Biotech Daily

Friday November 4, 2022

Daily news on ASX-listed biotechnology companies

*** ASX, BIOTECH UP: ACTINOGEN UP 8%; CYNATA DOWN 8%**

*** DR BOREHAM'S CRUCIBLE: CLINUVEL PHARMACEUTICALS**

*** $1.1b FOR 11 ARC CENTRES; SYNTHETIC BIOLOGY LAUNCHED**

*** CERTA 'FT011 ACTIVE AGAINST FIBROSIS, IN RATS'**

*** QUEENSLAND UNI, CASSOWARY 'PRECISION PAIN RELIEF'**

*** US BREAKTHROUGH STATUS FOR AVITA RECELL**

*** COGSTATE AGM MODEST DISSENT**

*** LHC CAPITAL, STEPHEN ABOUD REDUCE TO 5.6% OF BTC**

*** MERCHANT TAKES 5% OF NEUROTECH**

*** EPSILON LOSES DIRECTOR SIMON ROWE**

MARKET REPORT

The Australian stock market was up 0.5 percent on Friday November 4, with the ASX200 up 34.6 points to 6,892.5 points.

Fifteen of the Biotech Daily Top 40 stocks were up, 13 fell, 11 traded unchanged and one was untraded.

Actinogen was the best, up one cent or 8.3 percent to 13 cents, with 1.4 million shares traded. Emvision and Imugene improved more than five percent; Micro-X, Orthocell and Starpharma climbed three percent or more; Next Science, Impedimed, Paradigm and Polynovo rose more than two percent; Mesoblast, Nanosonics, Proteomics and Telix were up more than one percent; with Cochlear and Neuren up by less than one percent.

Cynata led the falls, down 2.5 cents or 7.8 percent to 29.5 cents, with 41,000 shares traded. Kazia lost 7.4 percent; Dimerix was down 6.25 percent; Antisense fell 4.65 percent; Alcidion, Atomo, Nova Eye and Prescient were down more than three percent; Medical Developments, Opthea, Pro Medicus and Resmed shed more than two percent; with Amplia, CSL and Immutep down one percent or more.

DR BOREHAM'S CRUCIBLE: CLINUVEL PHARMACEUTICALS

By TIM BOREHAM

ASX code: CUV

Share price: $19.50; **Shares on issue:** 49,410,338; **Market cap:** $963.5 million

Chief executive officer: Dr Philippe Wolgen

Board: Willem Blijdorp (chairman), Dr Wolgen, Brenda Shanahan, Dr Karen Agersborg, Susan Smith, Prof Jeffrey Rosenfeld, Prof Andrew Likierman

Financials (year to June 30, 2022): revenue $67.0 million (up 38%), net profit after tax $20.9 million (down 16%), dividend 4.0 cents a share (up 60%), cash balance $121.5 million (up 47%)

September quarter 2022: sales receipts $25.5 million, net operating expenses $8.27 million, net cash from operating activities $17.3 million, net cash $137.65 million.

Major identifiable holders: BNY Mellor 8.7%, Dr Wolgen 6.3%, Ender1 LLC (Sean Parker) 4.7%.

Move over Chairman Mao or - if you dare - China's increasingly permanent current Paramount Leader Xi Jinping. That's because Clinuvel is outdoing China in terms of the nation's famed manifestos, such as the Great Leap Forward, the Five-Year plan or - more recently - the enigmatic One Belt One Road initiative.

The skin disorders specialist has just unveiled its Strategic Update V, which follows Strategic Update I (October 2020), Strategic Update II (April 2021), Strategic Update III (November 2021) and Strategic Update IV (May 2022).

Dubbed "Clinuvel coming full circle", Strategic Update V is all about "facilitating access to [the company's] technologies and expertise in the form of healthcare solutions provided to target audiences".

This refers to the pending launch of a range of over-the-counter topical products, including one for "pigmentation stabilization" – a.k.a. safe tanning.

Clinuvel historians will know that when the company was known as Epitan it developed a safe tanning product, before changing tack with its now-approved prescription drug for a rare skin condition.

CEO Philippe Wolgen says the pending OTC launch "finalizes the sanctified journey we started 42 years ago".

But hang on! Dr Wolgen says that safe tanning is all about skin cancer protection for vulnerable audiences, rather than body beautiful types bronzing up ahead of the bikini season (see below).

The long march to approval

Clinuvel's core product Scenesse evolved from laboratory work by four scientists at the University of Arizona in 1987. In 1995, the owners applied for investigational new drug status with the US Food and Drug Administration (FDA), based on marketing claims of a "tanning solution by chemical induction".

The FDA demurred. Epitan was incorporated in 1999 and back-door listed on the ASX in 2000, before changing its name to Clinuvel in 2006. In 2003, the FDA knocked back the drug again, claiming it looked w-aaay too much like Botox.

The molecule was out licenced to an Australian team, which fronted the FDA again.

A former facio-cranial surgeon and almost professional soccer player, Dr Wolgen joined the company in 2005 and instilled a strict medical agenda.

Spurred by Swiss studies showing an 11-fold improvement in sunlight tolerability, Clinuvel honed its commercial strategy to focus on the rare skin intolerance condition erythropoietic protoporphyria (EPP). The first EPP patients were treated in Italy after the government agreed to subsidize part of the cost to users.

European regulators approved the drug for adult EPP use in 2014 and the company launched the drug there in 2016. The FDA approved the drug in 2019.

In 2014, the company rejected a $2.17 a share, $95 million takeover offer from Retrophin.

About Scenesse

A sub-cutaneous formulation of the peptide afamelanotide, Scenesse as an adult treatment for EPP, an inherited metabolic disorder causing a severe reaction to sunlight because of a dearth of the compound protoporphyrin nine (PPIX) in blood and tissues.

EPP is activated by visible light and ultraviolet radiation, causing tissue damage and howling pain. Scenesse binds to the melanocortin-1 receptor on skill cells and sets in motion a "cascade of cellular events" to activate melanin and create a prophylactic barrier.

About the size of a rice grain, the Scenesse shots are injected sub-cutaneously in a 16mg dose and ooze their goodness for two months (after which the patients have another one). EPP affects about one in 140,000 people, equating to about 5,000 to 10,000 sufferers.

Globally, 12,000 Scenesse doses have been administered to date. The drug is now widely reimbursed, including in the US where the treatment costs an average $90,000 to $140,000 annually, depending on the number of injections required.

Dr Wolgen says the US experience with Scenesse has been "well beyond our expectations".

While the company won't reveal its EPP market penetration - rivals are lurking – Dr Wolgen alludes to industry analysis suggesting a two to three percent share.

A topical opportunity

Clinuvel's over-the counter (OTC) strategy involves online-only sales of three photomedicine (dermato-cosmetic) products. The website goes live on March 1, 2023 under different branding.

The products target those most prone to skin cancers because they already have had a melanoma, or are immune compromised or otherwise genetically predisposed.

One is an ultra-high ultra-violet (UV) light protection sun cream called Cyacelle, targeting immune-compromised people or those otherwise vulnerable to skin cancer.

The 'fake tanning' product is an unguent to assist with cellular DNA skin repair.

When someone gets sun burn, the redness, in effect, reflects a strand of damaged DNA, which the enzymes repair in about 40 minutes. But the next time the damage occurs, the chance of the cells being replicated into pre-cancerous cells is higher.

"If you are able to fortify the enzymes that repair one single strand, you can make a claim that you assist DNA repair and that is what these enzymes do," Dr Wolgen says.

Organ transplant recipients are of special interest: an underappreciated fact is that 80 percent of fair-colored patients will develop skin cancer within 10 years, the result of the anti-rejection (immune suppressing) drugs.

About 150,000 organ transplants are carried out in the US and Europe a year.

"We started off with a dream of making a cream and making it topical, and we are coming back to a cream," Dr Wolgen says. "But [we] can only justify that position because [we] have gone into medical areas, not injected thousands of people with a hormone."

The beauty myth

In straying into the over-the-counter market, Clinuvel is going where the beauty product purveyors dare not go.

As Dr Wolgen puts it, the beauty giants "don't want to be associated with a melanoma or a horrible disease because you can't put that on a billboard … it's not sexy".

That's not to say the tanning product can't - or won't - be used off-label by healthy people. Indeed, stockbroker Wilsons cites the tanning product as a "unicorn opportunity" in a $US1.4 billion a year global market for sunless tanning products. Not that Dr Wolgen is buying that line.

"In our view the skin cancer prevention market is much bigger than the lifestyle tanning market."

A key factor is that at around EUR200 ($AUD305) for a 125-milligram tube, the product is priced as a serious pharmaceutical.

Under the influence

Clinuvel is adopting an influencer strategy to market its OTC unguents, but it's not about using those young girls who earn hundreds and thousands of dollars by shameless flogging beauty products to adoring followers.

Instead, the company has appointed about 60 paid 'ambassadors' across the three patient groups, some with terminal skin cancer.

"They talk about their ordeal," Dr Wolgen says. "They talk about the mission of reducing and preventing skin cancer because no one else wants to give them the air time."

The company also plans to recruit about 10 A-list celebrities "with some association with skin cancer or organ transplants". They must have one million followers or more and will be paid in Clinuvel shares.

Finances and performance

Clinuvel recorded sales receipts of $25.5 million in the September quarter 2022, the best quarterly result to date. The numbers reflect the peak treatment season for EPP sufferers in the US and Europe.

Net cash flows were a healthy $17.3 million, and with $137 million in the bank, the company won't be tapping the market for funds any time soon.

Being profitable, the company doesn't have to report quarterly, but does so in order to keep shareholders informed.

In the full year to June 30, 2022, the company generated $67 million of revenue (also from Scenesse sales, as well as a $20.9 million net profit.

These reported earnings were 16 percent lower, but management (not surprisingly) prefers the tax loss adjusted, pre-tax number of $34.3 million (34 percent higher).

Expenses during the year rose 44 percent to $32.6 million, but chief finance officer Darren Keamy said costs grew in a "controlled manner" to support the growth initiatives.

Dr Wolgen says Clinuvel's research and development budget of $175 million over five years will be funded by the cash on hand, as well as expected ongoing profits.

The company also intends to pay out 10 percent of earnings as dividends.

Over the last 12 months Clinuvel shares have traded between $40.56 (early November last year) and just over $13 (mid-June this year).

The stock peaked at $43 in October 2021 and five years ago were trading at a mere $7.60 a share.

The ‘Michael Jackson disease’: can Scenesse Beat It?

Meanwhile, Clinuvel is in the clinic with a pigmentation disorder called vitiligo, which affects about 45 million people. Known as the ‘Michael Jackson disease’ in some circles, vitiligo causes the skin to go pale, generally in blotches.

Trials have taken place since 2010 and are ongoing.

Clinuvel is also eyeing Scenesse for Xeroderma pigmentosum, or XP - not a spicy Chinese seafood sauce but an hereditary condition characterized by extreme sun sensitivity - leading to a very high risk of skin cancer and other medical problems.

Meanwhile, Clinuvel is working on a fast-acting afamelanotide variant called Prenumbra, for strokes and vascular disorders.

The company undertook a six-patient, proof-of-concept program for arterial ischaemic strokes and plans to expand this to a 12-patient effort by the end of 2022.

In case you’re wondering, the nexus with strokes is that afamelanotide is thought to improve blood flow and increase the delivery of oxygen and nutrients to deprived brain cells.

Dr Boreham’s diagnosis:

Dr Wolgen notes that the richest cuisines in the world have the least amount of ingredients - and the same applies to the life science sector.

In Clinuvel’s case, the company is now cooking up multiple dishes with Scenesse and - as discussed - they’re not all about skin protection.

Clinuvel is a remarkable ASX biotech success story, but ironically Dr Wolgen says the company has learnt much from failed businesses such as Pan Am, Enron and Lehmann Brothers.

“We are not unique or better executors but we are very good scholars at understanding what doesn’t work,” he says.

When we last covered the stock in October 2019, Dr Wolgen made it clear that the company would be targeting other indications and that investors expected it to do so.

Well - there’s some truth in advertising!

In the meantime, there looks to be further growth with Scenesse and EPP, while the OTC stuff could well be a case of the side dish usurping the main course.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. Unlike in his youth, he now realizes that using Reef Oil as a tanning aid is not the sun smart thing to do.

AUSTRALIAN RESEARCH COUNCIL

The Australian Research Council says 11 centres of excellent centres will receive $1,064.5 million, with Minister for Industry Ed Husic launching a Synthetic Biology centre.
The Australian Research Council said that “centres of excellence are focal points of expertise by which high calibre researchers collaborate to deliver research that benefits Australia, strengthens our international standing and addresses some of the major challenges of our time”.
The Council said that it would provide the centres for excellence $384.9 million over seven years, universities and collaborators would contribute a further $375 million, along with $304.6 million in cash and in-kind funding from the 221 partner organizations.
Separately, the Australian Research Council said that the Minister for Industry and Science Ed Husic had launched the Synthetic Biology centre of excellence at Macquarie University.
The Council said the centre had received $35 million in Australian Government funding and would focus on identifying and engineering “new microbes to turn biological waste to bio-fuels, bio-plastics and other useful products”.
Australian Research Council chief executive officer Judie Zielke said that the centre of excellence in Synthetic Biology was doing “vitally important work through the use of new microbes to turn waste into fuel and bio-plastics, which will mean a more sustainable environment for all Australians”.
“The production and use of bio-fuels also helps reduce the carbon footprint of transportation and other industries that rely on fuel,” Ms Zielke said.
“The centre’s contribution to building a bio-manufacturing industry in Australia will increase rural employment and investment and strengthen Australia's economy,” Ms Zielke said.

CERTA THERAPEUTICS

Melbourne’s Certa says data from a study of fibrosis in chronic kidney disease shows its FT011 is active against genetic markers of fibrosis, in rats.
In 2021, Certa said it had begun a 30-patient, randomized, double-blind, controlled phase II trial of oral FT011 for diffuse systemic scleroderma (BD: Sep 21, 2021).
Today, the company said the rat study, conducted at the University of Michigan, showed treatment with FT011 over 12 weeks “significantly reduced the fibrosis-associated gene response characteristic of the human [chronic kidney] disease”.
Certa said that treatment with FT011 resulted “in a remarkable reversal in the activation of genetic markers associated with fibrosis”.
Certa chief executive officer Prof Darren Kelly said “these findings indicate significant promise for FT011 as a potential novel therapeutic for the treatment of fibrotic diseases and support our plans to advance this investigational drug into later stage clinical trials”.
“The precision and insight gained from this transformative and disruptive research could change the way we identify and treat patients with chronic kidney diseases,” Prof Kelly said.
“We have identified the biological receptor related to fibrosis which gives us the potential to target fibrosis in a wide range of disease states,” Prof Kelly said.
"To our knowledge, there is no other drug on the market that does this,” Prof Kelly said.
Certa said top line data from its phase II trial of oral FT011 in scleroderma patients was expected to be released in early 2023.
Certa is a private company.

UNIVERSITY OF QUEENSLAND, CASSOWARY PHARMACEUTICALS PTY LTD

The University of Queensland says that Cassowary Pharmaceuticals Pty Ltd is developing "precision painkillers that are more accurate and less harmful to the liver".

The University said that the Australian Institute for Bioengineering and Nanotechnology's Prof Trent Munro was the scientific co-founder of the University spin-out company which was developing a range of "hyper-targeted pain medications".

In the University of Queensland media release, Prof Munro said the drugs would "help treat debilitating and chronic pain conditions associated with cancer, sciatica, post-herpetic neuralgia, a painful condition that can follow shingles, peripheral nerve injury and osteoarthritis".

Prof Munro told Biotech Daily that he could not disclose the nature of the compound but the company was working on its intellectual property strategy.

"What we can say is that it is not a naturally derived small molecule compound, but rather a rationally designed antagonist," Prof Munro said.

"We have a clinically validated target that was discovered by [the University of Queensland's Prof] Maree Smith," Prof Munro said.

"However, previous efforts to drug this target experienced observations of liver toxicity in long-term dosing in animal studies," Prof Munro said.

"As such we have taken a different approach to create a drug that is both more precisely targeted and will be primarily restricted to the periphery, limiting [central nervous system] exposure," Prof Munro said.

"Since we are just launching this program … we are not talking about the modality," Prof Munro said.

In the media release Prof Munro said "this type of targeted therapy reduces the potential side effects and safety issues associated with current pain treatments, and will also mean fewer doses are required".

"Creating drugs with these attributes could change the lives of millions of people who suffer from chronic neuropathic pain," Prof Munro said.

The University said that the Cassowary Pharmaceuticals' drug candidate targeted a molecule thought to be important in how the human body senses pain.

The University said that Cassowary receiving funding from the Federal Government's Medical Research Future Fund and would recruit candidates for clinical trials over the next 18 months.

Cassowary is a private company.

AVITA MEDICAL

Avita Medical says the US Food and Drug Administration has granted breakthrough device status for its Recell spray-on skin for soft tissue repair and vitiligo.

Avita said that FDA status afforded regulatory advantages including prioritized review and more intensive communication with the FDA throughout the review process.

Avita chief executive officer Jim Corbett said the company was "pleased that the FDA has recognized the therapeutic potential of our Recell System for our proposed soft tissue repair and vitiligo indications with the breakthrough device designations".

"We are hopeful that the designations will help ensure timely patient access to Recell as therapeutic treatments for both soft tissue repair and vitiligo, and we look forward to interacting with the agency in its review of Recell for these proposed indications," Mr Corbett said.

Avita was unchanged at $1.505.

COGSTATE

Cogstate says shareholders at its annual general meeting voted up to 8.43 percent against the adoption of a new constitution.
Cogstate said 9,931,275 votes (8.43%) opposed the new constitution, with 107,897,101 votes (91.57%), in favor.
The company said all other resolutions, including the adoption of the remuneration report, the re-election of Ingrid Player and Martin Myer as directors, the adoption of an employee equity plan, and an increase in the directors' pay pool passed by wider margins.
According to its most recent filing, Cogstate had 173,368,331 shares on issue, meaning that the 9,931,275 votes against the new constitution amount to 5.7 percent of the company, sufficient to requisition extraordinary general meetings.
Cogstate fell five cents or 2.75 percent to $1.77.

BTC HEALTH

Sydney's LHC Capital Partners says it has reduced its substantial holding in BTC from 19,500,000 shares (6.92%) to 15,705,222 shares (5.57%).
In a notice signed by chief executive officer Stephen Aboud, LHC said that between August 24 and November 2, 2022, it sold 3,794,778 shares in BTC at prices ranging from 4.2 cents to 6.2 cents.
BTC fell 0.2 cents or five percent to 3.8 cents.

NEUROTECH INTERNATIONAL

Merchant Group says it has become a substantial shareholder in Neurotech with 36,402,227 shares or 5.01 percent.
The Perth-based Merchant Group said that between March 15, 2021 and November 4, 2022, it bought shares in Neurotech, with the largest purchase 10,000,000 shares for $600,000, or six cents a share and the most recent purchase 8,500,000 shares for $850,000 or 10 cents a share.
Neurotech was up 0.2 cents or 2.3 percent to 8.9 cents with 3.9 million shares traded.

EPSILON HEALTHCARE

Epsilon says that director Simon Rowe has resigned as a director, effective from November 3, 2022.
Epsilon said that its was chair Josh Cui, deputy chair Alan Beasley and director Stuart Cameron.
Epsilon was unchanged at 3.3 cents.