Biotech Daily

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Daily news on ASX-listed biotechnology companies

Dr Boreham's Crucible: Patrys

By TIM BOREHAM

ASX code: PAB

Share price: 3.9 cents

Market cap: $70.96 million

Shares on issue: 1,819,596,905

Financials (June quarter 2021): revenue nil, cash burn $1.16 million, cash $10.91 million*****, quarters of available funding 9.39*

***** Includes $4 million in term deposits

Chief executive officer: Dr James Campbell

Board: John Read (chairman), Michael Stork (deputy chairman), Suzy Jones, Dr Campbell, Dr Pamela Klein

Identifiable major shareholders: Dr Dax Marcus Calder 10.2%, Stork Holdings (Michael Stork) 5.46%, Kemast Investments (Kerry M Stokes) 2.75%

The coronavirus pandemic continues to produce unexpected consequences - one of which is a shortage of monkeys.

We're not talking about the pesky rabies-ridden ones in Bali's Monkey Forest, but the two breeds of macaques - long-tailed and rhesus - favored by medical researchers for their physiological similarities with humans.

In the case of the rhesus monkeys, the US National Institutes of Health is investing $US29 million ($A40 million) in improving the facilities of the US National Primate Research Centres. China - the main breeding location for the long-tailed variety - has cut off supply to the West.

“The main problem is that demand exceeds supply,” says Dr James Campbell, head of antibody drug developer Patrys.

“There has been so much demand from developers of Covid vaccines.”

Dr Campbell says the Great Monkey Shortage is just one example of how the pandemic continues to present challenges for drug researchers.

The plague has also affected global supply lines and logistics - as evidenced by a glitch this week that knocked one-quarter from the company’s valuation (see below).

About Patrys (no, not the orange juice brand)

Patrys is developing a cancer therapy to tackle some of the most difficult solid cancers, including glioblastoma (brain cancer), triple negative breast cancer and pancreatic cancer.

Patrys was formed in December 2006 to consolidate human antibody technology acquired from German parties, but that program is now kaput because of manufacturing issues that emerged.

But not before the company raised funds for a phase II trial.

Dr Campbell took the reins in 2014 and licenced PAT-DX1 from Yale University in 2016.

The company’s lead program, PAT-DX1, is about inhibiting DNA damage repair (DDR), which is normally a good thing but not when the mechanism allows cancer cells to survive.

PAT-DX1 is a humanized and smaller version of deoxymab 3E10 (D3E10), a DNA damage repair antibody first identified in the inflammatory immune disorder lupus.

While most antibodies bind to the surface of cells, deoxymabs like PAT-DX1 penetrate into cells, then cross into the nucleus where they bind to the DNA and kill DDR-deficit or mutant cells.

Dr Campbell likens the DDR systems to a road crew that repairs any ‘potholes’ in the cell’s DNA sequence.

“If you have a DDR mutation, those holes aren’t patched up and that’s the basis of a range of cancers,” he says.

In other words, the road crew is on a smoko.

Transcending the blood-brain-barrier

Glioblastomas are the most common type of high-grade primary brain tumor and the most dangerous. They grow quickly and have thread-like tendrils that extend into other parts of the brain, which makes surgical removal very tricky indeed.

The average survival time after diagnosis is 12 to 18 months, and only 25 percent of glioblastoma patients survive beyond a year.

As the body's most important organ - although some may disagree - the brain has extra protection from foreign objects.

Specifically, the brain's capillaries have fewer 'holes' than capillaries elsewhere in the body, allowing the delivery of only essential nutrients and hormones. The downside of this protection barrier is that it's hard to get many therapeutic drugs into the brain.

Dr Campbell reckons only 1.5 percent of small molecules can transcend the blood-brain-barrier (including the glioblastoma drug candidate being developed by ASX peer Kazia Therapeutics).

Two decades ago, this didn't matter so much, because treatment was all about surgery or radiation.

"There's a heap of really interesting cancer drugs that just can't get into the brain," Dr Campbell says.

"We are in a strong position to go after cancers in the brain, whether they are primary or secondary cancers."

Indeed, Patrys has done quite a bit of pre-clinical work on treating brain metastases resulting from breast cancer.

"Outside of the potential in brain cancers we are also in a good position to go after other cancers with DNA damage repair mutations: triple negative breast cancers, pancreatic and colon cancer."

What's next?

Patrys is also broadening its portfolio with PAT-DX3, which is basically a full-sized version of the deoxymab antibody fragment PAT-DX1.

"As a larger molecule the mechanism of action is the same but the underlying pharmacology is different and PAT-DX3 stays in circulation longer than PAT-DX1," Dr Campbell says.

One idea for PAT-DX3 is deploying it as a vehicle to deliver other therapeutic 'payloads' (antibody drug conjugates, or ADCs).

Dr Campbell says antibody drug conjugates are particularly attractive in terms of delivering small molecules to a tumor site.

“We have an antibody that we know is attracted to a range of tumors. So, what would happen if we could put a payload on it?”

Think of PAT-DX3 as the bodily equivalent of a Qantas Cargo 747 carrying a million doses of Pfizer.

PAT-DX3 can be used for ADCs because it has more conjugation sites (amino acids) than the smaller PAT-DX1.

“You could conjugate a traditional small molecule, or some peptides,” Dr Campbell says.

“We have a payload delivery system for an anti-cancer agent, but the delivery system also has anti-cancer properties so there’s scope for really nice one-two punch.”

In July 2021 the company said animal models suggested PAT-DX3 could also cross the blood-brain barrier.

“Prior to this data, it had not been established whether the larger size of PAT-DX3 would limit its ability to cross the blood-brain barrier,” Dr Campbell says.

Patrys intends to follow this up with studies to compare the effects of both PAT-DX3 and PAT-DX1 on tumor reduction and survival in “range of primary and secondary brain cancer models.”

Parp! Parp!

If PAT-DX1 is progressed, it needs to be better than a current suite of so-called PARP inhibitors, which also inhibit DNA repair.

(PARP stands for the enzyme poly ADP ribose polymerase, but we all knew that already.)

The leading PARP drug is Astrazeneca’s lynparza olaparib, which is approved for a range of cancers. It is one of four approved PARP drugs that turn over $US2.3 billion a year.

“Generally, antibodies have fewer side effects than small molecules and we have the advantage that deoxymabs can transcend the blood-brain barrier,” Dr Campbell says.

He says both PAT-DX1 and PAT-DX3 have potential as a “tumor agnostic” therapy.

The company has been doing some work with Sydney’s Garvan Institute of Medical Research on pancreatic cancer, which is expected to be the second biggest fatal cancer by 2030.

(In the US there are about 60,000 cases a year).

Patrys is looking for local sites for a phase I trial, which will have a dose escalation component and will enrol solid cancer patients.

While doing the groundwork to get PAT-DX1 to clinic, the company is doing the drudge work of establishing stable cell lines, reproducing antibodies and getting toxicology down pat (excuse the pun).

This week the company reported a setback with this program, with its contract manufacturer unable to procure fermentation media equipment (no, not whisky stills) required for clinical-grade PAT-DX1 cell production.

As a result, the engineering run for PAT-DX1 is expected to be delayed until after September, with the tox studies rescheduled for the March quarter of next year. These delays were attributed to the impact of the pandemic on global reagent production and are "outside the control of either Patrys or its contract manufacturer".

Imagion that

Meanwhile, Patrys has a collaboration with the ASX-listed, US-based Imagion, which is working on cancer imaging.

"We have a way of getting across the blood-brain barrier and they have a compelling cancer diagnostic technology, so it's a collaboration that could well deliver some interesting insights," Dr Campbell says.

Finances and performance

Patrys' June quarter update reveals just under $11 million of cash, following a placement and rights issue that garnered $7.3 million late last year.

In 2018, the company raised $7 million partly by way of a placement which included Perth billionaire Kerry Stokes.

In December 2018, Patrys received a $3 million insurance payout, pertaining to its abandoned legacy program.

Patrys listed in July 2007 after a $25 million raising at 40 cents apiece. Under Dr Campbell's watch, shares in the reinvented Patrys have grown from one cent, to as high as six cents in mid-July.

Last week's PAT-DX1 delay doesn't look like the end of the world to us, but it was enough to knock 26 percent off the share price over two trading sessions.

Stokes aside, Patrys is backed by Canadian tech investor Mike Stork (who's also on the board) and Perth periodontist Dr Dax Marcus Calder.

Dr Boreham's diagnosis:

Dr Campbell sees any decent biotech outfit as an "alignment of intellectual capital, human capital and financial capital".

Naturally, he believes Patrys has all three of these magic ingredients.

"We have a differentiated asset that localizes a range of tumors and penetrates the cells and locks the DNA," he says.

"Drug development is long and rigorous and hard. We are systematically de-risking assets and we have a path to the clinic."

Dr Campbell says DNA damage repair and blood-brain barrier therapeutics are high on big pharma's shopping list, as is anything that targets the most problematic cancers.

"We are ready to talk to people", he says, adding that 60 percent of cancer antibody deals are enacted before phase I stage.

He concedes that Patrys might lack razzmatazz, but he's unapologetic about the company's rigorous approach to science.

"I've been criticized for not being a showman," he says. "That's a criticism I'm happy to take, because frankly we're doing our job properly."

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. He is surprised about the shortage of primates, given the degree of monkey-business surrounding last year's US election.