



TISSUE THERAPIES

Investor Update January / February 2015

VitroGro® ECM: Think Different



Dr Steven Mercer (CEO)
s.mercer@tissuetherapies.com



TISSUE THERAPIES

1. Introduction
2. Global Chronic Wound Market
3. Our Lead Product VitroGro[®] ECM
4. Strategy Update
5. Capital Raising
6. Summary



TISSUE THERAPIES

Section 1: Introduction



Tissue Therapies Ltd: Introduction

- An Australian biomedical company developing advanced technologies for more cost effective wound healing, tissue repair and scar prevention.
- Worldwide exclusive rights to commercialize VitroGro® technology: first product – VitroGro® ECM for difficult to heal wounds.
- Patents granted in the USA, Canada, Europe, China, Hong Kong, South Korea, Japan, South Africa, Australia and New Zealand (India under examination).
- Partnerships with Quintiles (hiring & support services) and Movianto (logistics) to minimize operational risk, restrain cost and optimize revenue.
- Attractive margin product; more **safe, convenient, and cost effective** than existing wound care treatments.
- Raising A\$7.7 million through a placement and entitlement offer at A\$0.21 per share to fund completion of the EMA review process and preparatory work for a US FDA diabetic ulcer clinical trial.

Corporate Overview



Key Statistics

Code	ASX: TIS
Listed	ASX, Frankfurt & Berlin
Share Price (30 Jan. 2015)	A\$ 0.29
52 Week High	A\$ 0.465
52 Week Low	A\$ 0.25
Shares Outstanding	263.3m
Market Cap	A\$ 76.4m
Net Cash (1 Jan. 2015)	A\$ 2.8m
Top 20 Shareholders	~50% of issued capital; institutional & private investors, directors, CEO

Major Achievements

Finalisation of protein formulation, VitroGro® ECM; Successful clinical trials	✓
Commercial-scale, efficient Good Manufacturing Practice (GMP) standard manufacturing	✓
Key commercial partners in place for start of sales (incl. Quintiles, Movianto)	✓
Strong health economics / savings data	✓
Science & clinical results papers published	✓

Major Priorities

CE Mark to treat venous ulcers (most reviewer questions resolved)
USA FDA diabetic ulcer clinical trial, sales approval & US launch
Execute international roll-out plan
Launch EU Sales rapidly, subject to granting of CE Mark
Initial focus: Germany, Austria, Switzerland, UK, Benelux

Top Shareholders (approx.)

Allan Gray Investment Management	16.5%
Asia Union Investments	8.0%
Directors, Employees & Related Parties	3.6%
Queensland Uni. of Tech.	3.1%

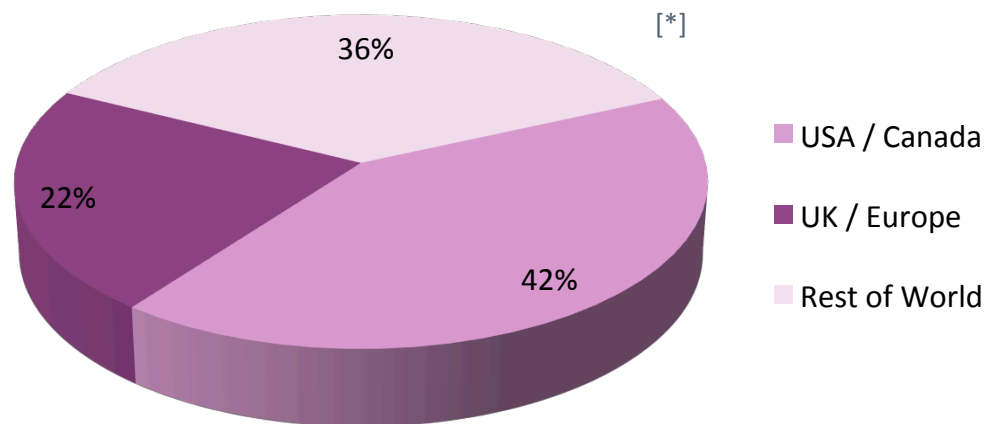


TISSUE THERAPIES

Section 2: Global Chronic Wound Market



Global Market: Hard to Heal Wounds US\$35 – 40Bn pa



- The USA and Europe are the largest combined market for chronic wound treatments.
- The global market is growing rapidly: at least 15% compound annual growth rate. ^[*]

[*] Data on file: Report Global Health Economic Projects LLC, USA, 2012 (contractor to Tissue Therapies Limited).

A growing problem = demand

- Chronic wounds: incidence increasing due to an ageing population and lifestyle choices.
- Increase in chronic venous insufficiency (CVI) and type II diabetes.
- CVI: the underlying condition for venous leg ulcers (VLU)
 - Half the adult population suffers from venous disease in the lower limbs (40-50% in men and 50-55% in women). ^[1]
 - Prevalence of CVI ranges from 2-7% in males and 3-7% in females. ^[1]
 - 70% of chronic ulcers in the lower limb are VLU. ^[1]
 - VLU's recurrence rate ranges from 54-70%. ^[1]
- Diabetes: the underlying condition for diabetic foot ulcers (DFU)
 - In 2014 9.3% (29.1 million people) of the US population have diabetes. ^[2]
 - In 2007 24 million people in the USA had diabetes. ^[3]
 - Incidence of DFU in the USA is approximately 6% and lower extremity amputation approximately 5%. ^[4]
 - Prevalence of DFU = 10.3% > 75 years of age and 6.5% at <44 years of age. ^[3]
 - DFU's recurrence rate 57.5%. ^[5]

High cost of treatment = need for a solution

- Chronic wounds are a growing problem with high costs of treatment: venous leg ulcers (VLU), diabetic ulcers (DFU) and pressure ulcers (PU).
- Chronic wound published annual cost estimates:
 - USA: VLU USD 18 billion ^[7]
 - USA: DFU USD 15 billion ^[7]
 - Europe: VLU Euro 6.5 billion ^[8]
 - UK (VLU, DFU, PU): GBP 2.3 to 3.1 billion ^[9]
- Health expenditure for treating chronic wounds as % of total health budget:
 - UK 2 – 3 % ^[9]
 - Europe 2% ^[9]
 - Scandinavia 2 – 4% ^[10]



TISSUE THERAPIES

Section 3: Our Lead Product VitroGro[®] ECM



VitroGro® ECM

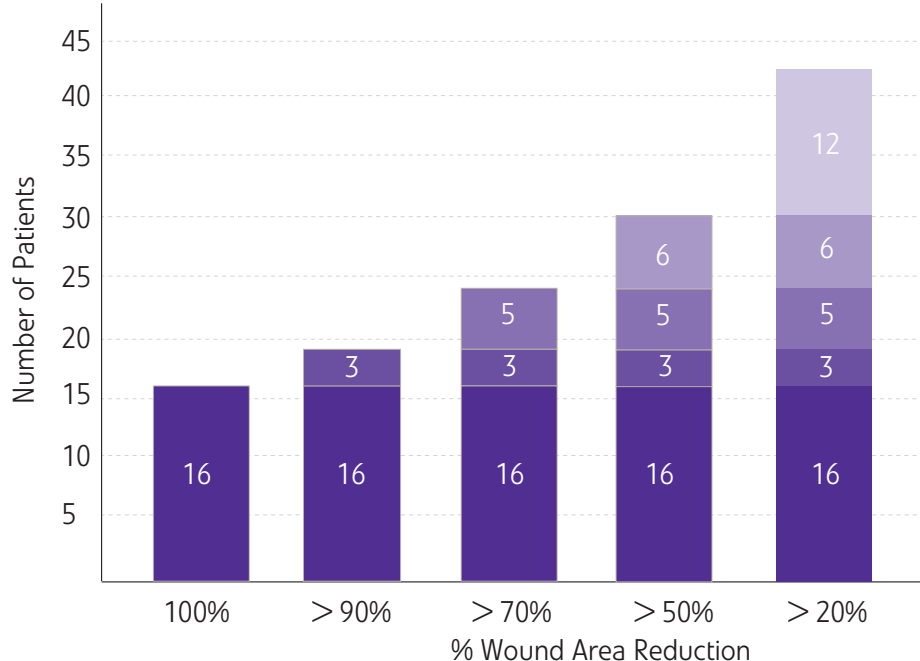


- VitroGro® ECM is a liquid formulation of a synthetic matrix protein that promotes healing and reduces pain in chronic wounds.
 - VitroGro® ECM replaces the degraded extracellular matrix (ECM) of chronic wounds.
 - The product is applied to the surface of a prepared wound and the liquid formulation allows the product to cover the irregular shape of wounds.
 - Skin cells attach to VitroGro® ECM proliferating and migrating onto the wound bed to initiate the healing process.
 - This restores the damaged dermis in the chronic wound reducing wound size over the course of weekly treatments.
- Development of commercial scale manufacturing of VitroGro® ECM is complete.

VitroGro® ECM: Clinical Effectiveness [11]

EU safety and effectiveness clinical trial : Venous Leg Ulcer (VLU) study

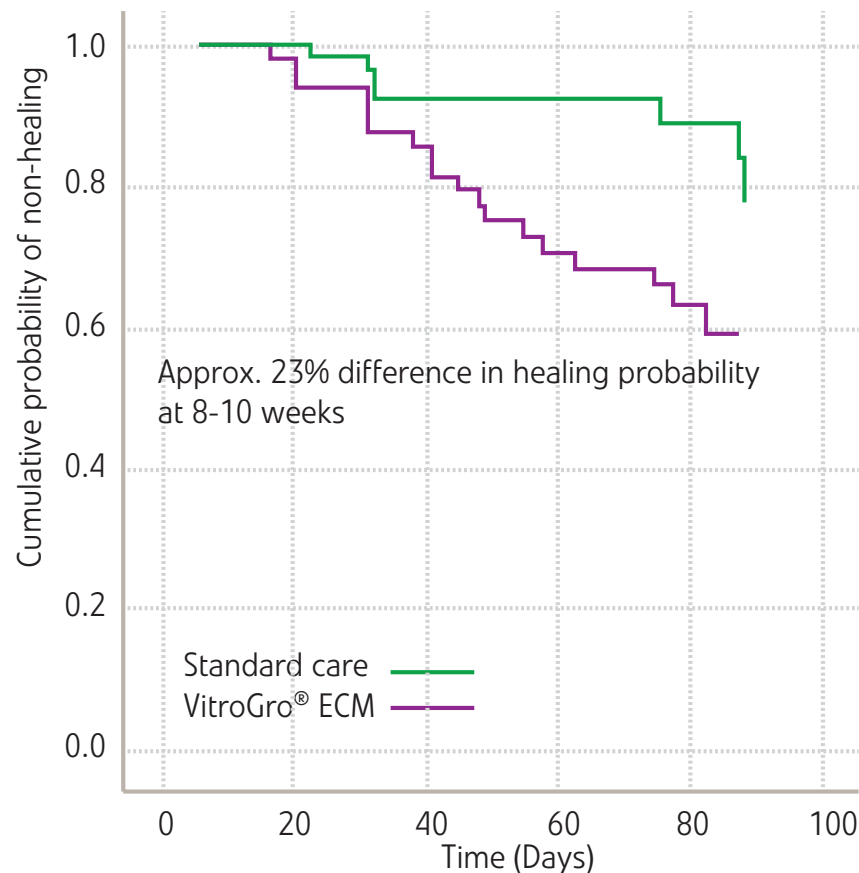
In human trials, VitroGro® ECM has demonstrated that it is an effective healing promoter able to take chronic wounds from a stalled non-healing state and move them towards healing.



Adapted from Harding K. et al. Int. Wound J. 2013.

- Results for 45 patients that completed the study:
 - Average age 74 years and had suffered venous ulcers that had not responded to expert care for an average of 37 months.
- All 45 study patients had no response to 4 weeks of expert care (run in period).
- Only change to care during study was application of VitroGro® ECM at routine dressing change.
- Strong results in 12 weeks:
 - 36% (16 out of 45 patients) completely healed (100% wound area reduction).
 - 67% (30 out of 45 patients) greater than 50% wound area reduction.
 - Median wound area reduction was 70%.

Venous Ulcer Cross Study Evaluation: Positive Health Economics ^[*]



- Data mined from German wound care networks (community and specialized clinic based care).
- Outcomes from EU clinical study and German standard care data analysed.
 - Number of matched standard care patients = 64
 - Approximately 23% difference in healing probability observed at the 8-10 week time point.
 - Statistically significant (Log rank test χ^2 11.46, $p=0.001$)
 - Not a head to head comparison study but results indicate a tangible benefit for using VitroGro® ECM.
- Further health economic analysis on expanded databases ongoing.

[*] Data on file, manuscript submitted to the German journal WundManagement.

Commercialisation: Partnership Structure

Tissue Therapies has in place partnerships to minimize operational risk, restrain cost and optimize revenue while maintaining flexibility and control

- **Quintiles**

- Outsourced HR for dedicated VitroGro® ECM Sales team; shared risk/reward: KPI based fee structure



- **Movianto**

- Integrated Logistics, Multi-lingual Customer Support, Order Entry, Supply, Accounts Receivable



- **Eurogentec**

- Manufacture of VitroGro® ECM Protein



- **Catalent**

- Fill and finish

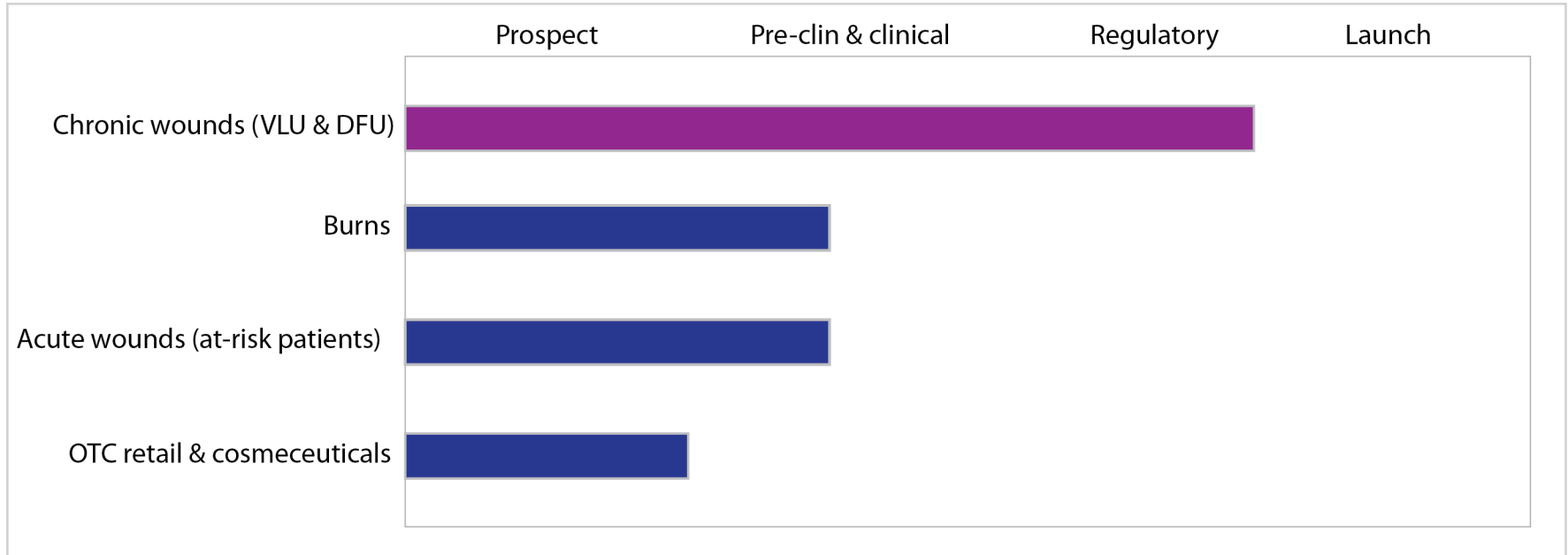


- **Queensland University of Technology (QUT)**

- Research & Development; only royalty payable is to QUT



Broad Product Pipeline



Extensive Library of Synthetic Proteins

- **Current Formulation:**
 - Global rollout for healing chronic wounds (diabetic & venous ulcers)
 - Additional applications e.g. pressure ulcers, burns, at risk surgical wounds
- **New Formulations:**
 - Additional tissue repair & scar avoidance products
 - Additional markets e.g. Pharmacy, OTC, consumer, first aid



TISSUE THERAPIES

Section 4: Strategy Update



CE Mark Update

- European Medicines Agency (EMA) review: final step: statutory 210 calendar day limit plus clock stop for questions.
- 180 day questions received and responses provided to the Notified Body (BSI) for submission to the EMA on 26 Feb. 2015
- EMA review Committee opinion should be advised to the Notified Body early April 2015 but experience has shown that the EMA timeline is not certain.
- The 120 day response resulted in approximately 65% of all questions being classified by EMA as “completely resolved”. The remaining questions have been addressed in the 180 day response but the acceptance of these will be subject to the approval of the EMA Review Committee.
- Benefits of EMA review:
 - Definitive regulatory approval for sale signed off by all EU member countries + 3 others.
 - To provide a robust regulatory package for approval for sale in multiple countries e.g. Turkey, Middle East, South Africa, Latin America, Russia, Taiwan, Canada and Australia.

Strategy Update

Unforeseen delays in the EMA review process for granting CE Mark have deferred the commencement of the FDA approval process for US sales. The Board has resolved that the opportunity cost of these delays is significant and the preparatory work for an FDA clinical trial in the US should proceed immediately.

Strategic Position:

- The regulatory approval process for the granting of CE Mark in the EU has exceeded internal timelines and expectations.
- The VitroGro® ECM application is thorough and meticulous but this does not guarantee that CE Mark will be granted imminently and contingency planning and risk mitigation for further potential delays are prudent.
- The appropriate risk mitigation strategy is to uncouple approvals and sales in the rest of the world from the EU CE Mark process.
- Starting an FDA diabetic ulcer trial in the USA will minimize risk and optimize future global sales by maximizing future market access. 2H 2015 start allows time for finalisation of contracts with clinical trial sites and manufacturing of VitroGro® ECM in required packaging for clinical trial use.

FDA Diabetic Ulcer Human Trial Design

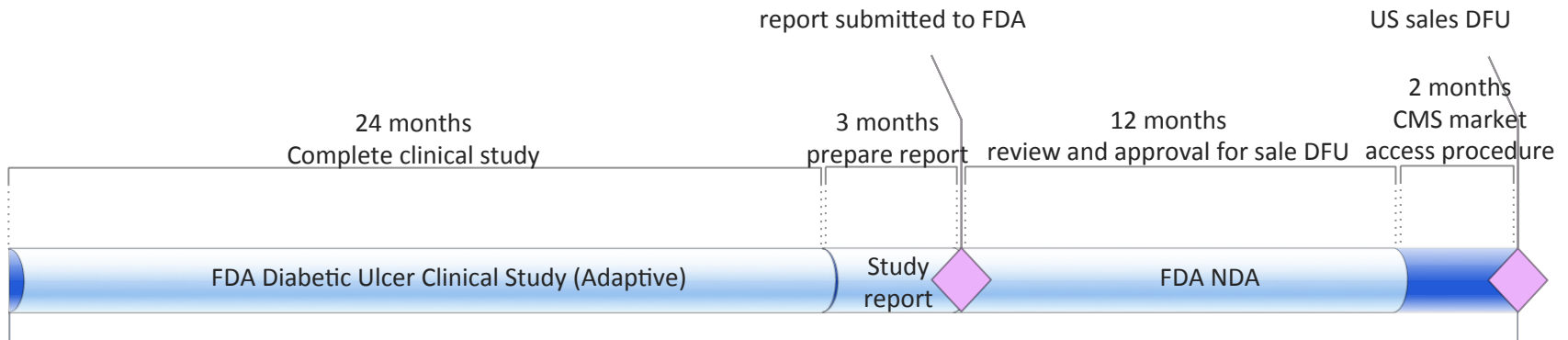
- Prospective randomized double blinded control trial of VitroGro® ECM v placebo.
- Planned as a 2 year clinical trial with sites in USA and EU, cost US\$10 million, with reporting anticipated 3 months after trial completion for submission to the FDA for approval for sale.
- Detailed analyses completed to calculate number of patients, delta over standard of care and statistical significance.
- Clinical trial sites and clinical investigators to be drawn from identified pool.
- Results to be used for FDA approval for sale for the treatment of diabetic ulcers and international approvals for sale.
- VitroGro® ECM protein FDA classification: combination device/biologic: practical commercial advantages:
 - No limit on number of clinical trial sites
 - Simplified reimbursement negotiations compared to devices
- Strong health economics compared to current global standard of care for venous ulcers: expected to be even better for diabetic ulcers.
- Most countries outside the EU accept FDA approval as basis for approval for sale.

Why an FDA Diabetic Ulcer Clinical Trial (instead of a venous ulcer trial)?

- Approval of VitroGro® ECM to treat both diabetic and venous ulcers will facilitate approval for sale in most countries in the world. Many countries outside the USA and EU accept either FDA approval or CE Mark as the basis for approval for sale e.g. Latin America, Asia, Middle East.
- The FDA diabetic ulcer clinical trial is designed to provide wound care clinicians with compelling data for the treatment of their diabetic ulcer patients, to compliment the clinical data already produced for the treatment of venous ulcers.
- An FDA diabetic ulcer clinical trial may also allow accelerated approval for sale in Japan under the Regenerative Medicine Promotion Law (2013).
- Strong clinical and live human cell data indicate that VitroGro® ECM may be even more effective at healing diabetic ulcers than venous ulcers.
- Health costs of diabetic ulcers are higher than venous ulcers and so health economic and cost savings of VitroGro® ECM treatment are likely to be even stronger than already shown for venous ulcers.
- The diabetic ulcer market is approximately the same size as the venous ulcer market but is growing faster.
- FDA diabetic ulcer clinical trial should have no impact on EU CE Mark approval or vice versa.

FDA Diabetic Ulcer Human Trial Indicative Timeline

- Tissue Therapies anticipates that following 3 – 6 months preparatory work, sales of VitroGro® ECM could start in the USA during the 2H of 2018 (subject to the FDA approval process proceeding as expected).



Strategy Summary

Key Strategic Objective:

Prevent Further Global Opportunity Cost of CE Mark Delays:

- Successfully complete final EMA review and granting of CE Mark.
- Commence FDA diabetic ulcer clinical trial during 2H 2015. Clinical trial expected to take 24 months & cost US\$10 million.
- Optimize size and speed of EU launch following CE Mark.
 - Initial concentration on Germany, Austria, Switzerland, UK: approx. 15% of global wound market^[1].
 - Countries outside EU that use CE Mark as important part of approval for sale: Russia, Turkey, Middle East, South Africa, Latin America, Canada, Australia.

Methods to Achieve Strategic Objective:

- Detailed protocol preparation underway for application to FDA to amend already approved venous ulcer clinical trial to diabetic ulcer trial.
- Sales, marketing and logistics preparation and execution for sales launch in EU and internationally: key commercial relationships in place.
- Health economic / reimbursement studies: 20 – 30% benefit from VitroGro® ECM
 - UK and German Government & private databases: matched patient outcomes and costs data.
 - Valid throughout EU and many other countries.
 - Designed to maximize market access.



TISSUE THERAPIES

Section 5: Capital Raising



Funding

Tissue Therapies intends to raise A\$7.7m (US\$6m) through a placement and an entitlement offer to fund:

- Completion of final EMA review, to seek approval for CE Mark and proceed with targeted country sales launches in the EU and internationally.
- Commence preparatory work for an FDA diabetic ulcer clinical trial.
- Provide working capital.

The Board estimates that a further A\$15 – 22m (US\$12 – 17m) will be required to fund the completion of the FDA clinical trial and submission for approval for sale and working capital requirements. It is expected that this funding will be secured from international strategic investors and this process will commence on completion of the capital raising.

Offer Overview

Offer Details	<ul style="list-style-type: none"> ● A Placement to institutional and sophisticated investors of approximately 19 million shares at an Offer Price of \$0.21 per new ordinary share to raise \$4 million with the ability to raise more subject to demand, followed by Entitlement Offer to existing shareholders targeted to raise \$3.7 million.
Pricing	<ul style="list-style-type: none"> ● The Offer Price of \$0.21 represents: <ul style="list-style-type: none"> ● 36.5% discount to the 10 business day Volume Weighted Average Price up to and including Fri. 30 January 2015 of \$0.33 ● 27.6% discount to the closing price on Fri. 30 January 2015 of \$0.29
Use of Funds	<ul style="list-style-type: none"> ● As well as providing the Company with working capital to meet the operational costs, TIS intends to use existing cash and the proceeds of the Equity Raising to proceed with: <ol style="list-style-type: none"> 1. Completion of all responses to successfully close out remaining questions from EMA reviewers to allow CE Mark to be granted. 2. Preparatory work for an FDA approved human prospective randomized double blinded control trial of VitroGro® ECM for the treatment of diabetic ulcers.
Other	<ul style="list-style-type: none"> ● New securities issued pursuant to the Placement will rank equally with Tissue Therapies existing securities. ● Morgans Corporate Limited and Baillieu Holst Limited are Joint Lead Managers to the Placement. ● There will be a top-up facility to allow existing shareholders to apply for additional shares under the entitlement offer.

Timetable

Activity	Date
Announcement of the Placement and Entitlement Offer	4 February 2015
Mailing of the Entitlement Offer details	5 February 2015
Ex-date	6 February 2015
Record Date for Entitlement Offer (7.00pm (AEDT))	10 February 2015
Information Booklet and Entitlement & Acceptance Form despatched	11 February 2015
Entitlement Offer opens	11 February 2015
Closing date for acceptances under Entitlement Offer (5.00pm (AEDT))	27 February 2015
New Shares quoted on deferred settlement basis	2 March 2015
Company notifies ASX of under subscriptions	4 March 2015
Allotment of New Shares under the Entitlement Offer	6 March 2015
Despatch of holding statements for New Shares issued under the Entitlement Offer	10 March 2015
Normal ASX trading for New Shares issued under the Entitlement Offer commences	10 March 2015

This timetable is indicative only and subject to change. The Directors may vary these dates, in consultation with the Underwriters, subject to the Listing Rules. The last date to extend the closing date is 24 February 2015. An extension of the Closing Date will delay the anticipated date for issue of the New Shares. The Directors also reserve the right not to proceed with the whole or part of the Entitlement Offer any time prior to issue of the New Shares. In that event, the relevant Application Monies (without interest) will be returned in full to Applicants.

Estimated Use of Funds

\$000's	Jan – Jul 2015
Opening cash	2,814
Capital raising *	7,687
Total Funds Available	10,501
 Outflows	
EMA expenditure	1,285
Preparation for FDA diabetic ulcer clinical trial	1,559
Marketing, sales and logistics	970
Manufacturing and stability testing	643
Market access expenditure	384
Intellectual property and regulatory costs	311
Research and development	587
Operating expenditure	
• Australian corporate salaries and Directors' Fees	1,034
• International consultants	393
• Registry, ASX, Audit & Tax Accounting & Insurance	178
• Other operating expenditure	374
Capital raising cost	461
Total Outflows	8,179
 Closing Cash	2,322

* It is expected that this capital raising will fund the Company through completion of the EMA review for EU sales and preparatory work for the FDA clinical trial. It is estimated that a further \$A15 – 22m will be required to complete the FDA diabetic ulcer trial and submission for FDA approval for sale and for working capital requirements. This investment will be targeted from strategic international investors and this process will commence at the completion of this capital raising.

Pro-Forma Balance Sheet

	31-Dec-14 Reviewed \$ 000's	Placement \$4M \$ 000's	Entitlement Offer \$3.7M \$ 000's	31-Dec-14 Pro-Forma
Current Assets				
Cash and cash equivalents	2,814	3,760 ^a	3,466 ^b	10,040
Receivables	92	-	-	92
Inventories	157	-	-	157
Current tax assets	189	-	-	189
Other assets	75	-	-	75
Total Current Assets	3,327	3,760	3,466	10,553
Non-Current Assets				
Inventories	9,381	-	-	9,381
Property, plant and equipment	202	-	-	202
Intangible assets	342	-	-	342
Other assets	2	-	-	2
Total Non-Current Assets	9,927	-	-	9,927
Total Assets	13,254	3,760	3,466	20,480
Current Liabilities				
Payables	839	-	-	839
Current tax liabilities	19	-	-	19
Provisions	318	-	-	318
Other liabilities	30	-	-	30
Total Current Liabilities	1,206	-	-	1,206
Non-Current Liabilities				
Other liabilities	90	-	-	90
Total Non-Current Liabilities	90	-	-	90
Total Liabilities	1,296	-	-	1,296
Net Assets	11,958	3,760	3,466	19,184
Equity				
Contributed equity	58,384	3,760	3,466	65,610
Reserves	51	-	-	51
Accumulated losses	(46,477)	-	-	(46,477)
Total Equity	11,958	3,760	3,466	19,184

Notes to the Pro Forma Balance Sheet:

Pro Forma Adjustments

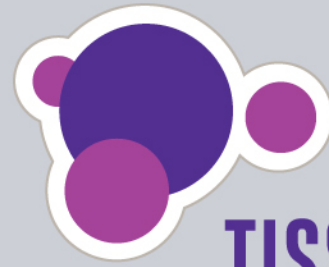
The Pro Forma Consolidated Statement of Financial Position has been prepared on the basis that the following significant transactions occurred as at 31 December 2014:

Material transactions since 31 December 2014:

- a) The issue of 19,047,642 New Shares arising from Placement, raising gross proceeds of \$4,000,005 less issue costs of \$240,000.

The Entitlement Offer:

- b) The issue of 17,557,218 New Shares under the Entitlement Offer, expected to raise gross proceeds of \$3,687,016 less estimated Offer costs of \$221,221



TISSUE THERAPIES

Section 6: Summary



VitroGro® ECM: Key Points

- CE Mark: Approximately 65% of EMA review questions completely resolved. Acceptance of final responses subject to the approval of the EMA.
- Proceed with FDA diabetic ulcer trial.
- Chronic wounds: large, fast growing market, no definitive treatment: US\$35 – 40 Bn per annum, 15% compound annual growth rate.
- VitroGro® ECM promotes **safe, convenient, cost effective** wound healing by replacing damaged skin scaffold.
- Commercial scale, efficient manufacturing process in place.
- Strong health economics supports reimbursement.



Summary of Key Risks

The major risks associated with an investment in TIS include:

- TIS may not obtain the regulatory approvals (such as the granting of CE Mark or FDA approval) that it requires for sale of its products or the reimbursement approvals required for sales growth, or such approvals may be subject to delay;
- TIS' clinical trials may prove unsuccessful;
- TIS currently has no material revenues. TIS intends to raise additional funds from international strategic investors later in 2015, which will have a dilutive effect on existing shareholders;
- TIS is dependent on the performance of its commercial partners and the retention of key consultants and personnel for its specialized business;
- TIS' value may be impacted if its intellectual property is not able to be adequately protected; and
- TIS may face competition from better resourced industry participants.

Disclaimer

- This document has been prepared by Tissue Therapies Ltd (the Company) to provide existing and prospective investors in Tissue Therapies Ltd with an update on the Company and its operations
- The information contained in the presentation is not intended to be an offer for subscription, invitation or recommendation with respect to shares in any jurisdiction.
- No representation or warranty, express or implied, is made in relation to the accuracy or completeness of the information contained in this document or opinions expressed in the course of this presentation. The information contained in this presentation is subject to change without notification.
- This presentation contains forward-looking statements which can be identified by the use of words such as “may”, “should”, “will”, “expect”, “anticipate”, “believe”, “estimate”, “intend”, “scheduled” or “continue” or similar expressions. Any forward-looking statements contained in this presentation are subject to significant risks, uncertainties, assumptions, contingencies and other factors (many of which are outside the control of, and unknown to, Tissue Therapies Ltd (“TIS”) and its officers, employees, agents or associates), which may cause the actual results or performance to be materially different from any future result so performed, expressed or implied by such forward-looking statements.
- There can be no assurance or guarantee that actual outcomes will not differ materially from these statements.
- The photographs of clinical subjects used in this presentation are illustrative of medical conditions associated with potential applications of VitroGro®. Actual clinical results may vary from those shown.

References

- [1] Luciana P *et al.* Venous ulcer: epidemiology, physiopathology, diagnosis and treatment. International Journal of dermatology 2005.
- [2] CDC-national diabetes statistics report 2014.
- [3] Driver VR *et al.* The costs of diabetic foot: the economic case for the limb salvage team. J. Vas. Surg. 2010.
- [4] Margolis DJ *et al.* Incidence of diabetic foot ulcer and lower extremity amputation among Medicare beneficiaries 2006 to 2008. Data Points Series publication 2011.
- [5] Dubsky M. *et al.* Risk factors for recurrence of diabetic foot ulcers: prospective follow-up analysis in the Eurodiale subgroup. International Wound Journal. 2013.
- [6] Chandon K *et al.* Human Skin Wounds: A Major and Snowballing Threat to Public Health and the Economy. Wound Repair Regen. 2009.
- [7] Press & announcements Organogenesis 26/09/13 Bradford-rice J. *et al.* 18th ISPOR annual meeting 2013 Presentation by “Analysis Group Inc. (A Health Economic Consultancy).
- [8] Posnett J. *et al.* The resource impact of wounds on healthcare providers in Europe. Journal of Wound Care. 2009
- [9] Posnett J. *et al.* The cost of skin breakdown and ulceration in the UK. The silent Epidemic. Smith and Nephew Foundation. 2007
- [10] Graves N *et al.* Modelling the direct health care costs of chronic wounds in Australia. Wound Practice & Research. 2014
- [11] Harding K. *et al.* Int. Wound J. Effectiveness of an acellular synthetic matrix in the treatment of hard-to-heal leg ulcers 2013, [Epub ahead of print].