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Orthocell Successfully Achieves all Endpoints in Pivotal Study for U.S. FDA Clearance of Nerve Repair Product Remplir™

- **Orthocell completes pivotal U.S. FDA 510(k) regulatory study validating Remplir™ as a safe and effective biological medical device for use in the surgical repair of peripheral nerves**
- **Regulatory study successfully met all endpoints, providing key data required to support a future U.S. FDA 510(k) marketing submission to commercially distribute Remplir into the US$1.6 billion[1] market**
- **Study results reinforce the previously published clinical results showing that 85% of nerve reconstructions performed using Remplir resulted in functional recovery of muscles controlled by the repaired nerve**
- **Orthocell remains on schedule to submit its Remplir U.S. 510(k) application in December CY24, with FDA clearance expected in the first quarter of 2025 and commencement of sales into the world's largest healthcare market soon thereafter**
- **The Company is well advanced in its commercial launch preparations with the recent appointment of U.S. sales and medical affairs executives to drive the market launch and sales of Remplir**
- **Remplir is already approved in the Australian, New Zealand and Singapore markets with rapidly growing sales and an increasing number of surgeons using and endorsing its unique repair qualities in clinical practice**
- **Orthocell has a strong balance sheet with circa $33 million in cash to drive the U.S. market launch, along with accelerating its regulatory program into other jurisdictions, including the key U.S. market, Canada, U.K., Europe and other ASEAN markets**

Perth, Australia; 02 December 2024: Regenerative medicine company Orthocell Limited (ASX:OCC, "Orthocell" or the "Company") is pleased to announce the successful completion of its Remplir™ 510(k) nerve repair study ("U.S. Regulatory Study" of "the Study"), validating Remplir as safe and effective for use in the surgical repair of peripheral nerves. The U.S. Regulatory Study is a key component of the FDA submission to gain U.S. marketing clearance and the Company remains on schedule to submit its 510(k) application in December CY24, with U.S. FDA clearance expected in Q1 CY25 and commercial distribution soon thereafter.

Orthocell *CEO and MD, Paul Anderson, said*: *"We are thrilled with the results from our U.S. Regulatory Study, validating the superior Remplir clinical outcomes, previously published in a highly regarded, peer reviewed journal. The Study results provide key data for the FDA submission to gain market clearance and start selling Remplir in the U.S. We believe Remplir will redefine the nerve repair market and become an important element in the success of nerve repair surgery."*

The Study was undertaken in collaboration with highly regarded research scientist Professor Bill Walsh, Director of Surgical and Orthopaedic Research Laboratories at the Prince of Wales Hospital in Sydney and the University of New South Wales, and Professor Minghao Zheng Winthrop Professor of Orthopaedic Research at University of Western Australia. The Study met all required endpoints and outcomes.

The Study outcomes reinforce the clinical results, indicating consistent and predictable return of upper arm and hand function following nerve repair with Remplir. The clinical results, published in peer-reviewed *Journal*

[1] USA nerve repair market size was estimated using referenced papers from both US and OUS databases and studies.

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of Reconstructive Microsurgery Open, showed 85% (23 of 27) of nerve repairs with Remplir, at 24 months post treatment, achieved functional recovery of muscles controlled by the repaired nerve.

Collectively, the positive outcomes from the U.S. Regulatory Study and clinical studies will assist the Company in driving into the U.S. market, estimated to be worth in excess of U.S. $1.6 bn[2] per annum and growing, and strengthens the Company's position to successfully execute its proven strategy to engage high quality distribution partners.

US 510(k) Study Overview

The primary objective of the Study was to generate critical data to demonstrate safety and performance outcomes equivalent to an FDA-cleared product, in support of an application to the FDA to gain U.S. market clearance. The Study was conducted using an established rat sciatic nerve injury model. Repair of surgically transected (severed) nerves was evaluated in 72 rats across 3 treatment groups: repair using suture only (control group), repair with Remplir, and repair with the predicate product (comparator). Nerve regeneration was measured at 4, 12 and 24 weeks post-treatment. The key outcome measures included restoration of motor and sensory function and the performance of Remplir in facilitating high quality nerve regeneration.

Summary of Results

All Study endpoints were achieved, demonstrating that Remplir is safe and effective for use in surgical repair of peripheral nerves, with outcomes comparable to the FDA-cleared control device. The positive findings, highlighting the performance of Remplir in facilitating nerve regeneration, provides key evidence to support a claim of *substantial equivalence***,** which is a critical component of the U.S. 510(k) regulatory application.

Use of Remplir to repair the severed sciatic nerves resulted in:

- **Return of motor function -** demonstrated by the return of function of the extensor muscle comparable to the opposite untreated leg by 12 weeks post-treatment;
- **Return of sensory function** - demonstrated by a withdrawal response to mechanical stimulus in the treated leg returning to normal (comparable to the opposite untreated leg) by 12 weeks post-treatment;
- **No adverse tissue reactions** providing strong evidence of biocompatibility;
- **Remodeling and integration into host nerve tissue** by 12 weeks post-treatment; and
- **The regeneration of high-quality nerve tissue** as demonstrated by the number of myelinated (mature) axons that were detected downstream of the repair site

Orthocell CSO, Professor Minghao Zheng, said: *"Use of Remplir did not induce inflammation or scarring, which are known to impede nerve regeneration. This outstanding local tissue response, combined with its optimal handling qualities, will be a key advantage for Remplir in nerve repair surgery. Use of Remplir will help surgeons to simplify the repair process, facilitate high quality nerve regeneration, and ultimately provide consistent and predictable outcomes to patients and support their return of function goals."*

Analysis of tissue and cellular responses

The nerve repair process following nerve injury involves a complex interplay between specialised cells and the surrounding tissue. Histological evaluation of the nerve tissue was conducted by experienced, blinded and independent pathologist revealing that use of Remplir supported healing and nerve regeneration after injury that was consistent with normal nerve repair processes.

[2] USA nerve repair market size was estimated using referenced papers from both US and OUS databases and studies.

Of particular interest was the response of macrophage cells, which play a key role in nerve regeneration by removing cellular debris, assisting device resorption and stimulating activity of other cell types, thereby creating a suitable environment for nerve regeneration. Macrophages at the nerve repair site successfully transitioned from a highly reactive inflammatory "M1" phenotype to the "M2" phenotype that promotes tissue healing and repair. Furthermore, the presence of Remplir around the nerve did not cause the macrophages to aggregate into multinuclear giant cells, which is a sign of foreign body inflammatory response. These results demonstrate that implantation of Remplir does not induce inflammation or scarring that may impede nerve regeneration.

Significance of Remplir US 510(k) Study results

In light of these Study results, published clinical data, and the rapid product adoption in existing markets, Orthocell believes Remplir will redefine the global nerve repair market and rapidly become an important element in nerve repair surgery to return function to paralysed upper limbs. Remplir's ability to integrate into nerve tissue, with an optimal resorption profile and no adverse reactions, provides ideal conditions for nerve regeneration. These properties, combined with Remplir's excellent handling characteristics will empower surgeons to perform these challenging surgical procedures and ultimately improve the lives of more patients suffering from complex spinal cord or traumatic nerve injuries.

Next Steps

With circa $33 million in cash and no debt, Orthocell is well-positioned to successfully launch Remplir in Singapore and other key markets including United States, South East Asia, Canada and the EU/UK. Importantly, the Company remains on schedule to submit its Remplir US 510(K) application in Q4 CY24, with progression into U.S. FDA clearance and commercial distribution soon thereafter.

Release authorised by:
Paul Anderson
Orthocell Ltd CEO and MD

For more information, please contact:

General & Investor enquiries

Paul Anderson
Orthocell Limited
CEO and MD
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

About Orthocell Limited

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

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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 a 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), New Zealand (WAND), UK (UKCA Mark) 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 and FDA engagement to confirm the path to the US market and prepare for partnering discussions.

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.

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