Biotech Daily

Friday March 26, 2021

Daily news on ASX-listed biotechnology companies

*** ASX, BIOTECH UP: IMMUTEP UP 33%; PRESCIENT DOWN 9%**

*** DR BOREHAM'S CRUCIBLE: CYNATA THERAPEUTICS**

*** PARADIGM FILES IND FOR PPS KNEE OSTEOARTHRITIS TRIAL**

*** IMMUTEP: BMS TRIAL DATA BACKS LAG3**

*** CRESO PLACEMENT RAISES $18m**

*** LBT DIRECTORS TAKE 25% OF FEES IN SHARES**

*** KAZIA REQUESTS 'REGIONAL LICENCE' TRADING HALT**

*** CANN GLOBAL REQUESTS 'REGULATORY MILESTONE' TRADING HALT**

*** CREDIT SUISSE TAKES 6% OF IDT**

*** REGAL FUNDS TAKES 19.8% OF VISIONEERING**

*** PYC LOSES DIRECTOR DR BERNARD HOCKINGS**

MARKET REPORT

The Australian stock market was up 0.49 percent on Friday March 26, 2021, with the ASX200 up 33.6 points to 6,824.2 points. Eighteen of the Biotech Daily Top 40 stocks were up, 16 fell, five traded unchanged and one was untraded. All three Big Caps fell.

Immutep was the best on a media release not published on the ASX (see below), up 11.5 cents or 33.3 percent to 46 cents, with 19.2 million shares traded. Paradigm climbed 10.4 percent; Actinogen and LBT were up more than seven percent; Amplia and Imugene improved more than four percent; Alterity and Proteomics were up more than three percent; Compumedics and Optiscan rose more than two percent; Medical Developments, Pro Medicus and Universal Biosensors were up one percent or more; with Avita, Cynata, Neuren, Next Science and Volpara up by less than one percent.

Prescient led the falls, down one cent or 8.7 percent to 10.5 cents, with 2.7 million shares traded. Dimerix, Opthea and Polynovo lost more than five percent; Antisense, Cyclopharm, Genetic Signatures, Mesoblast, Nova Eye, Starpharma and Uscom shed more than two percent; Oncosil, Orthocell, Pharmaxis and Resmed were down one percent or more; with Clinuvel, Cochlear, CSL and Nanosonics down by less than one percent.

DR BOREHAM'S CRUCIBLE: CYNATA THERAPEUTICS

By TIM BOREHAM

ASX code: CYP

Share price: 63 cents; **Shares on issue:** 143,276,594; **Market cap:** $90.3 million

Chief executive officer: Dr Ross Macdonald

Board: Dr Geoff Brooke (chair), Dr Paul Wotton, Dr Macdonald, Dr Stewart Washer, Dr Darryl Maher

Financials (December half 2020): revenue nil, operating loss $4.84 million (previously $2.54 million deficit), cash on hand $24.9 million (up 80%)

Identifiable major holders: Bioscience Managers Translation Fund 1 (10.3%) Fidelity International 9.9%, Fujifilm 5.8%.

Like any biotech with a platform technology, Cynata faces the dilemma of what commercial opportunity to pursue among myriad options.

The stem cell therapies developer doesn't have the resources to chase everything, so indications such as heart disease and strokes are side-lined because of the long duration and high cost of the studies.

"We have always tried to tailor clinical targets based on the company's capabilities," chief executive Dr Ross Macdonald says. "You cut your coat according to your cloth."

Rather than embarking on the "big grandstanding trials", he says Cynata will pursue the studies more likely to be successful and enhance shareholder value. "At the same time, they are not going to take forever and cost us a fortune."

To further the tailoring analogy, think of Cynata as the price-conscious Sires or Peter Jackson of the stem cell world, rather than a Henry Bucks or Saville Row.

Cynata's pluripotent stem cell approach

Cynata is based on its Cymerus platform technology that enables the company to manufacture stem cells without relying on material from blood marrow donors.

Rather, Cynata uses induced pluripotent stem cells (iPSCs), from which mesenchymal stem cells (MSCs) are derived via a patented differentiation process. MSCs are adult stem cells which are found naturally in a range of tissue sources such as bone marrow and fat.

The 'pluripotent' bit means the iPSCs have the ability to develop into any type of adult cell. As a result, the cells are cheaper to produce and consistent in quality and potency.

Currently these precursor cells are derived from embryos (raising religious issues) or bone marrow aspiration (painful). Cynata's cells can be derived from anywhere in the body - typically skin and blood - and grown in limitless quantities in the laboratory.

Cynata back-door listed in October 2013, based on Nobel Prize winning technology held by the University of Wisconsin-Madison, the centre of US stem cell research.

Tackling a pressing knee-d

Carried out with the University of Sydney, Cynata's phase III osteoarthritis program is funded by the National Health and Medical Research Council.

"The funding bodies in academia support the pre-clinical and academic research, but then there's the 'canyon of death' where funding is hard to generate," Dr Macdonald says. "The [Federal] Government has taken a view that it will bridge the gulf and support important translational work through these funding bodies, especially in osteoarthritis where there's no effective treatment."

"Everyone with osteo is frustrated that there's not much available to alleviate their condition and to allow them to return to normality, other than normal pain relief."

After the pandemic delays, Cynata has embarked on a dry run of recruiting a small number of the intended 440 patients.

Can Fuji mount a US push?

Japanese conglomerate Fujifilm (Fuji) holds the exclusive global rights to Cymerus to treat graft-versus-host disease (GvHD) and is responsible for trial costs and development.

GvHD is an immunological condition that afflicts bone-marrow recipients, when the donor's T-cells view the patient's healthy cells as foreign and attack them. It's usually fatal for patients resistant to conventional steroid treatment. When Cynata and Fuji struck their deal in 2019, Fuji was confident of getting a trial underway in the US by 2020. But given the pandemic, Fuji representatives could not travel to inspect the sites.

Cynata and Fuji are highly aware that Mesoblast have had a paediatric GvHD setback. A heavy-hitting US Food and Drug Administration advisory committee recommended that the agency approve the company's therapy, but the FDA itself said "not yet bud, you need to do an adult clinical study".

Cynata, however, is not in the loop on Fuji's emerging plans for non-Japanese markets.

"They don't give us too much insight into their strategies and nor do we expect them to do so because essentially it is none of our business."

Actually, it is Cynata's business in that the company stands to reap $60 million in milestone payments, plus a double-digit royalty. The next milestone - $2 million - is crystallized when Fuji finishes the trial.

Covid – an ‘ard nut to crack

Cynata’s slated local trial to treat Covid-induced acute respiratory distress syndrome (Ards) went nowhere - not such a bad thing because it reflects the scarcity of local patients in intensive care to enrol. An inflammatory process, Ards gives rise to fluid build-up and ultimately respiratory failure.

“We anticipated that when we started the trial last year, because Australia is doing a good job by shutting the borders,” Dr Macdonald says.

Now, the company is aiming for a trial of 24 patients from intensive care units at Sydney’s Westmead and Nepean hospitals and Melbourne’s Western Health. Cynata’s ‘big brother’ Mesoblast ran a small Ards trial in New York, but late last year was forced to cancel it for “futility” reasons. Cynata’s interest in Ards remains intact because it’s also seen in patients with conditions such as influenza and pneumonia.

Finances and performance

Trial funding aside, the Australian taxpayer now has a direct stake in the fortunes of Cynata after the company’s placement and rights issue that raised $18.3 million.

Why? The cornerstone investor was Bioscience Managers, which channels money for the Federal Government’s $500 million Biomedical Translation Fund (launched in 2016). The fund works on a co-investment principle, so the acquired 10.3 per cent investment stake is a joint investment between taxpayers and Bioscience Managers’ external investors.

“Bioscience Managers spent a long time kicking the tyres,” Dr Macdonald says. “They can only access publicly available information, but around that they built a very large investment case in stem cell and regenerative medicine technology.”

The raising was pitched at 70 cents a share, with some punters grumbling about the 10 percent discount and whether the dilutive effort was really needed.

“You have to be around to fight another day,” Dr Macdonald says. “It’s all well and good to say don’t raise capital and don’t dilute us, but if you want to generate value you have to spend a buck to make a buck. It would be delinquent of us not to.”

In a similar spirit of non-delinquency, in April last year Cynata raised $8.35 million in a placement and share purchase plan, at 60 cents apiece.

Where the money will be spent

Dr Macdonald says the funds from the latest raising will be used to progress the early-stage clinical programs that have produced decent results but are not subject to funding partnerships. They are kidney transplants, idiopathic pulmonary fibrosis (IPF) and diabetic foot ulcers. A progressive and ultimately fatal disease, IPF had had a bit of airplay because patients recovering from Covid-19 end up with scarred lungs (fibrosis).

While the data is still emerging, they're likely to have long term health effects. Diabetic foot ulcers are the sores that diabetics get on their lower feet and legs because of poor circulation.

Cynata this month inked a memorandum of understanding with the private Tekcyte, which has wound coatings for the delivery of mesenchymal stem cells. The compact is expected to lead to a deal with Tekcyte technology used in Cynata's diabetic foot ulcer product.

"Treating these wounds is complicated because they just don't heal," he says. "It's a very large unmet medical need which the medical community has been trying to resolve."

Like an even-handed dad, Dr Macdonald is reluctant to single out his favorite trial but he's especially enthused by the stem cell opportunities in kidney transplantations. Many more patients require kidneys than there are donors, so unless you're Kerry Packer with an obliging helicopter pilot there's a long waiting list.

Cynata is looking at potential centres for a small non-pivotal clinical study of perhaps 50 patients, locally and/or in Europe.

"We are now well down the track with a potential study site for this trial," he says.

Dr Boreham's diagnosis:

As with Mesoblast, Cynata has its fingers in more pies than a clumsy baker and one breakthrough indication would be enough to transform the company.

"There was a frustrating period where there didn't seem to be a lot happening, but like a duck, there was a lot happening under the water," Dr Macdonald says.

While Cynata paddles harder than a canard escaping the shooting season, its shares are trading at seven-month lows, despite the multi-pronged activity. And don't forget that in 2018, Sumitomo lobbed a non-binding, $2 a share cash offer for the company.

"You can point the finger to everything," Macdonald says of the share malaise. "The stem cell world still has its sceptics and that hasn't been helped by the bellwether stock [Mesoblast] not having good news recently."

"I see a lot of biotechs saying 'we can do this and we can do that', especially in the pre-clinical stage," he says. "Investors love that story but it's only when the rubber hits the road that [management] says 'oops we might have oversold that a bit'."

As Dr Macdonald mentioned at the outset, the company has tailored its programs to match its resources, expertise and the potential to commercialize the chosen indications. But it remains to be seen whether management's cloth-cutting skills will produce a vestment worthy of Pierre Carden or a garment to grace the shelves of Savers.

Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. He does possess a nice wardrobe of bespoke garments, but oddly enough none of them fits post the Covid lockdowns.

PARADIGM BIOPHARMACEUTICALS

Paradigm says it has filed its US Food and Drug Administration investigational new drug submission for a 930-patient phase III trial of pentosan polysulfate sodium.
Paradigm said that randomized trial would investigate pentosan polysulfate sodium (PPS), marketed as Zilosul, for knee osteoarthritis.
Today, the company said the submission was a “significant milestone”.
Paradigm said the trial was “on track” to start patient screening by July 2021, with 60 of the 65 planned trial sites prepared to begin recruitment.
Paradigm chief executive officer Paul Rennie said the company would provide further detail on the final study design and timing once the application had been opened following the 30-day review period with the FDA.
Paradigm was up 25 cents or 10.4 percent to $2.65 with 1.1 million shares traded.

IMMUTEP

Immutep says that a phase II/III combination trial of an anti-lymphocyte-activation gene 3 (LAG-3) antibody drug validates its LAG-3 antibody as an immune checkpoint.
Immutep republished a Bristol Myers Squibb media release saying a 714-patient trial of relatlimab combined with nivolumab (Opvido) for melanoma met its primary endpoint of progression-free survival.
Immutep said the results were “the much-anticipated validation of LAG-3 as the next immune checkpoint therapy” following programmed cell death protein (PD-1) and cytotoxic T lymphocyte-associated antigen (CTLA4).
In a media release not filed to the ASX, the company said that “until today, only relatively small, early-stage clinical data sets have been published regarding LAG-3”.
Immutep chief executive officer Marc Voigt said that the Bristol Myers Squibb trial results “validate LAG-3 as the next immune checkpoint”.
“Not since PD-1 and CTLA4 has there been a new immune check point enter the landscape to help patients,” Mr Voigt said.
"We believe LAG-3 will have many applications beyond melanoma, in multiple cancers and even in autoimmune disease,” Mr Voigt said. “As the only LAG-3 pure-play biotech in the space, we … have the greatest number of product candidates around LAG-3 under evaluation and look forward to advancing these to improve patients' lives.”
Immutep was up 11.5 cents or 33.3 percent to 46 cents with 19.2 million shares traded.

CRESO PHARMA

Creso says it has commitments to raise $18 million in a heavily oversubscribed placement at 19 cents a share, a 17.4 percent discount to the last traded price on March 23.
Creso said that, pending shareholder approval, investors would receive one option for every four shares purchased, exercisable at 38 cents each for 12 months.
The company said the funds raised would be used to acquire Halucenex Life Sciences Inc, for clinical development expand its range of hemp-based food additives, scale-up production at its Canadian subsidiary Mernova Medicinal Inc and progress a dual listing on the Over-The-Counter Quality Exchange second board (OTCQB) in the US.
Creso said Everblu Capital was the lead manager of the placement and the raising was supported by John Langley Hancock, the son of Gina Rinehart and grandson of Lang Hancock, S3 Consortium Holdings Pty Ltd and L1 Global Master Opportunities Fund.
Creso was up one cent or 4.35 percent to 24 cents with 87.6 million shares traded.

LBT INNOVATIONS

LTB says its non-executive directors will receive shares in lieu of cash for 25 percent of their fees until each director has invested 12 months' worth of fees in shares.
LBT said the number of shares to be issued would be determined by a monthly volume weighted average price of the company's shares.
The company said the shares would be issued subject to shareholder approval, and the directors would be reimbursed in cash if the resolution did not pass at the annual general meeting.
LBT chair Kate Costello said that "this new board policy sets a commitment to ensure all directors invest in, and support, the future of LBT Innovations".
"This is a positive indication of the long-term potential the board see in the company and builds alignment between the LBT board and feedback received from LBT Shareholders," Ms Costello said.
LTB was up 0.7 cents or 7.1 percent to 10.5 cents.

KAZIA THERAPEUTICS

Kazia has requested a trading halt "pending the release of an announcement about a regional licencing transaction".
Trading will resume on March 30, 2021 or on an earlier announcement.
Kazia last traded at $1.45.

CANN GLOBAL

Cann Global has requested a trading halt "pending the release of an announcement regarding a material regulatory milestone".
Trading will resume on March 30, 2021 or on an earlier announcement.
Cann Global last traded at 0.8 cents.

IDT AUSTRALIA

Sydney's Credit Suisse Holdings says it has become a substantial shareholder in IDT with 14,535,683 shares or 6.05 percent of the company/
Credit Suisse said that between November 23, 2020 and March 22, 2021 it bought, sold and borrowed shares with the single largest purchase 1,688,036 shares for $499,841 or 29.6 cents a share.
IDT was unchanged at 41.5 cents with five million shares traded.

VISIONEERING TECHNOLOGY

Regal Funds Management says it has increased its substantial shareholding in Visioneering from 77,487,914 shares (7.80%) to 454,656,490 shares (19.82%).
The Sydney-based said that between December 16, 2020 and March 23, 2021 it bought and sold shares, with the single largest purchase 382,352,941 shares for $6,500,000 or 1.7 cents a share.
Last month, Visioneering said it had raised $22 million in an "over-subscribed" placement at 1.7 cents per Chess depository interests (BD: Feb 17, 2021).
Visioneering was unchanged at 1.5 cents with 1.5 million shares traded.

PYC THERAPEUTICS

PYC says Dr Bernard Hockings has retired as a director after seven years on the board.
PYC was up one cent or 6.45 percent to 16.5 cents.