Biotech Daily

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Daily news on ASX-listed biotechnology companies

Dr Boreham's Crucible: Tissue Repair

By TIM BOREHAM

ASX code: TRP

Share price: 26 cents; **Shares on issue:** 60,464,843 (13,684,488 in ASX escrow)

Market cap: $15.7 million

Chief executive officer: Tony Charara

Board: Jack Lowenstein (chair), Mr Charara (co-founder and executive director), Bryan Gray, Dr Michael Silberberg (Max Johnston and Prof Craig Stamp resigned on April 28, 2023)

Financials (March quarter 2023): revenue nil, cash outflows $1.12 million, end -of-quarter cash $21.8 million, quarters of available funding 19.5

Identifiable major holders: Selene Holdings (NZ high net worth investor) 9.85%, Spark Capital Pty Ltd (Mr Charara) 8.1%, Creight Investments (Peter Scutt and Nadia Jacob) 5.01%, Welas Pty Ltd (Wales family trust) 3.83%, Washington H Soul Pattinson 3.6%, estate of Mark Deacon-Shaw 3.37%.

Cast one's eye over the sprawling ASX wound-healing landscape and there are plenty of exemplars of physical device-style solutions involving patches and lattices.

Companies that come to mind are Avita Medical - which this week won US Food and Drug Administration (FDA) approval for a key application - Polynovo, Aroa Biosurgery and Next Science.

The low-key Tissue Repair is taking a different, drug-centred approach with its topical hydrogel containing its active pharmaceutical ingredient (API) Glucoprime, which stimulates the immune system for improved-wound healing.

The Sydney-based Tissue Repair has also been buoyed by an FDA approval for a phase III trial to tackle the scourge of venous leg ulcers (VLU).

Remarkably, there's been no new VLU wound healing drug approved by the FDA in more than two decades. Many of the current therapies are derived from human placental tissue, which requires tissue to be harvested.

"Existing therapies are typically expensive and are mostly applied by healthcare professionals in hospitals or clinics," says Tissue Repair co-founder Tony Charara.

The early days

Tissue Repair was co-founded in 2012 by Mr Charara, based on technology acquired from Novogen but initially developed at the University of Sydney in the 1990s.

In 2012 Mr Charara also co-founded the healthcare agency Mable, of which he is CEO.

A market place for aged care and disability workers, Mable is a much bigger enterprise than Tissue Repair, but Mr Charara says he is "super passionate" about both companies.

As a JP Morgan mergers and acquisitions banker, Mr Charara was commissioned by Novogen to sell its over-the-counter drug business.

But Novogen also had the phase IIa wound care program, housed in the company's US business Glycotex.

Glycotex was slated for a separate listing, but the IPO was pulled in 2006.

Novogen then called on Mr Charara to sell Glycotex. "I did the rounds, but no one wanted to take on the development, they saw too much risk [because] wound care had been a graveyard of failures," Mr Charara says.

"When I looked at the data, I thought there was a genuine signal of efficacy … and fell in love with the program."

Mr Charara acquired the program with some close partners, notably the late chemist and co-inventor Mark Deacon-Shaw.

Tissue Repair listed in November 2021, having raised $22 million at $1.15 a share, for a $70 million market capitalisation. The company also raised $7.5 million in a pre-IPO round in April 2021.

In late April this year the company appointed Dr Michael Silberberg to the board. Dr Silberberg is therapeutic area head for facial aesthetics and medical affairs at Abbvie Inc.

How it works

Tissue Repair's platform is based on the active pharmaceutical ingredient Glucoprime, which in turn is based on molecules called beta glucans.

Glucoprime is a variant of the Glycotex GLYC-101 and has been used on more than 240 patients for venous leg ulcers and laser skin rejuvenation, in both clinical and 'real world evidence' studies.

When applied to the wound in a hydrogel form and covered in a compression bandage, Glucoprime acts as a decoy by simulating a yeast infection that stimulates the wound repair pathways.

The action attracts healing cells called macrophages to the site. These agents engulf the nasty bacteria and initiate an immune response, as well as tissue re-generation and collagen production.

"We are essentially providing a stimulus that allows the body's own pathways to heal by immune modulation of the wound area," Mr Charara says.

Beta glucans are commonly used as an adjuvant in vaccines to elicit an immune response.

"Glucoprime provides an effective and potent stimulus," Mr Charara says. "Our secret sauce is having a molecule that has been designed for maximum pattern recognition by macrophages."

Tackling VLUs

Having seen encouraging signals in the phase IIa data, Tissue Repair launched a phase IIb trial in 2016, aimed at replicating this treatment effect.

The program consisted of two trials enrolling 82 venous leg ulcers (VLU) patients and 42 patients who had undergone aesthetic laser treatment.

These trials confirmed the earlier efficacy signals and were "clinically and statistically significant".

A subsequent metadata analysis combining both phase II trials for VLUs showed a 60.2 percent reduction in wound size versus placebo at the 12-week mark, with a 'p' (probability) value of 0.031. (Less than 0.05 is good.)

In late May, the FDA cleared Tissue Repair to progress to phase III for chronic VLUs.

The two-year study aims to enrol 600 patients in each of two trials, one in the US and another in Australia. To date, 15 sites have shown interest in participating.

The company plans to submit a trial protocol to the FDA for final review, with enrolment expected to commence in early 2024.

The primary endpoints are the “incidence of complete closure over a 16-week treatment period” with secondary endpoints including reduced ulcer size and pain amelioration.

The US trial principal investigator is Prof Robert Kirsner of the University of Miami, who was also the prober-in-chief for Smith & Nephew’s VLU drug candidate HP802247 in 2016.

The lead investigator for the Australian study is Austin Health’s Prof Michael Woodward, who had that role for the phase IIa trial.

More than skin deep

The company’s secondary focus is on TR Pro+, a topical gel which contains a form of Glucoprime and can accelerate healing and improve skin quality after cosmetic and medical procedures.

TR Pro+ is a variant of Glycoprime for over-the-counter cosmetic use and as long as it doesn’t make claims it doesn’t need Australian Therapeutic Goods Administration approval.

The body beautiful industry wouldn’t describe them as such, but procedures such as laser resurfacing and dermabrasion are designed to break the skin and cause wounds.

Mr Charara says a recent phase IIb study of patients post cosmetic surgery showed the gel doubled the skin quality (as measured by wrinkling and elastosis).

The company says TR Pro+ is also supported by a “real-world evidence” study that involved 48 patients at 12 dermatology clinics, undergoing procedures including laser skin resurfacing and dermabrasion, as well as skin cancer removal, biopsies and cosmetic light treatments.

In the study, 39 patients (81.3%) gave a rating of four or five out of five, in terms of their perception of how their skin was healing and overall satisfaction with the product.

Of the patients who had undergone a previous procedure, all of them opined that TR Pro+ worked just as well or better than products used previously.

TR Pro+ was officially launched this month to dermatology and cosmetic clinics, with more than 160 clinics having registered their interest and trialling the product.

“We wanted to get something to market quickly as a secondary application,” Mr Charara says.

“Once we receive proof of validation we anticipate expanding nationally and exploring some of the interesting international markets.”

Finances and performance

Tissue Repair reported cash outflows of $1.12 million in the March 2023 quarter, with no revenue. The company's cash balance stood at a healthy $21.8 million at the end of March, with an expected research and development tax incentive still to be received.

The company says cash outflows "will increase in future quarters, in line with the acceleration of the chronic wound drug clinical program and commercialization of the aesthetic product".

Mr Charara says that with almost five years' funding at current burn rates, the company should be able to complete the phase III trial with its current resources. "I think we are one of the best funded small biotechs out there," he says. "Most have a runway of six to 12 months' cash."

Tissue Repair shares flopped 40 percent on debut, but this month spiked 10 percent (2.5 cents) after the FDA assent. The stock peaked at 67.5 cents on its initial public offer on November 18, 2021 and was as low as 20 cents in late March this year.

A tissue, a tissue they all fall

The wound care sector is dominated by device rather than drug companies, partly because of the difficulty in achieving 'gold standard' evidence via a double-blinded, placebo-controlled trial. This means it's hard to tell what products are effective.

"They are generally either open-label or active-only trials, or they compare [the drug candidate] with a proxy standard of care," Mr Charara says.

The last drug approved for VLU was Smith & Nephew's Regranex, in the mid-1990s. The FDA plonked a 'black box' warning on the drug over concerns about it being carcinogenic, but after further studies it was re-approved.

Smith & Nephew also tried to develop the aforementioned HP802247 (Allox), a spray-on skin for diabetic foot ulcers, but it foundered at phase III stage.

And of course, Brisbane's own Tissue Therapies (later Factor Therapeutics) failed to have its Vitrogro (VF001) combination drug and device approved, ultimately showing it was as good as the existing standard-of-care.

Reimbursement

Typically, venous leg ulcers cost between $15,000 and $20,000 to treat, so they leave a nasty gash in public healthcare budgets as well. Regranex achieved peak sales of around $US100 million and still sells for around $US1,500 for a 15-gram tube, enough for a month's treatment over a typical six-month course.

Naturally, Tissue Repair's US-centred reimbursement strategy is to show superior efficacy - the company is aiming for a 20 percent improvement - at a lower cost. The company expects a significant cost advantage given the yeast is relatively inexpensive.

"The regulatory pathway is simpler for devices which allows them to get to market sooner," Mr Charara says.

"However, a drug that receives FDA approval based on robust clinical evidence provides easier reimbursement and an easier path to market and sales post- approval."

Dr Boreham's diagnosis:

While Tissue Repair is replete with promise, investors aren't exactly sharing the love and the stock is trading well below cash backing.

"Normally if you have phase III asset and are fully-funded for a huge market with great economics, the valuations are usually high," Mr Charara says.

"In the current market dynamics, if you have a research and development element to your business model the market seems to just hate you."

While chronic wounds cost the US healthcare system around $US50 billion a year, Tissue Repair is targeting the $US1.7 billion global market for active (biologic) wound products.

There's also a $US3.4 billion market for "potentially relevant, minimally invasive cosmetic procedures".

The company also mentions potential applications for burns, surgical trauma, after sun care (a.k.a sunburn) and veterinary uses.

Of course, in the nearer term the upshot of the phase III trial process will determine whether investors regain that lovin' feeling for the tightly-held stock.

"Tissue Repair has a genuine shot at delivering the first drug to be approved to treat VLUs in almost two decades," Mr Charara says.

"This is a debilitating condition with significant unmet needs."

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. Next time he licks his wounds he will ponder if there is a better way.