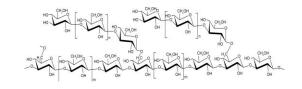


# **Tissue Repair Limited AGM Progress Update**

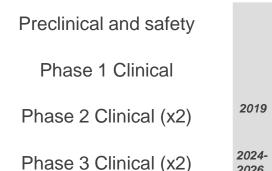
Tony Charara
Co-founder and CEO

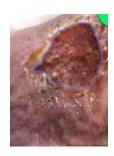
## Two separate workstreams in progress – chronic wounds (venous leg ulcers) and acute wounds (aftercare of medical and aesthetic procedures)

**Glucoprime®** 



#### **Chronic wounds (venous leg ulcers)**





#### Acute wounds (medical and aesthetic)

Preclinical and safety	
Phase 1 Clinical	
Phase 2 Clinical (x2)	
Real-World Evidence Study	2022
Product Launch – TR Pro+	2023
Case studies – new indications	2024+
TGA approval	





## Phase 3 screening has commenced - 7 sites online by the end of October 2024 (target 30 sites by Q1 2025) for both trials

#### **Current key site status**

Protocol	Site	PI	Randomization Pts/Month Target only	State	MUsT	Comments	SIV
BG002	11	Dr Ananian	1-2	CA		CTA Final	9/16/2024
BG002	14	Dr Cazzell	1-2	CA	Х		
BG002	18	Dr Costella	1-2	VA	Х	CTA Final	9/24/2024
BG002	21	Dr Ducharme	1-2	AZ		CTA Final	9/17/2024
BG002	23	Drs Frania/Iosue	1-2	OH		CTA Pending FE	10/10/2024
BG002	24	Dr Garrett	1-2	TX	Х	Pending Selection	
BG002	26	Dr Hanft	1-2	FL	Х	In Budget Negotiation	
BG002	28	Dr Le	2-3	OK	Х	CTA Final	9/18/2024
BG002	29	Dr Lev-Tov	.5	FL	Х	In Budget Negotiation	
BG002	32	Dr <u>Maislos</u>	4-5	TX		CTA Pending FE	10/16/2024
BG002	38	Dr Perlman	1-2	FL	Х	CTA Pending FE	
BG002	40	Dr Piraino	1-2	FL	Х	CTA Pending FE	10/21/2024
BG002	43	Dr <u>Reyzelman</u>	2-4	CA	Х	CTA Pending FE	10/28/2024
BG002	45	Dr Rutter	1-2	ОН		CTA Pending FE	10/9/2024
BG002	46	Dr Sanchez	1-2	TX	Х	Pending Selection	
BG002	47	Dr Seide	1	FL		Activated	9/11/2024
BG002	49	Dr Sigle	1-2	IL	Х	CTA Pending FE	10/31/2024
BG002	51	Dr Snyder	1	FL	Х	CTA Pending FE	10/15/2024
BG002	55	Dr Vlad	1-2	NC		In budget Negotiation	Local IRB
BG003	60	Dr Woodward (Austin)	1-2	AU - VIC		CTA pending FE	10/31/2024
BG003	65	Dr Daff (GVH)	1-2	AU - VIC		CTA/Budget with Site	10,01,202
BG003	75	Dr Bravo Ceballos (SCG)	2-3	AU - WA		CTA/Budget with Site	
BG003	76	Dr <u>Ghelber</u>	1-2	TX		Activated	9/12/2024
BG003	77	Dr Loder	1-2	MI		CTA Final	9/23/2024
BG003	78	Dr Leahy	1-2	AU-NSW		In Budget Negotiation	
BG003	82	Dr Oropallo	4-5	NY		CTA Pending FE	10/31/2024
BG003	85	Dr Puttaswamy (RNS)	3-7	AU - NSW		CTA/Budget with Site	
BG003	92	Dr Swain	1-2	FL		CTA Final	9/13/24

#### **Metrics Summary**

- **BG002** has 17 sites selected in the US. Sites Pending Selection (Sanchez, Garret).
  - Monthly Randomization estimates: 20 patients.
- BG003 has 9 ( sites selected, 5(+0) in Australia and 4 in the US.
   Monthly Randomization estimates: 14 26 patients

#### Highlights

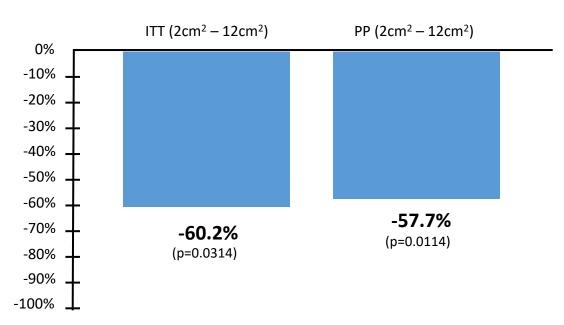
- 11 Site Initiation Visits (SIVs) completed in the US. 3 for BG003 and 8 for BG002. 6 additional SIVs have been scheduled. 16 SIVs in US and 1 SIV in AU.
- US combined BG002/BG003 Press Release for Study Initiation to occur once first patient randomizes. Expected PR pending first randomization.
- Major Australian Hospitals Participating Royal North Shore and Austin hospitals participating and expecting to have RPA also participate.



### Phase 3 refresher - Meta analysis on two Phase 2 trials for chronic wounds . . . this signal is what we are powering

Analysis included 147 patients from two Phase 2 trials which confirmed a strong signal of efficacy and demonstrated a 60% reduction in wound size vs placebo control (p=0.03).

Meta-analysis of all phase 2 patients. Mean wound reduction change between placebo and active in VLU size 2-12cm<sup>2</sup> n=147.



Meta-analysis of all phase 2 patients. Mean wound reduction change between placebo and active across a range of cohorts . VLU sizes 2-12cm<sup>2</sup> and 2-20cm<sup>2</sup>

Population	Dose TR-987 gel	Wound size	Adjusted difference in mean change (95% CL)	p-value
ITT	Low	2-12cmsq	-55.9 (-113.3, 1.52)	0.0562
ITT	Low	All	-31.6 (-68.60, 5.30)	0.0925
PP	Low	2-12cmsq	-58.0 (-103.0, -13.05)	0.0124
PP	Low	All	-41.6 (-72.41, -10.82)	0.0087
ITT	All	2-12cmsq	-60.2 (-114.9, -5.53)	0.0314
ITT	All	All	-33.2 (-65.36, -1.12)	0.0427
PP	All	2-12cmsq	-57.7 (-101.8, -13.47)	0.0114
PP	All	All	-44.3 (-71.16, -17.38)	0.0015

The percent change in ulcer area and actual change in ulcer area (cm2) was analysed using a general linear model with baseline ulcer area and duration of study VLU as covariates. Adjusted treatment effects for TR-987 0.1% gel (low dose) versus placebo and for TR-987 all doses combined (i.e. TR-987 0.1% or 1.0% gel) versus placebo were obtained overall for the ITT and PP populations for all patients from both studies combined and for the subgroup of patients with baseline ulcer area 2-12cm2, the proposed inclusion for the planned Phase 3 trials. Results are presented below in tables E2 (percentage change) and E3 (actual change) and graphically in figures E1 (percentage change) and E2 (actual change).



# We need affordable, effective new technologies to promote wound healing, TR987 has the potential to be a global scale front line therapy for chronic wounds > ease of use (topical), with excellent health economics having regard to efficacy

- Huge numbers
  - Around 300,000 Australians with chronic wounds
- High cost
  - \$5.1 billion in 2019
- Venous leg ulcers (VLUs) are the most common type of ulceration on the lower extremity and account for 70% of all leg ulcers
- Various estimates have been made from observational studies on the prevalence of VLU, ranging between 0.06% and 2%
- The number of affected patients is likely to be increasing globally with the UK reporting a 101% increase in VLU patients between 2012/2013 and 2017/2018
- Healing often delayed:

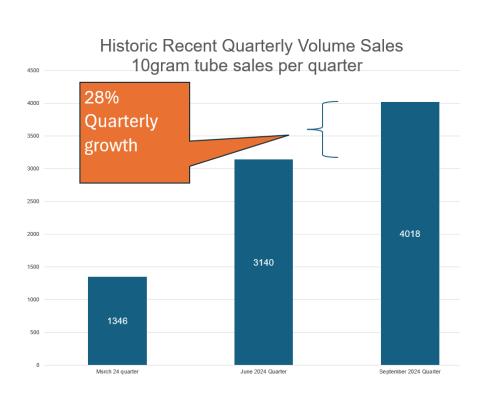
Suffering and poor quality of life



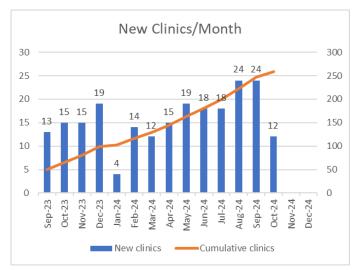
Associate Professor Michael Woodward. Past President of the Australian Wound Management Association, now Wounds Australia.



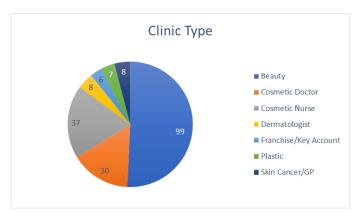
### TR Pro+ is growing and has demonstrated a strong signal of market acceptance. Around 35k per month in sales with consistent growth.



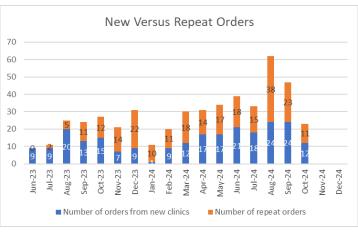
With minimal marketing spend and only c2.5 sales reps growth has largely been driven by direct out reach and conference participation



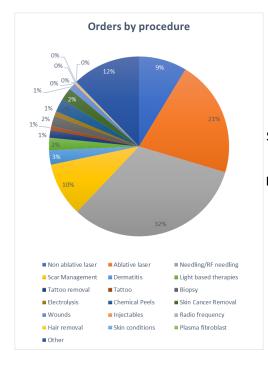
More than 250 clinics have purchased TR Pro+



Cosmetic clinics, including those with a nurse or doctor, are the most common customer



Orders are split 50:50 for new vs repeat



Laser resurfacing, skin needling and scar management are the most common procedures

### Expanding indications to increase distribution while still selling as cosmetic. TGA labelling not yet commenced.

- Medical
  - Biopsy
  - Hard-to-heal wounds
  - Skin cancer removal
  - Scar management
  - Dermatitis
  - Post solar keratosis treatment
- Aesthetic
  - Skin needling
  - Laser skin resurfacing
  - Chemical peels
- We are in active discussions with around 5-10 parties on distribution. We have received LOIs in aesthetics working through optimal partner

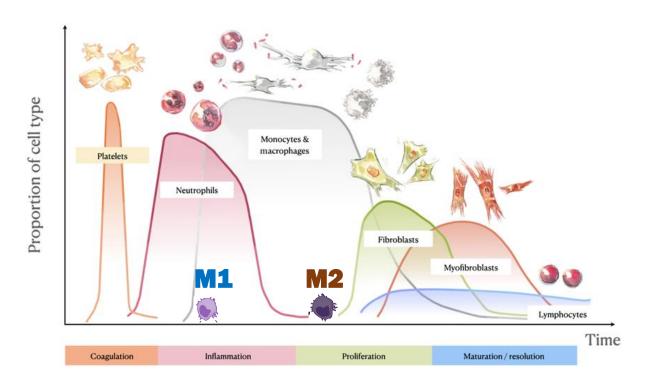








### New data on MOA Refresher - Macrophages co-ordinate the healing process



- Activation of macrophages by Glucoprime® draws neutrophils and other macrophages to the wound site during the inflammatory phase.
- M1 macrophages control the inflammatory phase (remove pathogens, prepare the site for repair) while M2 macrophages increase collagen to promote tissue repair, restore barrier function, and modulate scarring.



#### Further clarity on the novel mode of action

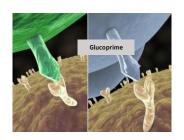
- The beta glucan in TR987®/TR Pro+® is purified from the cell wall of bakers' yeast.
- Beta glucans are complex polysaccharides composed of glucose monomers.
- TR987®/TR Pro+® is a hydrogel with purified beta glucan (Glucoprime®) as the active ingredient.



- Topically applied beta-glucan containing TR987®/TR Pro+® hydrogel is recognised by dermal macrophages.
- When receptors dectin-1 and TLR, are engaged the macrophages become activated and express genes that enable phagocytosis, protein synthesis and cytokine release.



- In this way TR987®/TR Pro+® initiates a mild innate immune response that attracts more macrophages as well as other immune cells like neutrophils and monocytes.
- Macrophages play a key role in re-modelling by releasing growth factors that aid in tissue repair and angiogenesis.



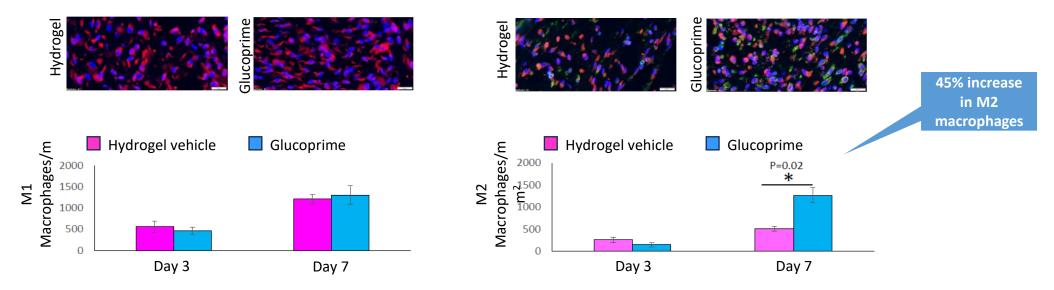


Confirmation of M2 macrophage stimulation

WA 12 month project with the University of South Australia (Prof. Allison Cowin) investigated the mode of action and found that Glucoprime<sup>®</sup>:



- **Accelerated healing** in wounded mice as evidenced macroscopically and microscopically
- Elicited an early release of TNF $\alpha$  and initiation of the inflammatory response from 24 hours
- Stimulated a 45% increase in M2 macrophages at Day 7



Together the in vitro and in vivo data supported accelerated healing arising through a shortened inflammatory phase and a faster onset of the proliferative phase.



### In summary Tissue Repair has a significant opportunity ahead with a track record of achieving goals and navigating challenges

TR Pro+TM  Medical and aesthetic wounds incl. burns	Australian TAM +AUD100M Global TAM +AUD1.5b	Generated revenue now with strong growth TGA approved with marketing commencing Q1 2025 Exploring approvals in China, UK and US Q1 2025 Exploring a significant number of third-party distribution opportunities
TR987® Device VLUs	Global TAM +US2b	Device approval targeted Q1 2025. Ability to entry chronic wound market with reimbursement
TR987® Drug VLUs		Phase 3 Trial initiation Sept 2024
Drug other chronic wounds	Global TAM +US20b	Exploring ability to undertake additional truncated trials (e.g. DFUs pressure ulcers) to support other indications

Dedicated founding team with significant venture, operations experience delivering growth outcomes in healthcare and highly regulated areas:

- Track record in delivering significant growth outcomes Myself and my co-founder founded Mable, Australia's largest healthcare delivery platform, delivering over 600,000 hours of care and support per month and a 75% CAGR over the preceding five years. The group processes +1B in healthcare funds. Over 20m hours of care and support delivered to date.
- Management team has a depth of experience COO, VP of Clinical, VP of Regulatory and CMC team, have depth of
  experience in sales and marketing, product development regulatory, clinical and analytical chemistry and manufacturing.
- o Co-founding team clear understanding of the science and MOA and trial design having been heavily involved in all operations across the Phase 2 program as well as authoring 3 recent patents as co-inventors.

Founder strategy has not changed and prospectus objectives remain in sight

Opportunity is still clear and real with Global Phase 3 assets trading at significant premiums to TR

(even with similar end market indications)

