ASX Announcement
Friday 28 October 2022

**SEPTEMBER 2022 - QUARTERLY ACTIVITIES REPORT & APPENDIX 4C**

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

**Key Highlights and Update**

**TR987® Drug**

- In response to the Type C meeting request in June, the FDA has broadly accepted as reasonable the Company's intended approach to chemistry, manufacturing and controls, raw material procurement and characterisation, and the proposed abridged toxicology program.
- Based on the recommendations within the FDA Type C meeting response, the Company is pleased to have greater clarity on key matters to progress into a phase 3 program, which was the main purpose of the meeting.
- The Company will continue to consult with its regulatory advisers and then seek further discussions with the FDA on the outstanding matters, with a view to holding an End of Phase 2 meeting in Q1 2023 to close out its phase 2 studies and seek approval for its phase 3 protocol.
- In addition to the three laboratory batches, the Company has manufactured four engineering batches of the API and two batches for phase 3 clinical supplies which are currently being analysed. Preliminary results on the two phase 3 clinical batches indicates similarity to the reference API and these will be used to produce GMP-standard finished product for use in the phase 3 clinical study.
- A second patent (17/845,098) has been granted which provides broad protection for the use of TR987® and Glucoprime® on any skin condition including burns, chronic wounds, surgical wounds, pressure ulcers and any post procedure wound whether surgical or cosmetic. The granting of the patent strengthens the planned commercialisation of TR Pro+™ both globally and in Australia.

**TR Pro+™ Aesthetic Gel**

- The real-world evidence study was closed on 15 September 2022 by which time 12 dermatology clinics had enrolled 102 patients who represented a broad cross section of ages and skin types.
- The results of a 48-patient cohort who completed both surveys were consistently positive. Notable outcomes at day 28 included:
    - patients' feelings towards perception of skin healing (81% of patients provided a 4 or 5 out of 5 rating)
    - satisfaction using TR Pro+™ (81% of patients provided a 4 or 5 out of 5 rating)
    - perception of skin healing (85% of patients provided a 4 or 5 out of 5 rating)
    - 100 percent of patients who had had a previous procedure reported that their overall healing using TR Pro+™ was similar or better than their prior use with other products

- A local contract manufacturer has been engaged to produce the initial batch of 10g tubes and 5 3g sample sachets to be available for the launch of TR Pro+™ in Q1 2023.
- A commercialisation strategy for TR Pro+™ has been finalised and implementation of this plan will follow production.
- A report on a phase 2 clinical trial which used TR Pro+™ (referred to in the article as TR987®) in patients who had undergone $CO_2$ fractionated laser skin resurfacing treatment has been accepted for publication in the highly regarded, peer reviewed journal of Dermatologic Surgery and will be available online from December 2022.
- The Company maintains its strong funding position with cash of $24.4m as of 30 September 2022. After reviewing its budget, it remains confident that the costs of the adjusted program of work required by the FDA can be fully funded from its current cash reserves to deliver a phase 3 outcome.

**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 | Completed | Q3 2022 | **YES** |
| Manufacturing Stage 3: GMP production | In progress | Q1 2023 | |
| Manufacturing Stage 4: phase 3 clinical supplies | In progress | Q1 2023 | |
| Analytical development | In progress | Q1 2023 | |
| Toxicology | FDA guidance provided and work in progress | Q2 2023 | |
| Approval to commence phase 3 trial | In progress | Q1 2023 (EOP2 meeting requested Q4 2022) | |
| Phase 3 trial – Contract Research Organisation appointment process | In progress | Q1 2023 | |
| Broader Clinical Scientific Advisory Panel | In progress | Q1 2023 | |
| | | | |
| **TR Pro+ (Aesthetics)** | | | |
| Market research Report | Completed | Q4 2021 | **YES** |
| Product Familiarisation Program | Completed | Q4 2022 | **YES** |
| Publication of phase 2 clinical trial on laser skin resurfacing | Accepted | Q4 2022 | **YES** |
| Initial Production Run | In progress | Q1 2023 | |

**Corporate and Financial Summary**

The Company's cash position was $24.4 million as of 30 September 2022. During the September 2022 quarter total cash operating outflows were approximately $1.4million, largely attributed to expenses associated with the development of TR-987® and commercialisation of TR Pro+™, partially offset by receipt of 2021FY R&D tax incentive.

A summary of the operating cash flow for the period 7 October 2021 to 30 September 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 Sep 2022 |
|---|---|---|
| Working capital and overheads[1] | 300,000[1] | 1,568,000[1] |
| Offer costs | 2,300,000 | 1,849,000 |
| Development of Chronic Wound Drug | 3,700,000 | 1,939,000 |
| Phase 2 Clinical Trials | 13,600,000 | 128,000 |
| Commercialisation of Aesthetic Product | 2,100,000 | 463,000 |
| Interest received | - | (13,000) |
| R&D tax incentive refunds | - | (293,000) |
| **Total** | **22,000,000** | **5,641,000** |

[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 September 2022 quarter, the Company received an R&D tax incentive refund for the 2021FY of $149,844.

The Company expects future favourable variances to its current budgets in the form of R&D Tax incentive inflows for FY2022 – FY2023 and beyond, which were not included in the use of funds statement in the Prospectus. Such R&D tax incentive refunds will further extend the Company's cash runway, assisting with execution of the Company's strategy and providing e a contingency should additional expenditure be needed to meet the Company's objectives for TR987® and TR Pro+™.

During the period ending 30 September 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 TR897®, 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. TR987® 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 2 clinical trial program.
2. Satisfactory feedback from the FDA on the manufacturing process to enable progression into the phase 3 trial.
3. Production of API for use in the phase 3 trial.
4. Manufacture of finished drug product (gel/API) in 10-gram tubes for use in the phase 3 trial.

Three laboratory scale batches of material have been produced successfully and are consistent with the reference material that was used in previous clinical trials.

The laboratory batches together with the four engineering batches and two in-process GMP batches completed to date have confirmed our ability to replicate the molecule used in the phase 2 studies. Based on our work aimed at stress testing the process and varying the parameters during the laboratory and engineering batches there is a high level of confidence that the process can be transferred at larger scale and into different equipment for commercial GMP manufacture.

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

| Stage | Update | Status |
|---|---|---|
| **Stage 1** Laboratory scale API | • Successful production of 3 laboratory scale batches | Completed |
| **Stage 2** Engineering API | • Successful production of 4 scale-up engineering batches.<br>• Production scheduled with the necessary equipment ordered. Batch record finalised and an agreement reached with contract manufacturer. | Completed<br><br>Expected completion Q1 2023 (validation completed by Q1 2023) |
| **Stage 3** GMP API | • Production of 2 GMP batches will commence immediately following successful production of the engineering batches. | Expected completion Q1 2023 (validation completed by Q1 2023) |
| **Stage 4** Production of API into finished gel (10-gram tubes) for phase 3 clinical supply | • Formulation of API material into gel and filling into 10-gram tubes for the phase 3 trial | Contract manufacturers to be appointed following RFI process. Expected completion Q4 2022 |

### 1.2 Analytical Update

The Glucoprime® API method development activities are continuing and together support an array of more than 20 tests that fully characterise the API and gel finished product. Tests relating to degradation products, linkage analysis, and protein fingerprinting are all currently in development.

Analysis of two engineering batches is in progress and the data generated so far shows a high level of consistency with the previous API material used in the phase 2 clinical trial.

The primary aim of the method development work is to support a comprehensive dossier for the FDA which describes in detail each of the specification tests and the respective method developments, as well as the test results prior to the phase 3 study.

## 1.3 CMO Update

Tergus Pharma (Durham, NC) has been selected as the CMO to produce the TR987® finished gel for validation and the phase 3 clinical 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 to the phase 3 clinical study and received a written response from the Agency in mid-September. In its response, the FDA broadly accepted as reasonable the Company's intended approach to:

- Chemistry Manufacturing and Controls - including release specifications for Glucoprime®
- Raw material - including the Company's yeast supply arrangements, characterisation and creation of a master cell bank facilitating long-term supply of this raw material
- Toxicology - including the Company's proposed abridged toxicology program consisting of an in vitro degradation analysis, a 28-day mini-pig toxicology study, and a maximal clinical use human study.

The Company also sought advice from the FDA on Fast Track Designation and/or Breakthrough Therapy Designation (FTD/BTD).

The FDA did not accept that TR-987® was eligible for Fast Track Designation and/or Breakthrough Therapy Designation (FTD/BTD), based on results from the Company's phase 2 study alone, stating that for this to be considered a further phase 2 trial would be required. The FDA did however note that if the Company adopted this route, it may only have to conduct a single confirmatory (phase 3) trial, rather the two phase 3 trials it has been planning and budgeting for. The FDA indicated that if results showed that TR-987® had the potential to address an unmet medical need in the treatment of venous stasis (leg) ulcers over the existing therapies, it could then submit a formal request for FTD/BTD status.

The FDA also accepted that the documentation and the yeast material is suitable for use in the phase 3 Glucoprime® API material.

Based on the recommendations within the Type C meeting response, the Company is pleased to have greater clarity on key matters to progress into a phase 3 program, which was the main purpose of the meeting.

The Company will continue to consult with its regulatory advisers and then seek further discussions with the FDA on the outstanding matters, with a view to holding a meeting with the FDA to close out its phase 2 studies and confirm protocols for its planned phase 3 trials.

**1.5 Phase 3 VLU Trial CRO Cost Estimate (RFI)**

Further discussions have been undertaken with the Contract Research Organisations (CROs) who completed the RFI document, and a final decision on who to appoint will be made in Q4 2022. The cost 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 TR987® phase 3 trial (ie: VLUs 2-12 cm2).

**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 EOP2 meeting submission, which will be requested in Q4 2022.

## 2. AESTHETIC COMMERCIALISATION TR Pro+™

### 2.1 Real-World Evaluation of TR-Pro+™ completed

The real-world evidence study concluded on 15 September 2022 by which time 12 dermatology clinics had enrolled 102 patients who represented a broad cross section of ages and skin types. Of these, 63 patients and 49 patients completed the surveys on days 6 and 28, respectively, with 48 patients completing both surveys. The results of the 48-patient cohort were consistently positive at day 28 for patients' feelings towards perception of skin healing ('Happy' - 81%), satisfaction using TR Pro+™ ('Satisfied' - 81%), perception of skin healing ('Well' - 85%). Notably, 100 percent of patients reported that their overall healing using TR Pro+™ was similar or better in comparison to their previous experiences using other products.

### 2.2 Commercial launch of TR Pro+™

A local contract manufacturer has been appointed to manufacture the initial batch of TR Pro+™ comprising 10g tubes and 3g sample sachets. We expect to have stock and samples in time for the product launch in Q1 2023.

A commercialisation strategy has been finalised and marketing materials are currently being prepared in the leadup to the TR Pro+™ launch

### 2.3 Conference Activity

During the quarter the Company attended the Australasian Beauty Expo and Wounds Australia 2022 Conference where TR Pro+™ was showcased. Both conferences provided opportunities to discuss the benefits of TR Pro+™ in detail and reinforced the interest from beauty clinics in its use in the aftercare across a range of cosmetic procedures.

### 2.4 Publication of TR Pro+ for use following laser skin resurfacing procedures

A report of a phase 2 clinical trial which used TR Pro+™ (referred to in the article as TR987®) in patients who had undergone $CO_2$ fractionated laser skin resurfacing treatment was accepted for publication in the highly regarded, peer reviewed journal of Dermatologic Surgery and will be available online from December 2022. This represents the first publication from the Company describing clinical studies using the Glucoprime® API.

### 2.4 Next Quarter Activities

- Complete data analysis of the real-world evidence study and development of a summary document
- Further development of the TR Pro+™ commercialisation strategy

For further information in relation to this release please contact Darryl Reed at darryl.reed@trtherapeutics.com 0419 557 663.

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

# 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 September 2022 |

| **Consolidated statement of cash flows** | | **Current quarter $A'000** | **Year to date (3 months) $A'000** |
|---|---|---|---|
| **1.** | **Cash flows from operating activities** | | |
| 1.1 | Receipts from customers | - | - |
| 1.2 | Payments for | | |
| | (a) research and development | (919) | (919) |
| | (b) product manufacturing and operating costs | (9) | (9) |
| | (c) advertising and marketing | (59) | (59) |
| | (d) leased assets | - | - |
| | (e) staff costs | (234) | (234) |
| | (f) administration and corporate costs | (348) | (348) |
| 1.3 | Dividends received (see note 3) | - | - |
| 1.4 | Interest received | 3 | 3 |
| 1.5 | Interest and other costs of finance paid | - | - |
| 1.6 | Income taxes paid | - | - |
| 1.7 | Government grants and tax incentives | 150 | 150 |
| 1.8 | Other (provide details if material) | 18 | 18 |
| **1.9** | **Net cash from / (used in) operating activities** | **(1,398)** | **(1,398)** |

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

| Consolidated statement of cash flows | | Current quarter $A'000 | Year to date (3 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** | **-** | **-** |

| **3.** | **Cash flows from financing activities** | | |
|---|---|---|---|
| 3.1 | Proceeds from issues of equity securities (excluding convertible debt securities) | - | - |
| 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 | - | - |
| 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** | **-** | **-** |

| **4.** | **Net increase / (decrease) in cash and cash equivalents for the period** | | |
|---|---|---|---|
| 4.1 | Cash and cash equivalents at beginning of period | 25,455 | 25,455 |
| 4.2 | Net cash from / (used in) operating activities (item 1.9 above) | (1,398) | (1,398) |
| 4.3 | Net cash from / (used in) investing activities (item 2.6 above) | - | - |

| Consolidated statement of cash flows | | Current quarter $A'000 | Year to date (3 months) $A'000 |
|---|---|---|---|
| 4.4 | Net cash from / (used in) financing activities (item 3.10 above) | - | - |
| 4.5 | Effect of movement in exchange rates on cash held | 328 | 328 |
| **4.6** | **Cash and cash equivalents at end of period** | **24,385** | **24,385** |

| 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 | 5,930 | 12,745 |
| 5.2 | Call deposits | 18,455 | 12,710 |
| 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)** | **24,385** | **25,455** |

| 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) | (1,398) |
| 8.2 | Cash and cash equivalents at quarter end (item 4.6) | 24,385 |
| 8.3 | Unused finance facilities available at quarter end (item 7.5) | - |
| 8.4 | Total available funding (item 8.2 + item 8.3) | 24,385 |
| 8.5 | **Estimated quarters of funding available (item 8.4 divided by item 8.1)** | **17.4** |

*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: 28 October 2022

Authorised by: Board of Directors
(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.