Biotech Daily

Friday June 23, 2023

Daily news on ASX-listed biotechnology companies

*** ASX, BIOTECH DOWN: 4D MEDICAL UP 10%; PATRYS DOWN 8%**

*** DR BOREHAM'S CRUCIBLE: TISSUE REPAIR**

*** COCHLEAR: UK OKAYS PARTIAL OTICON PURCHASE**

*** EBR RAISES $30m; SHARE PLAN FOR $5m MORE**

*** CHIMERIC SHARE PLAN RAISES $1.5m OF $5.25m; TOTAL $2.5m**

*** CHIMERIC TAKES $10.1m LIND FACILITY, CANCELS $30m L1 FACILITY**

*** RACE COMPLETES SHARE BUY-BACK**

*** INVEX WINS EUROPE PRESENDIN TBI ORPHAN DRUG STATUS**

*** ANDREW HARRISON REPLACES RESONANCE CEO MITCHELL WELLS**

MARKET REPORT

The Australian stock market fell 1.34 percent on Friday June 23, 2023, with the ASX200 down 96.3 points to 7,099.2 points. Six of the Biotech Daily Top 40 stocks were up, 26 fell, five traded unchanged and three were untraded.

4D Medical was the best, up 6.5 cents or 10 percent to 71.5 cents, with 1.2 million shares traded. Actinogen, Emvision and Medical Developments climbed more than four percent; Avita and Nova Eye were up more than three percent; with Resmed up by 0.6 percent.

Yesterday's 0.1 cent or 9.1 percent best, Patrys, led the falls, down 0.1 cents or 8.3 percent to 1.1 cents, with 2.8 million shares traded.

Dimerix and Telix lost five percent or more, despite Telix touching a record market capitalization of $4 billion for the second day in a row; Mesoblast and Proteomics fell more than four percent; Amplia, Cochlear, Cynata and Impedimed were down three percent or more; Clinuvel, Imugene, Kazia, Neuren, Pharmaxis, Polynovo, Prescient, Pro Medicus, Universal Biosensors and Volpara shed two percent or more; with Alcidion, Antisense, Genetic Signatures, Immutep, Nanosonics, Next Science, Opthea and Starpharma down by one percent or more.

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 in April, 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 approval for a key application - Polynovo, Aroa 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 its 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 raised $7.5 million in a pre-IPO round.

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 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, 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. “We are one of the best funded small biotechs out there. 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 warning on the drug over concerns about it being carcinogenic, but after further studies it was re-approved. Smith & Nephew also tried to develop 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.

COCHLEAR

Cochlear says the UK Competition Authority finds buying Oticon doesn't raise competition concerns but has stopped it buying the UK bone conduction implants business.

Cochlear says the UK Competition and Markets Authority concluded that its purchase of Oticon Medical "does not raise competition concerns" but prohibited acquisition of Oticon's bone conduction implants business saying it "would result in a substantial lessening of competition in the UK".

Last year, Cochlear said it would buy the Smørum, Denmark-based Oticon Medical for DKK850 million ($A184 million) (BD: Apr 28, 2022).

In April, the company said the UK Authority provisionally found that the proposed Oticon acquisition might lessen competition in the UK (BD: Apr 21, 2023).

Today, the company said it would buy the implants business at a "zero headline purchase price" which would allow it to supply Oticon Medical's base of about 20,000 cochlear implants.

Cochlear said the business was expected to add about $10 million in annual revenue, with integration costs to be determined but estimated to be $30 million to $60 million.

The company said the business was operating at a loss but that it was aiming for a long-term net profit margin of 18 percent.

Cochlear chief executive officer Dig Howitt said the company was "disappointed to be blocked from acquiring the acoustics business".

"We will still be able to offer Cochlear's technology to those customers into the future as our Baha sound processors are already compatible with Oticon Medical's Ponto acoustic implants," Mr Howitt said.

Mr Howitt said Cochlear was working with Oticon owner Demant to "ensure a seamless transition with continued access to current Oticon Medical technology for customers in the coming years".

"We plan to develop and commercialize next generation sound processors and services that will enable customers to transition to and benefit from Cochlear's technology platform over time," Mr Howitt said.

Cochlear said it expected the transaction to close by December 2023 and was conditional on customary closing conditions and receipt of competition approvals from the Australian Competition and Consumer Commission and the European Commission.

Cochlear fell $8.32 or 3.5 percent to $227.96 with 156,185 shares traded.

EBR SYSTEMS INC

EBR says it has "firm commitments" for $30 million through a placement of CHESS depositary interests (CDIs) at 91 cents each, with a share plan to raise $5 million more.

EBR said the placement and share plan price was a 7.1 percent discount to the last closing price.

The company said proceeds from the capital raising would support its regulatory and commercialization strategy, including finalizing its US Food and Drug Administration pre-market approval submission and its initial commercial launch.

In May, EBR said its Wise device trial met primary efficacy and safety endpoints and it planned to file a pre-market approval submission to the FDA (BD: May 22, 2023).

The company said the record date for the share plan was June 22, it would open on June 30 and close on July 19, 2023.

EBR said Bell Potter Securities, Morgans Corporate and Wilsons Corporate Finance were joint lead managers to the placement.

EBR fell four cents or 4.1 percent to 94 cents.

CHIMERIC THERAPEUTICS

Chimeric says its share plan has raised $1.5 million of a hoped-for $5.25 million, taking the total raised to $2.5 million.
In May, Chimeric said it had commitments from board and management to raise $1.04 million in a placement at 4.6 cents a share with a share purchase plan to raise a further $5.25 million (BD: May 15, 2023).
Today, the company said the share purchase plan shares were offered at the lower of either 4.0 cents or a five percent discount to the volume weighted average price in the five days up to June 16, 2023, which came to 3.5 cents a share.
Chimeric was up 0.4 cents or 11.1 percent to four cents with 2.5 million shares traded.

CHIMERIC THERAPEUTICS

Chimeric says it has a $10.1 million draw-down equity facility with New York's Lind Partners and has cancelled last year's $30 million facility with L1 Capital.
Last year, Chimeric said it had placed $500,000 of shares at 10 cents each with L1 Capital, under a $30 million, 24-month equity drawdown facility and would issue L1 Capital 15,000,000 options exercisable at 25.5 cents each by March 31, 2024. (BD: Jun 9, 2022).
Today, Chimeric said that it would receive $3.1 million from Lind for shares with a deemed value of $3.41 million within 24 months, with a further $7 million funded in minimal increments of $1 million "subject to mutual agreement and shareholder approval".
The company said it would pay Lind a $93,000 commitment fee.
Chimeric said it would issue Lind 24,000,000 shares at the subscription price, along with 41,891,892 options exercisable at 4.6 cents each within four years.
The company said that the subscription price was the lesser of 4.8 cents a share and 90 percent of the average of the three lowest 20-day volume-weighted average prices to the subscription, which at the date of this announcement was 3.3 cents.
Chimeric said Lind might elect when to provide with subscription notices for the shares with a fixed price of 4.8 cents a share until August 31, 2023 and thereafter at 4.8 cents with the aggregate subscription unlimited or at the subscription price, with the aggregate subscription amount in any one month limited to $120,000.
The company said that from July 1, 2024 to June 29, 2025 Lind subscription would be at the subscription price.
Chimeric said that Lind may, at its sole discretion, increase the maximum monthly aggregate subscription amount to $400,000, for two months only.
The company said that the total number of securities to be issued was limited to 103,333,333 shares, but "the limitation does not apply to any shares issued that are subsequently ratified by shareholders under Listing Rule 7.4".
Chimeric said that there was no security provided to Lind nor interest payable, other than if an event of default occurs.

RACE ONCOLOGY

Race says it has acquired 634,881 shares for $1,276,598, or $2.01 a share as part of its on-market share buy-back.
Last year, Race said it would conduct an on-market share buy-back of up to four million shares over 12 months (BD: Jun 9, 2022).
Today, Race said the 12-month buy-back period had expired, would not be renewed, and the shares had been cancelled, leaving 163,068,780 shares on issue.
Race fell six cents or 4.7 percent to $1.21.

INVEX THERAPEUTICS

Invex said the European Medicines Agency has granted Presendin orphan drug designation for the treatment of moderate to severe traumatic brain injury (TBI).
Invex said the designation gave Presendin 10 years of market exclusivity, clinical trial protocol assistance, access to the European centralized authorization procedure and certain fee reductions in the European Union.
The company said it was currently conducting a 240-patient, randomized, double-blind, placebo-controlled phase III trial of Presendin for idiopathic intracranial hypertension.
Invex was up 21.5 cents or 55.8 percent to 60 cents.

RESONANCE HEALTH

Resonance says Andrew Harrison has been appointed chief executive officer with managing director Mitchell Wells continuing as a director, effective from July 1, 2023.
Resonance said Mr Harrison was the founder and managing director of Capitol Health, and had worked in a range of industries, including radiology and medical artificial intelligence.
The company said Mr Harrison held a Bachelor of Commerce from Curtin University.
Resonance said Mr Harrison would be paid a base salary of $300,000 a year with short-term incentives of up to 30 percent of his salary and long-term incentives of up-to 30 percent of his salary.
Resonance chair Dr Martin Blake said that Mr Wells “had led the company as it has refashioned its internal compliance, technical and operational capabilities, to meet current and future challenges and to provide a solid foundation for future growth”.
Resonance was unchanged at four cents.