ASX Announcement
29 January 2025

Tissue Repair announces first patient randomisation for its Phase 3 clinical trial programme for TR987® as front-line therapy for the treatment of chronic venous leg ulcers

Tissue Repair Limited (ASX:TRP or the Company) announces first patient randomisation of its Phase 3 clinical trial program for TR987®, which involves the randomisation of 600 participants.

The Phase 3 program aims to confirm the promising results of previous studies, which demonstrated TR987®'s potential to significantly improve healing outcomes for patients with venous leg ulcers (VLUs).

Over the next two years several major Australian and American hospitals, universities, and complex wound centres, will participate in the clinical trials. Including Northwell Health, Barry University, the University of Florida and the John Peter Smith Hospital in the US.

In Australia, key hospitals involved in the clinical trials include Royal North Shore Hospital, Austin Health, Sir Charles Gardiner and the Royal Prince Alfred Hospital.

The Company's core focus is the chronic wound market. An ageing population, together with an increasing prevalence of obesity and diabetes, is driving an increase in the incidence of chronic, non-healing wounds that are resistant to traditional standard-of-care treatments[1]. In 2019, approximately 463 million adults (20-79 years), or 9.3 per cent of the global population, were living with diabetes. By 2045, this is expected to rise to 700 million, or 10.9 per cent of the global population.[2]

[1] Pharma Intelligence – Wound Care: Tissue-Engineered Skin Replacements and Active Wound Repair Modulators 2020

[2] International Diabetes Federation (IDF) Diabetes Atlas – Ninth edition 2019

TR987® offers a long-awaited solution for chronic wounds. In the US, chronic wounds affect approximately 6.5 million individuals and are estimated to cost up to US 50 billion annually (treating chronic wounds via primary and secondary diagnosis, including the cost of infections). This debilitating condition affects over 420,000 Australians annually and costs the healthcare system an estimated AUD 3.5 billion, or approximately two per cent of national healthcare expenditures. Chronic wounds can also significantly negatively impact the health-related quality of life of affected individuals.[3]

These factors contribute to an increasing number of patients requiring advanced chronic wound treatment and represent a significant cost burden on the healthcare system.

TR987® is a proprietary and patented B-D glucan molecule extracted from yeast. It is 100 per cent Australian-developed and has a unique mechanism of action that directly stimulates the immune system, leading to accelerated healing in chronic and acute wounds.

Across its Phase 2 trials in around 150 patients, TR987® demonstrated a 60% reduction in wound area ($p<0.03$) compared to placebo over a 12-week treatment period.

Further, its most recent phase 2B trial demonstrated a +20 per cent absolute improvement in the proportions of patients achieving 100 per cent wound closure. Should it replicate this signal in the Phase 3 program, it will be the first drug to deliver such an efficacy signal in a phase 3 clinical trial for chronic wounds.

This Phase 3 trial will be a significant milestone in developing the lead drug candidate for treating VLUs.

Randomising the first patient in the Phase 3 clinical trial program is a critical step in the Company's mission to introduce innovative regenerative medicine technology applicable to a wide range of wounds at a cost-effective price.

[3] Chronic wounds in Australia: A systematic review of key epidemiological and clinical parameters Laura McCosker, Link.

Dr Robert Kirsner, Chair of Dermatology at the University of Miami Miller School of Medicine and US Principal Investigator, emphasised the significance of this research, stating: "*The promise of delivering patients a 15%-20% improvement in absolute healing via an easy to use topical is much needed front-line therapy for patients suffering these debilitating wounds. Very few drugs or biologics have succeeded in hard-to-heal wounds, and this research is much needed to help improve outcomes for patients and caregivers alike."*

Associate Professor Michael Woodard, the Australian trial's Principal Investigator, said, "I have been involved in two Phase 2 trials now for TR987® for healing chronic wounds, and the most recent results are very encouraging. Very few products have been shown to promote wound healing, and the unique action of TR987® stimulating macrophages likely explains the positive results seen so far—a healing rate almost 60% greater than that of a placebo.

"We sorely need this, with over 250,000 Australians annually suffering from chronic wounds and often being subjected to pain, high treatment costs, and stigmatisation, sometimes for years. This novel approach is just what is required."

Alisha Oropallo, M.D., Medical Director of the Comprehensive Wound Healing Center and Hyperbarics at Northwell Health, said, "We look forward to beginning this important research to investigate the potential of TR987® further to address this critical unmet medical need. Should TR987® replicate its Phase 2 treatment effect of a 20% improvement in complete healing over the standard of care in these pivotal trials through a simple topical application, we believe it would be an exciting and significant step forward for patients and caregivers alike in treating this debilitating condition.

Tissue Repair Co-founder and CEO Tony Charara said getting to this point has been a significant effort from a small, dedicated team over many years.

"Glucoprime has the promise of achieving a world-first, cost-effective, efficacious universal healing agent that can be applied to all wound types in humans and animals.

"Should FDA approval be achieved, TR987® will be the first drug or biologic to be approved in around three decades in the US for chronic wounds. Randomising the first patient in the Phase 3 trial is a milestone for the Tissue Repair team to bring this regenerative medicine technology to market.

"We are optimistic that TR987® will set a new standard in chronic wound care, improving the lives of millions globally and setting the foundations for using the technology platform in multiple wound types," Mr Charara said.

Patients interested in participating in the clinical trial can learn more at https://triviastudy.com/ and register with their local clinic for screening.

This announcement has been approved for release by TRP's Board.

Ends

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Background

About the Phase 3 trial program

The Phase 3 program, referred to as the TRIVIA Study (**T**issue **R**epair Gel **I**n **V**enous Leg Ulcers **I**n **A**U/US), is a Phase 3 randomised, parallel-group, double-blind study that evaluates the efficacy, tolerability, and safety of TR987® gel versus standard of care in the treatment of chronic venous insufficiency leg ulcers. Two identical TRIVIA Studies are being conducted contemporaneously, each with 300 patients (600 combined) in Australia and the US. For more information, please visit www.triviastudy.com.

Further information is available at www.Clinicaltrials.gov. Interested parties can learn more by emailing info@trtherapeutics.com.

About Venous Leg Ulcers (VLUs)

Venous leg ulcers (VLUs) are the most common type of ulceration on the lower extremity, accounting for 70% of all leg ulcers (O'Donnell et al., 2014). Various estimates have been made on the prevalence of VLU, ranging between 0.06% and 2% (Ruckley et al., 2002; Fischer, 1981; Jawien et al., 2003; Carpentier et al., 2004). In the U.S., up to 2 persons in 1000 have active VLUs, with prevalence increasing to 20 persons per 1000 people by age 80 (approximately 0.5 million in the US) with an annual direct medical care cost of US$2,500 per month per patient (US$15Bil annually) The mean total cost of treating VLU was estimated at $15,732.

Global prevalence estimates run into the millions, with estimates of mark size on wounds ranging from USD20b-USD50b.

About TR987®

The active pharmaceutical ingredient in TR987® gel is a patented and proprietary insoluble particulate (1,3) (1,6)-β-glucan derived from a yeast cell wall via a specific purification process. The process yields a glucan of a size and configuration that appears to have a distinct immunologically based mechanism of action.

When the TR987® hydrogel is applied topically, the active ingredient moves to the dermis, where it engages with specific cell surface receptors located on macrophages (Dectin-1 and TLR2), the key immune cells involved in managing the healing process. The macrophages subsequently become activated and instigate the production of an array of cytokines and growth factors. The entire healing process involves many different cellular factors that need to be switched on and off at the appropriate times and in the correct concentrations. M1 macrophages control the early inflammatory stage of healing, while M2 macrophages control the proliferative re-building stage. Studies have shown that TR987® can stimulate greater numbers of M2 macrophages (almost double) and, through this, effectively control the inflammation phase, ensuring that it is not too severe nor extends for too long, both of which have been shown to compromise skin quality. The positive impact on M2 macrophages results in accelerated healing with less downtime and superior skin quality.

Venous leg ulcers are in a continual state of inflammation and cannot progress to the re-building stage. M1 macrophages dominate these wounds, with relatively few M2 macrophages. By stimulating greater numbers of the M2 macrophages, TR987® is likely able to 'reset' the wound environment, allowing the inflammation to be modulated and new tissue to be laid down, leading to the wounds closing.

About Tissue Repair

Tissue Repair Limited (ASX TRP) is a Phase 3 advanced biotechnology company developing second-generation wound healing agents. The Company's core focus is completing Phase 3 clinical trials in chronic wounds for its lead drug candidate TR987®, with a secondary focus on commercialising TR Pro+®, a post-procedure topical gel to accelerate healing and improve skin quality following cosmetic and medical procedures, as well as other acute wound products in its pipeline. The Company's longer-term strategy is to commercialise its proprietary Glucoprime® API to treat a variety of wounds and skin conditions.

Note regarding forward-looking statements

This media release contains forward-looking statements regarding TR987® and its ongoing clinical development by Tissue Repair Pty Ltd. These statements are based on current expectations and projections of future events and are subject to risks and uncertainties. Readers are cautioned not to place undue reliance on these forward-looking statements. If underlying assumptions prove inaccurate or if known or unknown risks or uncertainties materialise, actual results could differ materially from the expectations of Tissue Repair Pty Ltd.

Risks and uncertainties include but are not limited to, challenges and uncertainties inherent in product research and development, including the uncertainty of clinical trial outcomes, regulatory approval processes, and eventual product commercialisation; manufacturing and supply chain complexities; competition from new or existing products, technological advances, or intellectual property challenges; potential product safety or efficacy concerns that could lead to regulatory action or withdrawal; changes in healthcare regulations and policies, including cost-containment measures; and shifting market or patient needs.

Tissue Repair Pty Ltd undertakes no obligation to update any forward-looking statement in light of new information, future events, or developments except as required by applicable laws or regulations.