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## Glucoprim® hydrogel

(TR987® for chronic wounds; TR Pro+™ for damaged or wounded skin)

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

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# Executive Summary



## Unique platform technology

- Technology platform is a unique immunogenic active ingredient, Glucoprime®, that improves wound healing
- The immunomodulatory mechanism of action suits different indications, allowing multiple applications
- Glucoprime® may satisfy FDA requirements as a new chemical entity which could allow 5 years of exclusivity



## Differentiated drug label strategy provides valuable opportunity

- Core focus is on realising value from the Glucoprime® technology through drug approval of the chronic wound product, TR987®, to treat chronic wounds
- Chronic wounds represent a significant opportunity; costing the US federal healthcare system up to US\$50bn<sup>(1)</sup>. Tissue Repair is initially targeting the US\$1.7bn global market of active wound care products (biologics)
- Existing wound care treatments are dominated by medical devices, scaffolds and human placental-derived products
- Tissue Repair aims to provide a topical gel targeting a superior and more cost-effective outcome than alternative therapies



## Phase 3 clinical trials commencing in 2023

- Positive signal for wound healing demonstrated in clinical trials to date, most recently completing a phase 2 chronic wound clinical trial in late 2020 under an FDA approved protocol (randomised, double-blind and placebo-controlled)
- Planned phase 3 trials aiming to prove superior in-use outcomes to the current in-market treatments



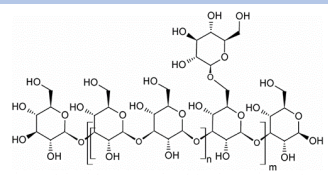
## Commercialisation of aftercare product for medical and cosmetic treatments

- Secondary strategy to commercialise TR Pro+™ for post-procedure aftercare of medical and cosmetic procedures (such as laser skin resurfacing)
- Supported by clinical data from a phase 2 trial on laser skin resurfacing showing improved skin quality (elastosis and wrinkling) at 28 days
- In the USA alone, an estimated US\$3.4bn was spent on potentially relevant minimally invasive cosmetic procedures<sup>(2)</sup>

## Glucoprime®

### The Technology

Tissue Repair's immunomodulatory active ingredient, Glucoprime® stimulates the body's natural innate immune response to assist wound healing



### The Benefits

- The immunomodulatory mechanism of action seeks to offer significant clinical benefits to patients undergoing treatment for acute or chronic wounds including:
  - closure for wounds which have stalled and become chronic;
  - lower cost of hospitalisation and medical treatment;
  - enhanced patient quality of life;
  - improved healing of wounded or damaged skin; and
  - improved aftercare of cosmetic and medical procedures.

### The Evidence

- The drug product, containing the Glucoprime® API, has been used on over 240 patients across two indications in phase 1, phase 2, and real-world evidence studies
- All phase 2 trials have been conducted as randomised, double-blind and placebo-controlled studies
- Tested on chronic wounds (venous leg ulcers; n=82) with a positive signal of efficacy<sup>(1)</sup>:
  - 20.4% (p=0.13) and 28.1% (p=0.087) difference in incidence of complete closure VLU 2-12cm<sup>2</sup> (ITT and PP groups, respectively)<sup>1</sup>
  - 25.7% (p=0.071) and 31.7% (p=0.042) difference in incidence of at least 90% wound closure (ITT and PP groups, respectively)<sup>1</sup>
- Tested following laser skin resurfacing (n=40), achieving a significant improvement in skin quality (assessed by elastosis and wrinkling) at day 28<sup>2</sup>
- Real-world evidence study (n=48) with 85% of patients considering their wound to be healing 'well/very well', and 81% of patients 'satisfied/very satisfied' with their experience using TR Pro+, at day 28.

### The Potential

- Potential to be used across a variety of applications and indications

# Glucoprime® – Mechanism of action

- Primary target is macrophages which are activated to trigger the expression of genes that enable phagocytosis, protein synthesis and cytokine release



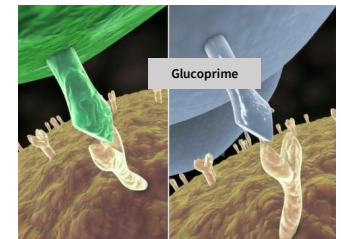
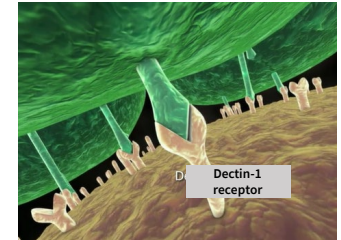
- $\beta$ -glucans in fungal cell walls bind to the dectin-1 and TLR2 receptors to initiate macrophage activation






- TR Pro+ is a non-infective particulate,  $\beta$ -glucan containing product isolated from yeast cells. The active ingredient is Glucoprime®
- TR Pro+ is designed to leverage the body's natural response to a yeast infection.



- In laboratory and clinical studies TR Pro+ has been shown to promote wound healing by activating the genes in macrophages <sup>(1)</sup>
- Cytokines and growth factors are released which attract helper cells like fibroblasts, monocytes and additional macrophages that assist in wound repair
- Utilises the normal innate immune response



# Two indications targeting different conditions

	Market	Product	Strategy	Stage of clinical development					Commercial launch		
				Preclinical	Ph 1	Ph 2A	Ph 2B	Ph 3			
Primary focus	#1	Chronic wounds	TR987®	<ul style="list-style-type: none"> <li>Achieve FDA and TGA approval as a topical drug for use in venous leg ulcers</li> <li>Obtain reimbursement in the US and Australia</li> </ul>						Clinical trial expected in 2023* (venous leg ulcers)	2025 (following FDA/TGA approval)
	#2	Cosmetic and medical procedures	TR Pro+™	<ul style="list-style-type: none"> <li>Commercialise as a post-procedure aftercare product</li> <li>Initially launched as a 'cosmetic' product while seeking TGA approval</li> </ul>						Product developed for launch leveraging existing phase 2 trials	2023
	#3	New indications	Potential for a variety of products	<ul style="list-style-type: none"> <li>Invest in the research and development of additional products and build clinical evidence for a broader range of indications</li> </ul>						R&D potentially commencing in 2023	

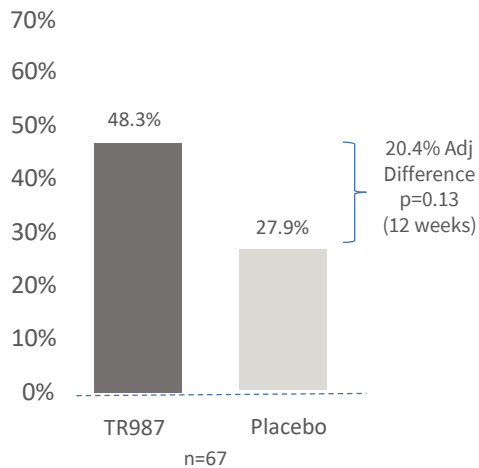
\* Pending FDA approval

# Clinical Study – chronic wounds (2020)

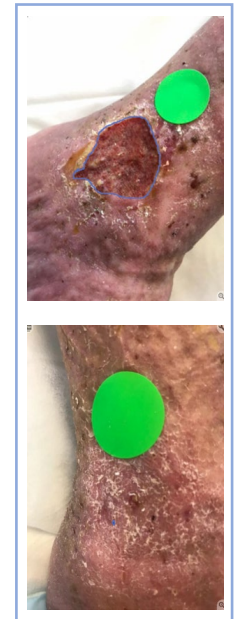
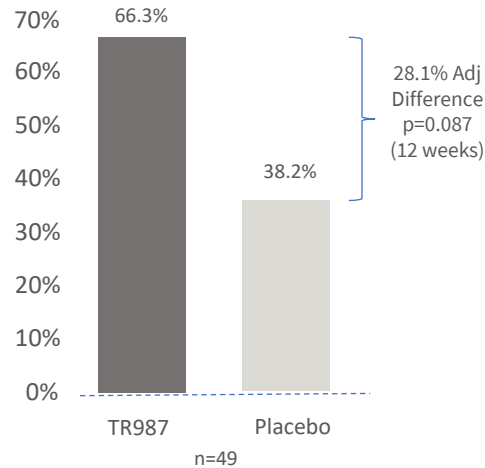
## Phase 2B: Study of the Efficacy of TR 987, beta-1,3-1,6-D-glucan, in the Treatment of Chronic Venous Insufficiency Ulcers (BG001, Australia/USA, 2020).

To assess the time to heal within 12 weeks between chronic VLU treated with TR987<sup>®</sup> gel and Standard of Care (SoC) versus placebo gel and SoC.

Adjusted Incidence of Complete Closure (2-12cm<sup>2</sup>)  
2020 phase 2B (Intention to Treat) 100% healed



Adjusted Incidence of Complete Closure (2-12cm<sup>2</sup>)  
2020 phase 2B (Per Protocol) 100% healed



7.53cm<sup>2</sup> ulcer had been present for 208 weeks and was healed in 10 weeks (Heidelberg Repatriation Hospital Melbourne).

TR987<sup>®</sup> 2020 phase 2B FDA VLU trial PP and ITT groups (adjusted difference based on logistic regression analysis, controlling for factors known to affect healing),

*TR987<sup>®</sup> confirmed a strong signal of efficacy to heal chronic venous leg ulcers after 12 weeks treatment*



# Key product advantages – TR987<sup>®</sup> for chronic wounds

## Strong efficacy signal from well designed trials

- No drug or biologic appears to have been approved in chronic wounds since REGRANEX gel in 1997, and as such a drug indication for chronic wounds supported by high quality clinical data drives reimbursement and is highly prized
- Positive signal for efficacy in wound healing (including key FDA accepted endpoints) demonstrated in clinical trials

## Aiming to prove superior in-use outcomes over current therapies

- Existing therapies are typically expensive and require application by healthcare professionals in a hospital setting. Many are derived from human placental tissue
- Tissue Repair aims to provide a superior in-use alternative to these therapies, without a reliance on harvesting human tissue and the ease of a topical gel in contrast to a complicated patch or scaffold

## Positive safety profile

- TR987<sup>®</sup> has a positive safety profile across its clinical program to date
- TR987<sup>®</sup> has been tested across different indications on over 240 patients with no significant adverse events attributable to the drug product

## Ease of use

- Administered topically onto the wound – no complicated bandages or patches
- Can be used in combination with standard of care products, including compression bandaging
- Capable of being administered by a nurse/caregiver or in the home directly by the patient

## Stable over a long shelf life

- Preliminary stability testing of TR987<sup>®</sup> suggests a three-to-five-year shelf life at room temperature may be achievable with no refrigeration or freezing required



# Milestones and initiatives over the short-to-medium term – TR987<sup>®</sup> for chronic wounds

## Completed

- Completion of FDA Type C meeting with positive outcomes for raw material, CMC and abridged toxicology program
- Appointment of two CMOs to manufacture the Glucoprime<sup>®</sup> API and finished gel product
- Production of three laboratory batches that confirmed reproducibility of Glucoprime<sup>®</sup> API
- Generation of four engineering and two GMP batches to confirm batch consistency and generate Glucoprime<sup>®</sup> API for phase 3 trial
- Ongoing method analysis and validation to support the 20+ characterisation tests
- Engagement of Principal Investigator (Prof. Robert Kirsner, Miami) for phase 3 VLU trial
- Engagement of US-based consultancy to undertake a reimbursement landscape assessment for the US (Q4 2022)

## Planned

- Initiation of a 28-day minipig study as part of the toxicology program to support product safety (Q3 2023)
- Finalisation of the phase 3 protocol (Q1 2023)
- End of phase 2 meeting with FDA (Q1 2023) to enable commencement of phase 3 trial
- Appointment of CRO to manage phase 3 trials in the US and Australia (Q1 2023)
- Initiation of stability programs for Glucoprime<sup>®</sup> API and finished gel (Q4 2022/Q1 2023)
- Establishment of a collaboration with an Australian research group to elucidate further information around the mode of action to support the FDA application

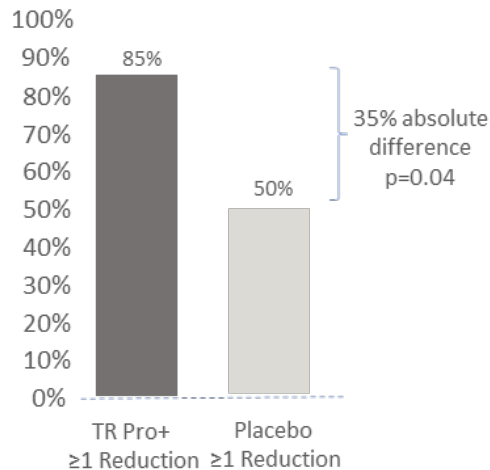
# Clinical Study – laser skin resurfacing (2020)

## Phase 2B: Study to Evaluate a Novel Macrophage Activating Gel for Optimization of Healing and Skin Quality After CO<sub>2</sub> Laser Resurfacing of the Chest (TR987-2016-FullChest, USA, 2020).

To evaluate the efficacy of TR Pro+™ active gel compared to placebo in accelerating wound healing following fractionated CO<sub>2</sub> laser resurfacing of the chest for treating wrinkles and photo-damaged skin.

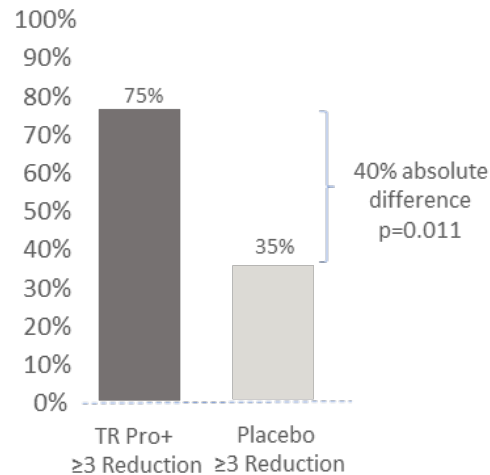
### Wrinkling

Proportion of patients with at least 33% improvement at 28 days



### Elastosis

Proportion of patients with at least 33% improvement at 28 days



Day 1



Day 28

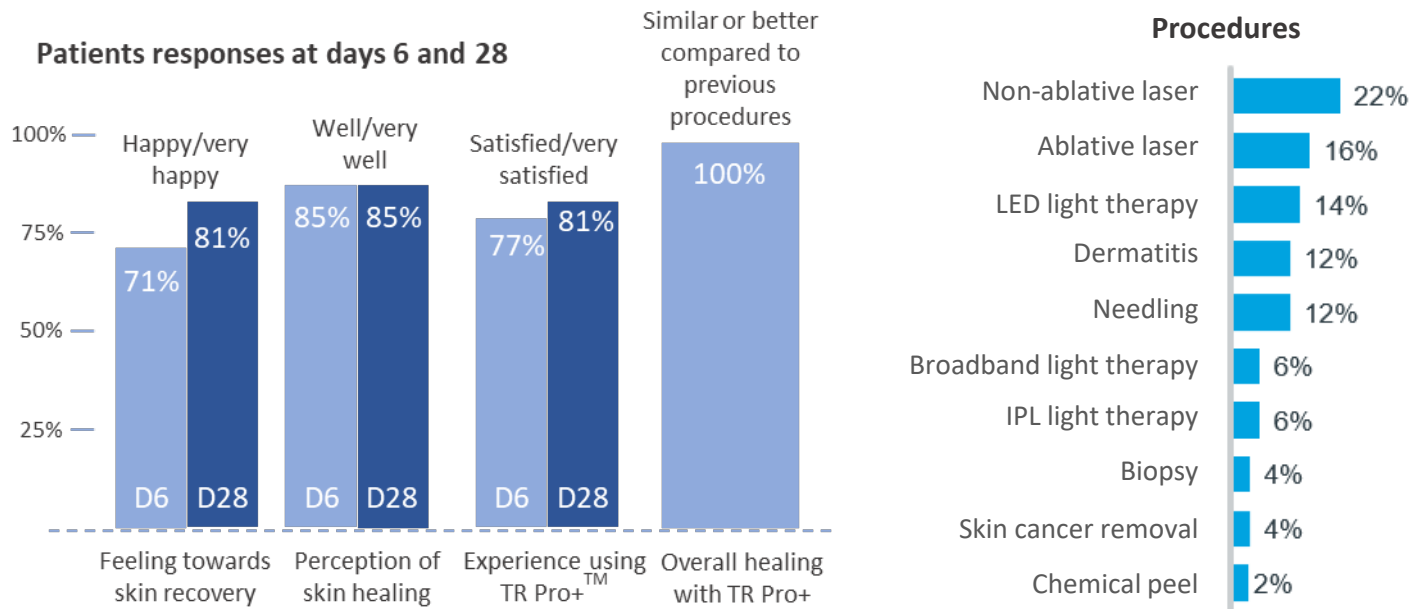


(Typical patient response following 5-day treatment treatment with TR Pro+)

*TR Pro+™ demonstrated a significant improvement in skin quality, as assessed by wrinkling and elastosis, after 28 days*

# Real-world evidence study (2022)

A real-world evidence study<sup>(1)</sup> was done with 12 dermatology clinics in Australia in patients (n=48) who had undergone a range of cosmetic and medical procedures. The program was run independently and patients provided anonymous feedback at day 6 and day 28 following the procedures.



Healthcare professionals who consider TR Pro+ appealing<sup>(1)</sup>

86%

Dermatologists interested in learning more about the phase 2 laser skin resurfacing trial<sup>(2)</sup>

84%

# Milestone and initiatives over the short-to-medium term – TR Pro+™ for the aftercare of cosmetic and medical procedures

## Completed

- Comprehensive market research program undertaken with various healthcare professional specialists
- Real-world evidence study (n=48) across 12 dermatology clinics in Australia
- Insight generation and lead development through interactions at dermatology, plastic surgery, wound, tattoo and beauty conferences
- Publication of the phase 2 laser skin resurfacing trial in the peer reviewed journal, Dermatologic Surgery (expected Q4 2022)
- Appointment of an Australian-based CMO to produce finished gel TR Pro+™ in preparation for launch

## Planned

- Commercial launch of TR Pro+™ to dermatology and beauty clinics (Q1 2023)
- Production of an initial batch of 10g tubes and 3g sample sachets (Q1 2023)
- File TGA application to include beta-glucans as an accepted active ingredient (Q3 2023) for Listed (AustL) therapeutic goods
- Continue to explore opportunities for use of Glucoprime® in other indications (eg: tattoo removal) (2023)
- Investigate opportunities for distribution of TR Pro+™ in global markets (2023)

# Milestone and initiatives over the short-to-medium term – additional developments

## Completed

- Two patents accepted which each afford 21 years of protection:
  - claims to the method of manufacture of a unique isolated biological polysaccharide
  - claims to the use on any skin condition including burns, chronic wounds, surgical wounds, pressure ulcers and any post procedure wound whether surgical or cosmetic
- Work undertaken to examine opportunities relevant to the Government R&D tax initiative
- Assessment of IT and Quality requirements undertaken with actions implemented as required.

## Planned

- A third patent application is being prepared to cover the structure of the beta glucan molecule (ie: Glucoprime®)
- Trademark applications are ongoing for US, UK, Australia and Canada

