



Biotech Daily

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Daily news on ASX-listed biotechnology companies

Dr Boreham's Crucible: Race Oncology

By **TIM BOREHAM**

ASX code: RAC

Share price: \$2.09; **Shares on issue:** 159,402,311; **Market cap:** \$333.15 million

Financials (June quarter 2022): receipts nil, cash outflows \$2.155 million, cash of \$33.5 million, quarters of available funding: 15.6

Chief executive officer: Phillip Lynch

Board: Dr John Cullity (chair), Mr Lynch, Dr Daniel Tillett (chief scientific officer), Mary Harney

Identifiable major shareholders: Dr Tillett 8.5%, Dr Cullity 5.1%, Merchant Opportunities Fund 2.8%

Race Oncology's chief scientific officer Daniel Tillett says there was more than a smidgen of luck in the company's discovery that its repurposed bisantrene for leukemia had wider potential applications.

The supportive data had always existed; it's just that someone needed to join the dots and Dr Tillett did so by reading a scholarly journal. "We got incredibly lucky," he says.

Given the drug's additional properties "we have gone from having, frankly, a boring old chemotherapeutic drug to being a targeted agent in a couple of hot areas".

The "boring" part was repurposing bisantrene - now known as the zestier Zantrene - as a therapy for acute myeloid leukemia (AML).

AML is an aggressive cancer that sees only one-third of patients surviving beyond a year.

The company still has a keen interest in AML, but the hot bit is Zantrene's properties as an inhibitor of the cancer-causing protein called the fat mass and obesity associated protein (FTO).

Believe it or not FTO is also known in medical circles as 'fatso' and this has nothing to do with Fatso the Wombat, the much-loved unofficial mascot of the 2000 Sydney Olympics.

In mid-2020 scientists at Los Angeles' City of Hope identified two "potent small molecules that appear to suppress tumor growth in multiple cancers even when other treatments cease to work, possibly due to the development of drug resistance".

One of these was bisantrene, of course.

The Race so far

Okay - let's start at the start.

Race was founded in 2013 when US physician and entrepreneur Dr William Garner reviewed medical literature about the old oncology drug bisantrene, which was approved by French authorities for AML in 1990. But a series of corporate takeovers meant the drug was never commercialized.

The drug was developed in the 1980s by French group Lederle Laboratories as an anthracycline - a chemotherapeutic - but without the common cardiotoxicity that resulted in more cancer patients dying of heart failure than the cancer itself.

Extensive clinical trials covering 2,000 patients confirmed both the drug's cardio-protective and anti-tumor activities.

Lederle was taken over by American Cyanamid, which had no interest in the drug. Bisantrene ended up in the hands of the Nevada-incorporated Update Pharma, owned by Dr Garner, pharmaceutical scientist Dr John Rothman and Dr Peter Molloy.

Race listed in July 2016 via a resources company shell, raising \$4.3 million at 20 cents apiece.

Comings and goings

Race has had a few management and ownership changes in its short-listed life.

Best known as head of the then ASX-listed influenza drug house Biota, Dr Molloy resigned from Race in May 2020 to devote his attention to anti-infectives house Firebrick Pharma (which listed on the ASX in January this year).

Race was then run by a tag team of executive chair Dr John Cullity and Dr Tillett.

With a long medical commercial background at drug companies, including Johnson & Johnson's consumer division, Phillip Lynch joined Race as a director in May 2020. He took over as chief executive in September of that year, with Dr Cullity resuming as non-executive chairman.

In October 2020 chief medical officer Prof Borje Andersson joined as an executive director and chief medical officer, but quit the board in December of that year to focus on the CMO role. He retired altogether in February 2021.

Dr Garner was a director and Race's biggest shareholder. He quit the board in October 2020 and sold down his shareholding in the latter part of 2021.

Now the biggest holder, Dr Tillett remains a director and chief scientific officer.

What's the go with FTO?

Race believes Zantrene is applicable for not just AML, but extramedullary AML and solid tumors such as breast and kidney cancers and melanoma.

Extramedullary AML is when tumors grow outside the bone marrow, similar to metastatic solid cancers. In effect, the tumors escape from the bone marrow, enter the surrounding bodily tissue and behave like solid tumors.

Dr Tillett notes that in 10 percent of cancers, the doctors have no idea where the cancer originated (cancer of unknown primary).

Nicknamed FTO, the protein plays a critical role in cancer development and progression, primarily because it regulates cancer stem cells and immune evasion. In other words, FTO promotes the growth, self-renewal, metastasis and immune escape of cancer cells.

"It looks like the drug has multiple mechanisms of action," Dr Tillett says. "If you use it as a high dose, it works like a chemotherapeutic drug; if you use it at a low dose its works like an FTO inhibitor with a very different mechanism of action."

He says Zantrene looks to have wider applicability than AML if used constantly in low doses, rather than more infrequent high-dose cancers as in the past.

In the clinic ...

In 2020, Race reported the results of a phase II study using Zantrene for relapsed or refractory AML patients, carried out at Israel's Chaim Sheba Medical Centre.

The trial recruited 10 patients aged between 22 and 80 years, all of whom had failed at least three treatment options.

Seven of them had relapsed after receiving an allogeneic stem cell transplant (using tissue from someone else). Four of them had extramedullary AML - and these patients were the four who responded to the treatment.

Now, Chaim Sheba is conducting a phase Ib/II trial of Zantrene in combination with two standard chemo drugs, also to treat relapsed/refractory AML patients.

Locally, Race has received ethics approval for its own trial of extramedullary AML patients, to be carried out by the contract research organization Parexel. The trial expects to enrol 60 patients across 10 sites, with a 'two in one' trial design. A high-dose arm high will test Zantrene as a single agent, while the low-dose arm will combine Zantrene with Inqovi (decitabine and cedazuridine).

As with the previous Israeli trial, the study is open-label, which means both the patient and the doctor know the treatment they are receiving. It also means the company does not have wait until the end of the trial and the final 'unblinding' to report results.

The trial is expected to take 36 to 40 months. Recruitment was meant to have started in the December 2021 quarter but Covid got in the way.

"Almost all AML patients are treated in public hospitals," Mr Lynch says. "But what works in our favor is that you can't delay treatment, unlike a dodgy knee."

... and the mouse cage

Last month, the company released the results of mouse trials pertaining to cardio protection and melanomas, carried out with the University of Newcastle.

In the case of heart protection, mice dosed with Zantrene and doxorubicin maintained healthy tickers, even at higher doses.

In the case of melanomas, a novel combination of Zantrene and BRAF/MEK inhibitors (immunotherapies) showed a diminution of melanoma tumors, an immune cell response and reduced expression of "immune evasion genes" (which is a good thing).

Dr Tillett describes the melanoma results as "really positive, both as an enhancement for immune-oncology and overcoming checkpoint inhibitor resistant cancers".

He adds: "We chose a really difficult model that really doesn't respond to anything in the immunotherapy space and we were able to get a response."

In March, pre-clinical work showed that Zantrene was able to kill a range of kidney cells, both on its own and in combination. Mr Lynch says Race has the funding for a human solid tumor trial: "we just have to figure out the highest probable, commercial and best patient opportunities to progress."

In the near-term investors can expect updates on in-vitro breast and melanoma work and, of course, news from Israel about the dose-finding stage of the AML trial.

The heart of the matter

Meanwhile, Race is bolstering its case that Zantrene is less damaging to the ticker. Mr Lynch says the company is mulling the idea the combined with a chemotherapeutic it would reduce heart muscle damage caused by chemotherapeutics.

Recent in-vivo (mouse) models support both the cardio-protective and efficacy aspects.

“We hope to move that into the clinic and provide chemotherapeutics that are more effective and will mitigate heart damage in the future.”

Other cardio-protective drugs have been found, but they have protected the cancer as well. “You need to hit both birds with the one stone and ... that’s what makes this discovery really exciting.”

Dr Tillett says cardio-protection is becoming more important because cancer patients are living long enough for heart failure to be a problem.

Financials and performance

Astonishingly, Race has activated a share buy-back facility at a time when so many biotechs are running out of cash and will struggle to raise more.

Yes - you heard correctly! The company has more capital than it needs and doesn’t want to hang on to cash for the sake of it.

Mr Lynch says the move is a tangible manifestation of management’s belief that the shares are under-valued

“Everyone says their shares are under-valued even when they are over-valued, but they rarely put their money where their mouth is,” Mr Lynch says.

“We have always been explicit that we will only raise capital we need.”

Race has the right to buy back four million shares, implying a circa \$8 million investment at current prices. So far, the company has bought back 110,000 shares in the narrow pricing windows available.

Race has \$33 million in the bank, having last year raised \$44 million in an oversubscribed share purchase plan.

The company only sought to raise \$29.7 million and rather than keeping the cash for a rainy day the company returned the excess amount to the subscribers.

Over the last 12 months Race shares have traded between \$1.50 (mid-June this year) and a record \$3.86 (mid-November last year). Since listing the stock has traded as low as five cents, in mid-2019.

Dr Boreham's diagnosis:

With what Dr Tillett describes as a “new team, new opportunity and new strategy”, with both the old and new programs ticking away.

Meanwhile, the old AML and cardioprotective programs are ticking away.

Dr Tillett says he feels “incredibly lucky” that Zantrene has turned out to be so promising in tackling FTO.

(But hey, Daniel, don't companies make their own luck?)

As with other drug re-purposers such as Recce and Paradigm, Race has the benefit of the big dollars the former owners sunk into the compound.

Ultimately, Race's future will be determined by the cancers that are the most 'commercial'. Mr Lynch says Race has no intention to get beyond 'pre revenue' stage, which implies a deep-pocketed partner will take any drug to market.

“We don't intend to be doing this in five years' time,” he says. “There are better qualified people than us to take the drug all the way.”

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. He will plump for Fatso over Perry the Bull - Birmingham's official Commonwealth Games mascot - any day.