Biotech Daily

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Daily news on ASX-listed biotechnology companies

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 certainly 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 (via the Medical Research Future Fund).

“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.”

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

“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.”

The trial, by the way, is dubbed SCUlpTOR: “stem cells as a symptom - and structure - modifying Treatment for medial tibiofemoral OsteoaRthritis”. But you don’t need to know that.

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.

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

But now the company is aiming for a local trial called Mend, predicated on recruiting 24 patients from intensive care units at Sydney’s Westmead and Nepean hospitals and Melbourne’s Western Health.

An inflammatory process, Ards gives rise to fluid build-up and ultimately respiratory failure.

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

The government's support for the knee trial 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). Because the fund works on an equal co-investment principle, 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 devised patented wound coatings for the delivery of mesenchymal stem cells. The compact is expected to lead to a deal by which Tekcyte's technologies are 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," Dr Macdonald 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."

He also admits the company could do more "investor outreach" to manage expectations, which tend to exceed the pace of development.

“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.