29 April 2022

MARCH 2022 APPENDIX 4C

Tissue Repair Limited (ASX TRP, TR or the Company) is pleased to update the market on its progress in the March 2022 quarter and attaches its Appendix 4C Quarterly Cashflow Report for the period.

Key Highlights and Update

- Progress on a submission to the FDA (proposed for filing in May 2022) which, if endorsed will provide clarity on the substantive matters for the company to progress into a Phase III clinical program for its lead drug candidate TR-987.
- Strong funding position with cash of $25.6m as at 31 March 2022, sufficient to complete the planned Phase III trial.
- The Company was granted a patent during the quarter - "**AN ISOLATED BIOLOGICAL POLYSACCHARIDE COMPOUND, METHODS OF USE AND METHODS OF MANUFACTURE THEREOF"** - which provides a further 21 years of protection on the process of manufacture of its unique and proprietary immunogenic molecule.
- The Company has now enrolled physicians at eight clinics to evaluate its TR Pro+ aesthetic product. It is intended this real-world evaluation will include 100-150 patients.

TR-987 Wound Drug Candidate

The Company is progressing the pre-requisites for a Phase III clinical trial program approval and commencement including:

- **Manufacturing** – the Company is currently on track to produce its GMP API material by September 2022 and has successfully produced three laboratory scale batches that are consistent with the reference material used in previous clinical trials. The Company believes it is on track to deliver the manufacturing data required for a Phase III clinical trial approval by the FDA.
- **Analytics** - the Company is complying with all previous FDA recommendations with respect to the characterisation of TR-987. More than 20 discrete tests are being used to evaluate the lot-to-lot consistency of the API and will be utilised to establish release specifications for commercial and clinical production.
- In conjunction with its toxicology and regulatory experts, the Company has developed a toxicology program for submission to the FDA in its upcoming meeting request in May 2022.
- The Company is in the later stages of selecting an additional CMO and supplier of specialised equipment to produce the finished product for the Phase III clinical trial and future ongoing commercial manufacture.

Aesthetic Commercialisation (TR Pro+)

- Following the positive market research conducted in January 2022 the Company is progressing with a product familiarisation program to provide a real-world evaluation of TR Pro+ by physicians and patients.
- The Company is pleased to report it has enrolled eight clinics where physicians and patients are commencing an evaluation of the product. The company program will include a total of 15-20 clinics with c100-150 patients providing feedback and evaluation of the product.

- The Company has been delayed in the commissioning of production of the commercial supply of 10-gram tubes given the delays in supply chains globally but is pleased to report is has selected a vendor for the production of an initial run of 20,000 TR Pro+ 10g-tubes for sampling and commercial sale. It is expected that this inventory will be available in September 2022.

Summary of Current Work Streams and Next Quarter Activities

Milestone	Status	Completion Timing (Calendar year)	Success
TR-987 Wound Drug			
Manufacturing Stage 1: lab scale	Completed	Q1 2022	**YES**
Manufacturing Stage 2: engineering scale	In progress	Q3 2022	
Manufacturing Stage 3: GMP production	Yet to commence	Q3/Q4 2022	
Manufacturing Stage 4: Phase III clinical supplies	Yet to commence	Q4 2022	
Analytical development	In progress	Q4 2022	
Toxicology (as part of FDA type C meeting, to be requested in May)	In progress	Q3/Q4 2022	
Approval to commence Phase III trial	Yet to commence	Q4 2022 (subject to currently intended submission	
Phase III trial – Contract Research Organisation appointment process	In progress	Q3/Q4 2022	
Broader Clinical Scientific Advisory Panel	In progress	Q3/Q4 2022	
TR Pro+ (Aesthetics)			
Market research Report	Completed	Q4 2021	**YES**
Initial Production Run	CMO selected for initial inventory of 20,000 units	Q3 2022	
Product Familiarisation Program	In progress	Q4 2022	

Corporate and Financial Summary

The Company's cash position was $25.6 million as of 31 March 2022. During the March 2022 quarter total cash operating outflows were approximately $796,000, largely attributed to expenses associated with the development of TR-987 and commercialisation of TR Pro+.

A summary of the operating cash flow for the period 7 October 2021 to ending 31 March 2022 compared with the proposed use of funds in the Company's Prospectus dated 7 October 2021 is shown below:

	Use of Funds under Prospectus	Actual use of funds for the period ending 31 Mar 2022
Working capital and overheads[1]	300,000[1]	934,000[1]
Offer costs	2,300,000	1,841,000
Development of Chronic Wound Drug	3,700,000	491,000
Phase III Clinical Trials	13,600,000	4,000
Commercialisation of Aesthetic Product	2,100,000	327,000
Total	**22,000,000**	**3,597,000**

[1]The Company raised $7.5million via a convertible note in April 2021 (pre-IPO) which has been allocated to fund a significant portion of the working capital and overheads of the Company. The working capital and overhead cash outflows are broadly in line with the forecast budget. The Company believes the working capital outflows are consistent with the requirements for an ASX listed biotech Company of its size.

Research & Development (R&D) Tax incentive refunds were not included in the use of funds statement in the Prospectus. Any R&D tax incentive refunds received would further extend the runway and assist with executing the Company's strategic objectives.

In accordance with Listing Rule 4.7C, payments made to related parties and their associates included in items 6.1 of the Appendix 4C were $51,000. This includes payments for remuneration of director fees to executive and non-executive directors in the normal course of business at commercial rates, excluding reimbursements of out-of-pocket expenses.

KEY OPERATIONAL UPDATES

1. TR-987 DRUG DEVELOPMENT

1.1 Manufacturing Update

The Company's manufacturing initiatives are focussing on the delivery of four components

1. Manufacturing new API (drug substance) material consistent with the reference material used in the previous Phase IIB clinical trial program.
2. Satisfactory feedback from the FDA on the manufacturing process to enable progression into the Phase III trial.
3. Production of API for use in the Phase III trial.
4. Manufacture of finished gel / API (drug product) in 10-gram tubes for use in the Phase III trial.

The Company is currently on track to produce GMP-standard API material by September 2022 and has successfully produced three laboratory scale batches of material that are consistent with the reference material that was used in previous clinical trials.

Within the laboratory scale batches the Company has optimised the manufacture process, including the incorporation of several process developments. The Company is pleased to report that it now has a batch process that produces API material of the purity and immunogenic potency consistent with its previous Phase IIB clinical reference material which was previously produced by Novogen.

The purpose of these laboratory batches was to confirm the base process, examine critical parameters and test alternate mechanical technologies. Not all four laboratory batch drug substances were intended to match the standard characterisation, but importantly, the results from each laboratory batch varied as predicted based on our process understanding. Critical parameters were identified, and no further laboratory batches are expected to be required to progress this process to a production scale. Despite the process development initiatives, the first three laboratory batches have material consistency with the original reference material.

The Company's manufacturing status is summarised in the table below:

Stage	Update	Status
Stage 1 Laboratory scale API	Successfully completed production of 3 laboratory scale batches	Completed
Stage 2 Engineering API	• Preparatory work commenced to produce 2 engineering batches. • Production scheduled with the necessary equipment ordered. Batch record finalised and agreement reached with contract manufacturer.	Commenced Expected completion July 2022
Stage 3 GMP API	GMP production will commence immediately following successful production of the engineering batches.	Expected completion September 2022
Stage 4 Production of API into finished gel (10-gram tubes) for Phase III clinical supply	Formulation of API material into gel and filling into 10-gram tubes for the Phase III trial	Contract manufacturers to be appointed following RFI process

1.2 Raw material yeast supply

An in-principle agreement has been reached between the Company and AB Mauri (one of the largest global suppliers of food grade yeast) to support the supply of yeast raw material for GMP production, both for Phase III and ongoing commercial production.

This in-principle agreement contemplates AB Mauri maintaining a longer term separate yeast supply via a dedicated master cell bank of a specific strain of yeast as well as advanced characterisation of the raw material yeast to ensure consistency of API and the immunogenic mechanism of action of the final drug substance.

1.3 Analytical Update

The FDA has provided significant guidance to the Company on the specific tests required to characterise and test its drug product and drug substance, for both commercial production and for the Phase III pivotal trial.

The Company has now assembled a matrix of more than 20 tests to characterise the API and gel finished goods/product with corresponding laboratory partners and vendors. The matrix of tests has been used to analyse the laboratory scale production batches and reference material batches to determine consistency and will be used to further analyse engineering and GMP production batches. Included in the specification tests are proprietary tests designed to measure potency from human harvested macrophages which directly measure the immunogenic impact on human cells.

Method development work continues on each of these specification tests with the key aims to:

1. submit a complete dossier of all 20+ specification tests and the respective method developments to the FDA prior to Phase III approval; and
2. develop a complete analytical dossier for submission to the FDA containing the results for each test method across:
    a. historic reference material used in the Phase IIB clinical program
    b. dataset on the 3 laboratory scale batches
    c. dataset on the 2 engineering scale batches
    d. dataset on the 2 GMP scale engineering batches

1.4 Regulatory Update

The Company is aiming to submit an FDA meeting request in May 2022 which will seek clarity on key matters required to progress into the Phase III clinical study. The Company previously anticipated an FDA meeting request in February 2022 to cover a subset of matters. However, it has since decided to request a more substantial meeting which seeks to clarify a broader set of matters required to facilitate progression into the trial program. The Company now expects to submit the request in May 2022 which should allow recommendations and responses to be tabled by the FDA in July 2022.

Should the FDA endorse the plans, program and recommendations contained in this meeting request the Company will have sufficient clarity on the substantive items required to obtain Phase III clinical trial approval in Q4 2022. The Company believes the program of work detailed in the FDA submission can be fully funded with the current cash reserves to deliver a Phase III outcome.

The content to be included in the expanded type C meeting request to the FDA is based on input from a range of experts covering regulatory, clinical and pre-clinical aspects. Key plans and proposals to be submitted to the FDA for approval or guidance include matters relating to:

- Chemistry Manufacturing and Controls – that the FDA endorse the company's proposed manufacturing and analytical plans including the proposed 20+ specification tests.
- Raw material – the FDA endorse the yeast supply and characterisation and support the creation of a master cell bank facilitating long term supply.
- Toxicology – the FDA endorses the Company's proposed toxicology program consisting of additional tests including *in vitro* analysis, mini-pig toxicology studies and maximal clinical use human studies to be conducted in conjunction with the Phase III clinical trial program.
- Clinical trial – the FDA provide guidance on certain elements related to a Phase III clinical trial protocol.

1.5 Phase III VLU Trial CRO Cost Estimate (RFI)

A Request for Information (RFI) has been sent to five Contract Research Organisations (CRO) during the March 2022 quarter. The RFI is intended to gather comparative estimates of costs to conduct the required double-blind, randomised Phase III clinical trial. The RFI included details of the clinical trial design including an estimate of the number of subjects needed, the number of sites required, and the services requested (project management, clinical operations, data management, statistical analysis, investigator training etc.).

The Company has received preliminary responses and is pleased to report that the costings to conduct the Phase III clinical trial program at this preliminary stage are in line with the estimates contained within the prospectus.

1.6 Scientific Advisory Board (SAB)

The Company is in the process of establishing a broader scientific advisory board and key leading clinical experts in the treatment of chronic wounds. The company has had initial discussions with a leading wound healing expert who has conducted a number of high profile chronic wound clinical trials similar to the proposed phase III TR pivotal clinical trial.

1.7 Next Quarter Activities

Key activities for the June Quarter include

- Finalisation of the yeast specifications, testing, cell bank characterisation and associated documentation for the FDA meeting.
- Fine tuning of certain analytical methods required to determine sugar content and composition.
- Compilation of testing data, methods, protocols and reports for the FDA briefing document.

2. AESTHETIC COMMERCIALISATION TR Pro+

2.1 Real-World Evaluation of TR-Pro+ commenced

As reported in the December Quarter update the Company completed a market research program composed of interviews with 15 healthcare professionals (eg: dermatologists and cosmetic surgeons) and a further survey of 57 healthcare professionals. TR Pro+ was received positively by the group with some 86% of HCPS in the survey indicating they were likely to recommend the concept.

The Company has progressed in Quarter 3 with a product familiarisation program (ie: a real-world evaluation) of TR Pro+ by physicians and patients.

Information materials, a survey questionnaire, and an evaluation program have been developed for physicians and patients to appraise TR Pro+ as a post-procedure topical product following its use in targeted procedures, with a focus on its ability to aid and accelerate skin healing and skin quality.

2.2 Commercial production of TR-Pro+

The Company has selected a vendor to produce an initial run of 20,000 TR Pro+ 10-gram tubes to be used for samples and commercial sale. It is expected that this inventory will be available in September 2022.

2.3 Conference Activity

The Company has secured space at a number of relevant healthcare professional conferences to showcase TR Pro+ and facilitate networking and product discussions with relevant doctors. Among these, the Company will have a booth at the Annual Scientific Meeting of the Australian College of Dermatologists (ACD) which will be held in Adelaide in early May 2022.

2.4 Next Quarter Activities

- Completion of the PFP program for TR-Pro+ and analysis of results

Appendix 4C

Quarterly cash flow report for entities subject to Listing Rule 4.7B

Name of entity	
Tissue Repair Limited	
ABN	**Quarter ended ("current quarter")**
20 158 411 566	March 2022

Consolidated statement of cash flows		**Current quarter $A'000**	**Year to date (9 months) $A'000**
1.	**Cash flows from operating activities**		
1.1	Receipts from customers	-	-
1.2	Payments for		
	(a) research and development	(530)	(667)
	(b) product manufacturing and operating costs	-	-
	(c) advertising and marketing	(23)	(30)
	(d) leased assets	-	-
	(e) staff costs	(203)	(590)
	(f) administration and corporate costs	(183)	(717)
1.3	Dividends received (see note 3)	-	-
1.4	Interest received		
1.5	Interest and other costs of finance paid	-	-
1.6	Income taxes paid	-	-
1.7	Government grants and tax incentives	-	-
1.8	Other (provide details if material)	143	(51)
1.9	**Net cash from / (used in) operating activities**	**(796)**	**(2,055)**

2.	**Cash flows from investing activities**		
2.1	Payments to acquire or for:		
	(a) entities	-	-
	(b) businesses	-	-
	(c) property, plant and equipment	-	(4)
	(d) investments	-	-
	(e) intellectual property	-	-
	(f) other non-current assets	-	-

Consolidated statement of cash flows		Current quarter $A'000	Year to date (9 months) $A'000
2.2	Proceeds from disposal of:		
	(a) entities	-	-
	(b) businesses	-	-
	(c) property, plant and equipment	-	-
	(d) investments	-	-
	(e) intellectual property	-	-
	(f) other non-current assets	-	-
2.3	Cash flows from loans to other entities	-	-
2.4	Dividends received (see note 3)	-	-
2.5	Other (provide details if material)	-	-
2.6	**Net cash from / (used in) investing activities**	**-**	**(4)**

3.	**Cash flows from financing activities**		
3.1	Proceeds from issues of equity securities (excluding convertible debt securities)	-	22,000
3.2	Proceeds from issue of convertible debt securities	-	-
3.3	Proceeds from exercise of options	-	-
3.4	Transaction costs related to issues of equity securities or convertible debt securities	(20)	(1,908)
3.5	Proceeds from borrowings	-	-
3.6	Repayment of borrowings	-	-
3.7	Transaction costs related to loans and borrowings	-	-
3.8	Dividends paid	-	-
3.9	Other (provide details if material)	-	-
3.10	**Net cash from / (used in) financing activities**	**(20)**	**20,092**

4.	**Net increase / (decrease) in cash and cash equivalents for the period**		
4.1	Cash and cash equivalents at beginning of period	26,614	7,764
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(796)	(2,055)
4.3	Net cash from / (used in) investing activities (item 2.6 above)	-	(4)

Consolidated statement of cash flows		Current quarter $A'000	Year to date (9 months) $A'000
4.4	Net cash from / (used in) financing activities (item 3.10 above)	(20)	20,092
4.5	Effect of movement in exchange rates on cash held	(183)	(182)
4.6	**Cash and cash equivalents at end of period**	**25,615**	**25,615**

5.	Reconciliation of cash and cash equivalents at the end of the quarter (as shown in the consolidated statement of cash flows) to the related items in the accounts	Current quarter $A'000	Previous quarter $A'000
5.1	Bank balances	7,898	8,890
5.2	Call deposits	17,717	17,724
5.3	Bank overdrafts	-	-
5.4	Other (provide details)	-	-
5.5	**Cash and cash equivalents at end of quarter (should equal item 4.6 above)**	**25,615**	**26,614**

6.	Payments to related parties of the entity and their associates	Current quarter $A'000
6.1	Aggregate amount of payments to related parties and their associates included in item 1	51
6.2	Aggregate amount of payments to related parties and their associates included in item 2	-

Note: if any amounts are shown in items 6.1 or 6.2, your quarterly activity report must include a description of, and an explanation for, such payments.

The amount at 6.1 includes Director fees (including superannuation) for directors and related parties.

7.	**Financing facilities** *Note: the term "facility' includes all forms of financing arrangements available to the entity.* *Add notes as necessary for an understanding of the sources of finance available to the entity.*	**Total facility amount at quarter end $A'000**	**Amount drawn at quarter end $A'000**
7.1	Loan facilities	-	-
7.2	Credit standby arrangements	-	-
7.3	Other (please specify)	-	-
7.4	**Total financing facilities**	**-**	**-**

7.5	**Unused financing facilities available at quarter end**	-

7.6 Include in the box below a description of each facility above, including the lender, interest rate, maturity date and whether it is secured or unsecured. If any additional financing facilities have been entered into or are proposed to be entered into after quarter end, include a note providing details of those facilities as well.

8.	**Estimated cash available for future operating activities**	**$A'000**
8.1	Net cash from / (used in) operating activities (item 1.9)	(796)
8.2	Cash and cash equivalents at quarter end (item 4.6)	25,615
8.3	Unused finance facilities available at quarter end (item 7.5)	-
8.4	Total available funding (item 8.2 + item 8.3)	25,615

8.5	**Estimated quarters of funding available (item 8.4 divided by item 8.1)**	**32.2**

Note: if the entity has reported positive net operating cash flows in item 1.9, answer item 8.5 as "N/A". Otherwise, a figure for the estimated quarters of funding available must be included in item 8.5.

8.6 If item 8.5 is less than 2 quarters, please provide answers to the following questions:

8.6.1 Does the entity expect that it will continue to have the current level of net operating cash flows for the time being and, if not, why not?

Answer: N/A

8.6.2 Has the entity taken any steps, or does it propose to take any steps, to raise further cash to fund its operations and, if so, what are those steps and how likely does it believe that they will be successful?

Answer: N/A

8.6.3 Does the entity expect to be able to continue its operations and to meet its business objectives and, if so, on what basis?

Answer: N/A

Note: where item 8.5 is less than 2 quarters, all of questions 8.6.1, 8.6.2 and 8.6.3 above must be answered.

Compliance statement

1 This statement has been prepared in accordance with accounting standards and policies which comply with Listing Rule 19.11A.

2 This statement gives a true and fair view of the matters disclosed.

29 April 2022

Date: .....

By the Board

Authorised by: .....
(Name of body or officer authorising release – see note 4)

Notes

1. This quarterly cash flow report and the accompanying activity report provide a basis for informing the market about the entity's activities for the past quarter, how they have been financed and the effect this has had on its cash position. An entity that wishes to disclose additional information over and above the minimum required under the Listing Rules is encouraged to do so.

2. If this quarterly cash flow report has been prepared in accordance with Australian Accounting Standards, the definitions in, and provisions of, *AASB 107: Statement of Cash Flows* apply to this report. If this quarterly cash flow report has been prepared in accordance with other accounting standards agreed by ASX pursuant to Listing Rule 19.11A, the corresponding equivalent standard applies to this report.

3. Dividends received may be classified either as cash flows from operating activities or cash flows from investing activities, depending on the accounting policy of the entity.

4. If this report has been authorised for release to the market by your board of directors, you can insert here: "By the board". If it has been authorised for release to the market by a committee of your board of directors, you can insert here: "By the [*name of board committee – eg Audit and Risk Committee*]". If it has been authorised for release to the market by a disclosure committee, you can insert here: "By the Disclosure Committee".

5. If this report has been authorised for release to the market by your board of directors and you wish to hold yourself out as complying with recommendation 4.2 of the ASX Corporate Governance Council's *Corporate Governance Principles and Recommendations*, the board should have received a declaration from its CEO and CFO that, in their opinion, the financial records of the entity have been properly maintained, that this report complies with the appropriate accounting standards and gives a true and fair view of the cash flows of the entity, and that their opinion has been formed on the basis of a sound system of risk management and internal control which is operating effectively.