## JULY 2022 APPENDIX 4C

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

### Key Highlights and Update

### TR-987 Drug

- A request for a Type C meeting was filed with the FDA in June, seeking clarification on all the substantive matters required for progression into a Phase III trial. The FDA has indicated a written response to the information tabled by the Company will be communicated by early to mid-September 2022. A comprehensive briefing package accompanying the meeting request was filed with the FDA on 28 July 2022.
- Once the FDA provides feedback from this meeting, the Company will have sufficient clarity on the substantive items required to progress the Company towards a Phase III clinical trial.
- Concurrent to undertaking this FDA regulatory activity, the Company is manufacturing Phase III clinical API. Production of three GMP batches of API to formulate the TR-987 gel for use in the Phase III trial is expected to be completed in September 2022.
- The Company welcomes Professor Robert Kirsner to its Scientific Advisory Board. Professor Kirsner holds tenure at the School of Medicine, University of Miami and was the Principal Investigator in a clinical trial using spray-on skin with a similar target indication to that planned for the TR 987 Phase III trial (ie: VLUs 2-12 cm2).
- The Company is also in discussions with Professor Gary Ostroff, a tenured professor at the School of Medicine, University of Massachusetts, and anticipates Professor Ostroff also joining its advisory board. Professor Ostroff was the inventor of 'betafectin', a soluble glucan injectable which progressed into a Phase III trial in the mid-1990s as an alternative to antibiotic therapy.
- A patent has been granted and published as US Patent No. 11,384,160 on 12 July 2022 entitled "Method of Making a Beta Glucan Compound" which provides a further 21 years protection on the method of manufacture for Glucoprime, the company's proprietary active ingredient.

### TR Pro+ Aesthetic Gel

- The Company continues to progress its real-world evaluation of the aesthetic product, TR - Pro+. Nineteen clinics have registered, and Day-6 surveys have been received by more than 40 patients with half of these providing additional feedback at Day-28.
- Interim preliminary data from the evaluation is positive with patients providing feedback on measures such as their experience using TR Pro+ (4 out of 5) and their perception of skin healing (4.4 out of 5). The patient feedback has been positive, consistent with the market research outcomes in highlighting the benefits of TR Pro+ in relieving post-procedure symptoms and healing skin. The program is expected to be completed in September 2022 and provides additional confidence in the lead up to product launch.
- The Company continues to seek quotes from Australian-based companies to produce an initial run of 20,000 10ml tubes and 20,000 3ml tubes/sachets of TR Pro+. It is expected that this inventory will be available in Q1 2023.
- The company maintains its strong funding position with cash of $25.5m as of 30 June 2022, which based on current estimates should be sufficient to complete the planned Phase III trial.

**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 | Commenced | 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) | Yet to commence | Q3/Q4 2022 | |
| Approval to commence Phase III trial | Yet to commence | Q4 2022 (pending successful FDA meeting) | |
| 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 selection for initial inventory of 20,000 units under way | Q4 2022/Q1 2023 | |
| Product Familiarisation Program | In progress | Q4 2022 | |

**Corporate and Financial Summary**

The Company's cash position was $25.5 million as of 30 June 2022. During the June 2022 quarter total cash operating outflows were approximately $638,000, largely attributed to expenses associated with the development of TR-987 and commercialisation of TR Pro+, partially offset by receipt of 2020FY R&D tax incentive.

A summary of the operating cash flow for the period 7 October 2021 to 30 June 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 30 Jun 2022 |
|---|---|---|
| Working capital and overheads[1] | 300,000[1] | 1,196,000[1] |
| Offer costs | 2,300,000 | 1,849,000 |
| Development of Chronic Wound Drug | 3,700,000 | 949,000 |
| Phase III Clinical Trials | 13,600,000 | 39,000 |

| | | |
|---|---|---|
| Commercialisation of Aesthetic Product | 2,100,000 | 363,000 |
| Interest received | - | (10,000) |
| R&D tax incentive refund | - | (143,000) |
| **Total** | **22,000,000** | **4,243,000** |

[1]The Company raised $7.5million via a convertible note in April 2021 (pre-IPO), which has funded 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.

During the June 2022 quarter, the Company received an R&D tax incentive refund for the 2020FY of $143,376. In addition, in July 2022, the Company received $149,844 for its 2021FY R&D tax incentive refund.

The Company expects future favourable variances of the R&D Tax incentive inflows for FY2022 – FY2023 which were not included in the use of funds statement in the Prospectus. The estimated R&D tax incentive refunds will further extend the runway and assist with executing the Company's strategic objectives and provide a contingency should additional expenditure be required to meet the Company's objectives for TR-987 and TR Pro+.

During the period ending 30 June 2022, overall spend was lower than estimated in the use of funds as set out in the Prospectus largely due to timing differences associated with commissioning of key work streams including chemistry manufacturing and control (CMC) work for the Company's drug candidate TR-897, and development work streams associated with commercialisation of TR-Pro+. The Company anticipates cash outflows in future quarters will increase in line with the acceleration of the chronic wound drug clinical program, and commercialisation of the aesthetic product.

In Accordance with Listing Rule 4.7C, payments made to related parties and their associates included in item 6.1 of the Appendix 4C totalled $70,000. This includes remuneration of 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 drug product (gel/API) 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 which will be validated by the end of the year. Three laboratory scale batches of material have been successfully produced which are consistent with the reference material that was used in previous clinical trials.

The laboratory scale batches have provided an opportunity to optimise the manufacture process which has led to a reduction in the overall time and cost of production. Several positive process refinements have also been made. The Company is confident that it now has a reliable batch process to produce API material of the purity and immunogenic potency consistent with its previous Phase IIB clinical reference material which was previously manufactured by Novogen.

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 | • Successful completion of 4 scale up engineering batches.<br>• Production scheduled with the necessary equipment ordered. Batch record finalised and agreement reached with contract manufacturer. | Commenced<br>Expected completion August 2022 (validation completed by year end) |
| **Stage 3** GMP API | • GMP production will commence immediately following successful production of the engineering batches. | Expected completion September 2022 (validation completed by year end) |
| **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. Expected completion Q4 2022 |

### 1.2 Supply of raw material (yeast)

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 for Phase III and ongoing commercial production.

This agreement stipulates 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 the Phase III pivotal trial.

The Company has now assembled an array of more than 20 tests to characterise the API and gel finished goods/product with corresponding laboratory partners and vendors. A selection of these tests has been used to analyse the laboratory scale production batches and reference material batches to demonstrate 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 assess the immunogenic impact on human cells.

Method development work continues with the primary aim of developing a comprehensive dossier for the FDA which describes in detail each of the 20+ specification tests and the respective method developments, as well as the test results prior to the Phase III study.

### 1.4 Regulatory Update

The Company submitted an FDA Type C meeting request in June to seek clarity on key matters required to progress into the Phase III clinical study. The FDA has indicated a written response to the information tabled by the Company will be communicated by early to mid-September 2022. A detailed briefing package accompanying the meeting request was filed with the FDA on 28 July 2022.

The FDA package contents were based on input from a range of experts covering regulatory, clinical and pre-clinical aspects. Specifically, FDA guidance is being sought for the following aspects:

- Chemistry Manufacturing and Controls – that the FDA endorses the company's proposed manufacturing and analytical plans including the proposed 20+ specification tests.
- Raw material – the FDA approves 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 abridged toxicology program to be conducted in conjunction with the Phase III clinical trial program.
- Clinical trial – the FDA provides guidance on certain elements related to a Phase III clinical trial protocol.

If the FDA ratifies the plans, program and recommendations put forward for this meeting the Company will have sufficient clarity on the substantive items required to obtain a 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.

### 1.5 Phase III VLU Trial CRO Cost Estimate (RFI)

RFI's have been received from five Contract Research Organisations (CROs) which outline comparative estimates of costs to conduct the required double-blind, randomised Phase III clinical trial. Further due diligence on two of the CROs is needed before a final decision is made in Q3/Q4 2022. The estimates provided so far are consistent with those contained within the prospectus.

### 1.6 Scientific Advisory Board (SAB)

The Company has appointed Professor Robert Kirsner to its Scientific Advisory Board. Professor Kirsner is a Tenured Professor, Chairman and holds the endowed Harvey Blank Chair in Dermatology in the Department of Dermatology and Cutaneous Surgery at the University of Miami Miller School of Medicine. He currently serves as director of the University of Miami Hospital Wound Center and Chief of Dermatology at the University of Miami Hospital. Professor Kirsner was the Principal Investigator in a clinical trial using spray-on skin with a similar target indication to that planned for the TR 987 Phase III trial (ie: VLUs 2-12 cm2).

The Company has also identified and had discussions with several candidates with expertise in the management of chronic wounds and expects to formally appoint SAB members in Q4 2022.

### 1.7 Next Quarter Activities

- Continued progression of the analytical methods required to characterize the active ingredient and the finished hydrogel product.
- Compilation of the briefing package to accompany the FDA Type C meeting submission, which will be filed on 28 July 2022.

## 2. AESTHETIC COMMERCIALISATION TR Pro+

### 2.1 Real-World Evaluation of TR-Pro+ commenced

The Company has progressed its Product Familiarization Program (PFP) having registered 19 Dermatology clinics. More than forty patients have so far provided feedback at Day-6 post use with 19 of those providing additional feedback at Day-28. The types of procedures that have been used

include laser ablation, micro needling, chemical peels, and broadband and intense-pulsed light treatments.

Interim preliminary data from the evaluation is positive with patients providing feedback on measures such as their experience using TR Pro+ (4 out of 5) and their perception of skin healing (4.4 out of 5). The patient feedback has been positive, consistent with the market research outcomes in highlighting the benefits of TR Pro+ in relieving post-procedure symptoms and healing skin. The program is expected to be completed in September 2022 and provides additional confidence in lead up to product launch.

The Company anticipates completing the PFP in Q3 2022 and will work with IQVIA (program coordinators) to develop a compelling summary that builds on the clinical data to support the use of TR Pro+ as an effective aftercare product for aesthetic procedures.

### 2.2 Commercial launch of TR-Pro+

Additional quotes are being sought from Australian-based manufacturers to produce an initial batch of 20,000 10ml tubes of TR Pro+. The Company expects to have stock available in Q1 2023 at which time TR Pro+ can be officially launched.

Details around a staged approach to launching in specific target markets are being developed.

### 2.3 Conference Activity

The Company recently showcased TR Pro+ at three conferences: the Australasian College of Dermatologists Annual Scientific Meeting, the Plastic Surgeons Conference, and the Brisbane Tattoo Expo. These fora provided opportunities to discuss the benefits of TR Pro+ in detail, and importantly, uncovered insights about how best to communicate these benefits to each target audience. The benefits of TR Pro+ resonated well with audiences at all conferences, with strong interest in the use of the product as a post procedure topical following a variety of procedures

### 2.4 Next Quarter Activities

- Completion of the PFP program for TR-Pro+ and analysis of results
- Development of a commercialisation strategy for TR Pro+

# 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 | 30 June 2022 |

| **Consolidated statement of cash flows** | | **Current quarter $A'000** | **Year to date (12 months) $A'000** |
|---|---|---|---|
| **1.** | **Cash flows from operating activities** | | |
| 1.1 | Receipts from customers | - | - |
| 1.2 | Payments for | | |
| | (a) research and development | (348) | (1,015) |
| | (b) product manufacturing and operating costs | - | - |
| | (c) advertising and marketing | - | (30) |
| | (d) leased assets | - | - |
| | (e) staff costs | (223) | (813) |
| | (f) administration and corporate costs | (263) | (980) |
| 1.3 | Dividends received (see note 3) | - | - |
| 1.4 | Interest received | 10 | 10 |
| 1.5 | Interest and other costs of finance paid | - | - |
| 1.6 | Income taxes paid | - | - |
| 1.7 | Government grants and tax incentives | 143 | 143 |
| 1.8 | Other (provide details if material) | 42 | (9) |
| **1.9** | **Net cash from / (used in) operating activities** | **(639)** | **(2,694)** |

| **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 (12 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 | (8) | (1,916) |
| 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** | **(8)** | **20,084** |

| **4.** | **Net increase / (decrease) in cash and cash equivalents for the period** | | |
|---|---|---|---|
| 4.1 | Cash and cash equivalents at beginning of period | 25,615 | 7,764 |
| 4.2 | Net cash from / (used in) operating activities (item 1.9 above) | (639) | (2,694) |
| 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 (12 months) $A'000 |
|---|---|---|---|
| 4.4 | Net cash from / (used in) financing activities (item 3.10 above) | (8) | 20,084 |
| 4.5 | Effect of movement in exchange rates on cash held | 487 | 305 |
| **4.6** | **Cash and cash equivalents at end of period** | **25,455** | **25,455** |

| 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 | 12,745 | 7,898 |
| 5.2 | Call deposits | 12,710 | 17,717 |
| 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)** | **25,455** | **25,615** |

| 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 | 70 |
| 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**<br>*Note: the term "facility' includes all forms of financing arrangements available to the entity.*<br>*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) | (639) |
| 8.2 | Cash and cash equivalents at quarter end (item 4.6) | 25,455 |
| 8.3 | Unused finance facilities available at quarter end (item 7.5) | - |
| 8.4 | Total available funding (item 8.2 + item 8.3) | 25,455 |
| 8.5 | **Estimated quarters of funding available (item 8.4 divided by item 8.1)** | **39.8** |

*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.

Date: 29 July 2022
.....

Authorised by: The Board
.....
(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.