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: 62 cents

Market cap: $72.2 million

Shares on issue: 116,450,037

Financials (March quarter 2020): receipts $15,000, cash outflows $666,000, cash on hand $2.56 million, number of quarters of available funding: four

Executive chairman: Dr John Cullity

Board: Dr Daniel Tillett (CSO, COO), Dr Cullity, Chris Ntoumenopoulos, Dr William Garner, Phillip Lynch, Prof Borje Andersson

Identifiable major shareholders: William James Garner 11.75%, Dr Daniel Tillett 7.90%, Merchant Opportunities Fund 6.15%, Dr Molloy 3.43%

Have you ever looked under the couch cushion and found a fortune in long-lost coins?

It sounds incredible but the same thing can happen with forgotten drugs - even ones that have been approved.

In the case of Race, the 'sofa cushion' moment came in 2013 when US physician and entrepreneur Dr William Garner reviewed medical literature about a cancer drug called bisantrene.

Bisantrene underwent 15 years of clinical trials and was even approved by French drug keepers in 1990, but a series of corporate takeovers consigned the drug to the back of the Chesterfield.

Race has revived efforts to commercialize bisantrene, not so much for re-purposing but for the drug's original remit of treating the difficult acute myeloid leukaemia (AML).

Despite the progress with alternative drugs in the ensuing decades, recent trial results shows the drug is promising for treating AML patients on their last legs.

The big trouble with the current drugs (anthracyclines) is that they can cause cardiomyopathy or, in executive chairman Dr Cullity's words: "a floppy bad heart".

Bisantrene was developed in the 1980s by French group Lederle Laboratories as a "next generation" version of an anthracycline.

By modifying the basic anthracycline molecule, the inventors aimed to maintain the same DNA binding effects but reduce the cardiotoxicity.

Give me a sense of (re)purpose

In the 1980s and 1990s, more than 40 clinical trials covering 2,000 patients confirmed both the lack of cardiotoxicity and the anti-tumor activity.

"We got efficacy (data) and a King Kong-sized file on safety, based on hundreds of patients," Dr Cullity says.

Generally speaking, acute myeloid leukaemia is an aggressive cancer resulting in only 34 percent of patients surviving for more than a year. The odds reduce to 20 percent on the first relapse and eight percent on the second.

The trials (carried out mainly in France) showed a complete remission rate of 38 to 72 percent, or an average 48 percent across 85 patients.

(OK- one trial showed a mere five percent remission rate, but the wrong dosage was used.)

Gallic authorities approved the drug in 1990, but then a chain of takeovers meant that Lederle's oncology division ended up with American Cyanamid.

One way or the other, interest waned and it was bye-byes time for bisantrene.

Race was formed in July 2016 to acquire bisantrene from the Nevada-incorporated Update Pharma, owned by Dr Garner, pharmaceutical scientist Dr John Rothman and Peter Molloy.

Dr Molloy is best known as head of the ASX-listed Biota, which developed the influenza drug Relenza before moving to the US.

Race listed in July 2016 via the shell of Coronado Resources, raising $4.3 million at 20 cents apiece.

The CEO since listing, Dr Molloy resigned in May to head up a company called Firebrick Pharma.

Since then the whole shebang has been run by Dr Cullity and Dr Daniel Tillett, the company's CSO-cum-COO*****.

Dr Cullity's career took him from his childhood playground of Cottosloe Beach in Perth to a University of Western Australia medical degree and then to the London School of Economics and Wharton Business School.

He also had stints at the World Health Organisation, the World Bank, and big pharma Sanofi before joining the New York biotech deal shop Torreya Partners.

Doctors Garner and Molloy one day dropped in for some corporate advice, which led to Dr Cullity eventually being invited to join the Race board.

***** chief scientific officer cum chief operating officer.

Clinical trials

Race shares went on a romp in mid-June after the company unveiled the results of a phase II trial for relapsed or refractory AML patients, carried out at Israel's Sheba Medical Centre.

The trial was open label, which means both the patient and the doctor knew the treatment they were receiving. A placebo control group was inappropriate.

The trial enrolled 10 patients aged between 22 and 80, who 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 tumors outside the bone marrow, known as extramedullary AML. Interestingly, these were the four who responded.

Of these patients, one achieved complete remission and three achieved partial remission: an overall clinical response of an "impressive" (the company's words) 40 percent.

This compares with "hospital experience" of a 20 to 30 percent response rate and is in line with the 20 to 50 percent response with the old trials. But four of 10 patients is a very small sample group.

Apart from lesser side effects such as mouth ulcers and low platelet counts, no major adverse events were recorded.

Dr Cullity says in such cases the response to the therapy is more crucial than the survival experience, because the multiple treatments the patients have received muddy the picture.

“How do you unscramble the egg?” Dr Cullity asks. “The answer is you will never know what intervention was the key driver for survival because (the patients) have had the kitchen sink thrown at them.”

Prof Borje Andersson, the chair of Race’s clinical advisory board, says the patients were at high risk of not responding at all and the company would have been happy with a 10 percent response rate.

A global leukaemia and stem cell transplant expert based at MD Anderson Cancer Centre in Houston, Texas, Prof Andersson adds the side effects were similar to the results from three decades ago, using the same 250 milligram dose.

The primary endpoints of the trial were overall survival over 24 months, as well as leukaemia-free survival over the two years.

“While we must study the drug further, it appears that with this kind of response bisantrene-based therapy may have potential to serve as an important bridge to an allogeneic stem cell transplantation in patients who otherwise have few therapeutic options,” he says.

What’s next?

While there’s been a lot of action with acute myeloid leukaemia therapies over the last decade, there are various treatment sub-sectors.

“You need to be wary about where the best value is,” Dr Cullity says. “You want to drive around traffic, not into it.”

With the dexterity of the Michael Schumacher of old, Race’s management is now steering the company through a five-step program, including three further potential acute myeloid leukaemia trials.

The company is talking to Sheba about running a phase II program for relapsed and/or refractory AML, but based on a combination therapy.

“I can’t tell you the exact size but it will be much larger,” Dr Cullity says.

In the US, the company is pondering a separate trial for paediatric AML patients who have received large - and possibly maximum - doses of cardiotoxic anthracyclines.

“It’s a real tragedy when kids have induction therapy, move into durable remission and are transplanted, but then are left with an underperforming heart,” Dr Cullity says.

“They can’t kick a soccer ball or in the worst-case scenario they require a heart transplant.”

This effort is being overseen by Dr Jaap Boelens, head of paediatric leukaemia at New York’s Memorial Sloan Kettering Cancer Center.

Race is also considering a third trial to target the 25 percent of AML patients supposedly in remission with measurable residual diseases, or MRD.

MRD-positive patients have an approximate 20 percent chance of two-year survival, but with MRD-negative cases the odds improve to 80 percent (post bone marrow transplant).

Dr Tillett says an MRD therapy could allow the company to enter a market that’s larger and less competitive than the broader market for ‘salvage’ acute myeloid leukaemia.

The fourth and fifth stages refer to proof-of-concept combination trials for the use of bisantrene for breast and ovarian cancer.

With two million new breast cancer and 200,000 new ovarian cancer cases a year, these are both bigger markets than AML.

Financials and performance

Race ended the March quarter with a cash kitty of $2.56 million, having burned the Devil’s number of $666,000 during the stanza.

The company also raised $1.69 million in a placement corner-stoned by the ubiquitous biotech investor Merchant Opportunities Fund.

Dr Cullity says the clinical results provide Race with solid grounds to pursue “sensible, titrated and balanced capital formation” - which to you and I means a likely capital raising.

Race is also eyeing a US Food and Drug Administration priority review voucher - a.k.a. a Willy Wonka golden ticket - for a paediatric therapy. These vouchers are fungible (transferable) and currently are being bought and sold on the secondary market for up to $100 million.

In June, the company settled the outstanding matter of a limited recourse loan granted to Dr Molloy when he joined.

The loan was by way of four million Race shares issued at a deemed 20 cents apiece and funded by an $800,000 loan.

The loan became payable on Dr Molloy’s departure, and was settled via a buy-back (and cancellation) of 2.22 million shares with a deemed value of 36 cents apiece.

Shareholders will vote on the buy-back proposal at a general meeting to be held in late July or early August.

The June 16 results sent Race shares soaring 16.5 cents, or 52 percent to 48 cents and they have since further elevated to record levels.

In July 2019, the stock plumbed a low of 4.5 cents, at which point your columnist backed up the truck and piled in … in his dreams.

Dr Boreham's diagnosis:

Drug repurposing is a popular sub-sector of life sciences and need we mention Paradigm Biopharmaceuticals with its program to treat osteoarthritis with a very old blood-thinning drug?

The benefit of 'rebirthing' lies in the ability to leverage millions of dollars of past investment - $200 million in the case of bisantrene - which leads to a cheaper and faster route to approval.

Reviving a drug for essentially the same purpose - which Race is attempting - is less risky than re-inventing it for an entirely different indication.

"In short we have reset bisantrene; it was a long time between drinks," Dr Cullity says. "We have now put it in a small yet precise phase II experiment and the drug is talking to us."

If the drug 'talks' some more with the expanded trials, this company is indeed is off and Race-ing.

Just watch those chicanes along the way.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. He has not found a wonder drug behind his sofa cushion but did retrieve a dozen bottle tops and a long-lost remote control.