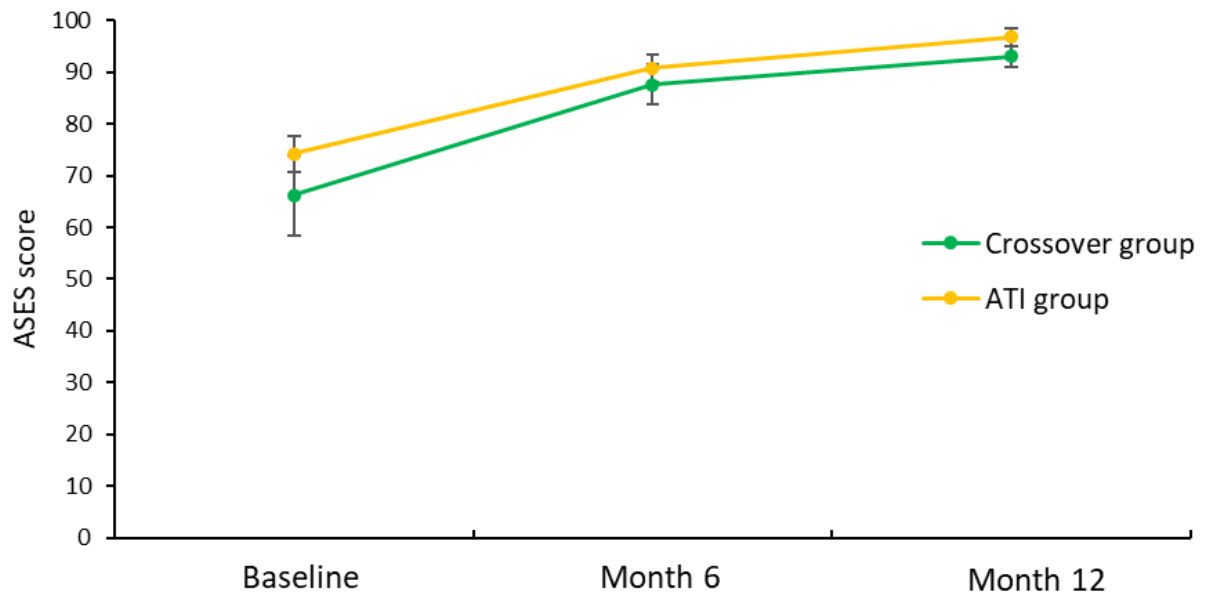
Assessment of Shoulder Disability and Function

The American Shoulder and Elbow Surgeons Shoulder Assessment (ASES) score is a standardized method for assessing outcomes of shoulder and elbow surgery. It comprises assessments of pain and function with a combined ASES/Shoulder Function score ranging from 0-100, with a higher score indicating better outcomes. **A change in ASES score of 12 points (from pre-treatment score) represents the smallest change in score that patients would perceive as a meaningful improvement. An ASES score of 78.6 or more is considered by patients as a "successful outcome".**

Participants receiving OrthoATI™ experienced a meaningful and sustained improvement in pain and return of shoulder function after treatment.

- **The average ASES score improved by 26.8 points** from 66.2 pre-treatment to 93.0 at 12 months post-treatment (Figure 2). The improvement in ASES score was sustained over the assessment period;
- **The mean improvements in ASES score pre-treatment to 6 (21.4) and 12 (26.8) months post-treatment were greater than the smallest change (12) that would be considered clinically meaningful;**
- At 6 months post-treatment, 78% (7 of 9) of participants reported an ASES score of 78.6 or better (successful outcome), improving to 100% (9 of 9) of participants at 12 months post-treatment, i.e achieved a level of shoulder function consistent with a successful outcome;
- Participants in the crossover group had similar improvements in ASES score to those seen in the original OrthoATI™ group (Figure 2).

Figure 2 – American Shoulder and Elbow Surgeons Assessment (ASES)



Mean ASES score at baseline (pre-treatment), and at 6 and 12 months post-treatment with ATI.

Subsequent treatment

No patients in the crossover group required subsequent treatment (e.g. surgery/injection) for their shoulder injury within the 12 month follow-up period.

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 including the rotator cuff, elbow, gluteal, patellar and achilles. Treating physicians and insurers are constantly seeking advances in new treatments that are safe, effective and cost efficient. OrthoATI™ addresses these demands by enabling the accelerated regeneration of injured tendons, directly addressing the underlying cause of injury, replenishing degenerative tissue with healthy mature tendon derived cells. The treatment has been shown to support patients in their return to recreational activities, the workplace and competitive sports. Ortho-ATI™ 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.

Accessing OrthoATI™

OrthoATI™ is available in Australia, New Zealand, and Hong Kong, via the Special Access Scheme, for patients who have failed conservative treatment options such as exercise programs, corticosteroid and platelet rich plasma injections. Under SAS approval, doctors can prescribe use of therapeutic goods prior to regulatory approval if they can justify that the product has significant advantages for their patient over existing approved products or where there are no approved products currently available.

Release authorized by Paul Anderson, Managing Director
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About Orthocell Limited

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™, a collagen medical device which facilitates tissue repair and healing in a variety of dental and orthopaedic reconstructive applications. Striate+™ was the first product approved for dental GBR applications and is cleared for use in US FDA (510k), Australia (ARTG) and Europe (CE Mark). Remplir™, for peripheral nerve repair, recently received approval in Australia (ARTG). 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.