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*Daily news on ASX-listed biotechnology companies*

# Dr Boreham's Crucible: Prescient Therapeutics

**By TIM BOREHAM**

**ASX code:** PTX

**Share price:** 7.0 cents; **Market cap:** $44.8 million; **Shares on issue:** 640,553,010*****

**Chief executive officer:** Steve Yatomi-Clarke

**Board**:** Steven Engle (chairman), Mr Yatomi-Clarke, Dr James Campbell, Dr Allen Ebens

**Financials (year to June 30, 2020):** interest income $70,361, cash burn $3.32million, cash balance $20. 3 million*******

**Identifiable major shareholders:** Australian Ethical 6.48%, Retzos Executive Pty Ltd 4%, Andrew Morrison Stewart 1.6%

***** After $6.5 million share purchase plan and $7m placement that resulted in 246,292,429 additional shares being issues.
****** Paul Hopper resigned in January this year
******* Post capital raisings

Prescient chief Steve Yatomi-Clarke deploys a racy analogy to describe the immune-oncology house's re-emphasis on its trendy Car-T technology and away from its legacy therapies.

He likens the company's foundation assets to the "nice reliable woman you are happy to take home and meet your parents".

The Car-T program isn't quite the "flashy stuff" of a Tinder date, but much more likely to get investors' blood pumping.

“With the introduction of Car-T, I reckon we have both substance and sizzle,” he says. “The business is very different now.”

Investors appear to agree, having flocked to the company’s $6.5 million share purchase plan at 5.5 cents a share, which was followed by a surprise $7 million placement.

## A Prescient move

Prescient evolved from oncology house Virax Holdings, which acquired the ‘old’ part of its current portfolio through the acquisition of Aktivate Therapeutics in October 2014.

A corporate finance director at broker Paterson Securities, Mr Yatomi-Clarke took over from Rob Crombie in February 2016. A biochemist and molecular biologist by training, Mr Yatomi-Clarke was involved in big-ticket deals including Halcygen’s acquisition of the former Faulding operations (the precursor to Mayne Pharma).

In essence, Prescient’s foundation programs are PTX-100 and PTX-200, which dwell in different disciplines of targeted therapies. A pathway inhibitor, PTX-100 has the ability to block a cancer growth enzyme, thus disrupting oncogenic pathways called Ras and Rho mutations.

Meanwhile PTX-200 is currently in early stage trials, focusing on blood and solid cancers that display these mutations.

## Turning poodle cells into rottweilers

In May this year, Prescient acquired its Omnicar Car-T program from the University Pennsylvania (known to its Ivy League alumni as ‘Penn’, and not to be confused with the public ‘Penn State’) “the home of Car-T therapy”.

“Car-T is game changing,” Mr Yatomi-Clarke says. “It’s stealing headlines for all the right reasons.”

In developing Omnicar, Prescient is focusing on the disadvantages, rather than benefits, of Car-T.

## Please explain? Okay - here we go...

Car-T enhances the work of T-cells, the soldiers of the immune system that rely on their receptors binding to problematic proteins called antigens. Once they bind, the T-cells can tear the infected cell apart with the ferocity of a rottweiler.

Ideally, T-cells will kill cancer cells without the person even knowing of the imminent danger. But if the cancer evolves, that antigen (protein) becomes invisible to the immune system and the T-cells can’t sniff it out.

“We solved that problem by adding a bespoke receptor capable of recognizing a cancer antigen, called a chimera (chimeric antigen receptor),” Mr Yatomi-Clarke says. “This is half the patient’s T-cell with an introduced receptor.”

The genetically engineered cells are grown by the millions in a lab and then re-injected in a patient.

“The patient is getting a turbo-charged version of their own cells ... you are putting a new nose on the dog to turn it into an attack dog.”

## Moving on from ‘Betamax’ tech

While Penn State developed Car-T therapies, big pharma Novartis can lay claim to launching the first commercial Car-T therapy. The drug, Kymriah (tisagenlecleucel) was approved by the US Food and Drug Administration for blood cancers in 2017 and turns over $US1 billion ($A1.38 billion) a year.

A mere eight years after the initial Car-T stuff was discovered, Mr Yatomi-Clarke reckons the technology is akin to those bulky 1980s video cameras that required a suitcase and a brick-like battery. (Not that that stopped annoying Francis Ford Coppola wannabes from filming their entire Viva holiday and insisting you watch the evidence).

“As wonderful as it is, with any first-generation technology there are shortcomings,” Mr Yatomi Clarke says. “These include the time and cost of a bespoke treatment and the safety and control aspects of dispensing a living medicine. Patients have died from a severe inflammatory response.”

He adds the T-cells can lose their ‘nose’ and become poodles again if the cancer cells mutate - as they are wont to do.

Omnicar involves halving the Car-T-cells, which are then ‘armed’ only by adding a certain component. Thinks of two strands of molecular Velcro that need to join each other to be active. This means that the clinicians can continue to administer all of the T-cells upfront, but can control the activity post infusion.

“For the very first time, clinicians can have control of a living cell once it is inside the body. If there is a deleterious event you can switch off the therapy, but T-cells are ready to be ‘enlisted’ again,” he says. “This feature on its own will be immensely powerful, taking this to new patients, new indications and even things beyond cancer.”

## Beating big pharma to the prize

Omnicar came about after Mr Yatomi-Clarke scoured the world for suitable technologies; and eventually spoke to a Penn boffin who suggested the know-how that eventually formed the platform.

“I couldn’t believe what I saw,” he says. “At that stage the patent wasn’t public and the data was unpublished, so no one knew about it.”

The terms of the global exclusive licence are confidential, but heavily back-ended with normal milestones.

Skeptical investors have asked why Prescient sniffed an asset overlooked by giants such as Novartis. Mr Yatomi-Clarke says the bespoke technology didn't fit the big pharma strategy, which at the time was focused on a so-called CD19 target for blood cancers.

"Being a small company, we were target agnostic. We weren't bringing the agenda of a big company, we were going to develop it like a platform," he says.

"No one else was looking and that really helps."

**For your eyes only**

There's a venerable learning institution other than Penn involved in the Omnicar story: Oxford University.

That's because the aforementioned novel molecular binding system (the 'Velcro') was devised at the University (technically, a cluster of 39 separate colleges).

These interlocking thingies go by the title of "Spycatcher/Spytag", which is intriguing because we thought espionage rings were the preserve of Cambridge. Anyway, the secret's out about Oxford's crucial role. As Mr Yatomi-Clarke puts it: "We licenced the sports car from Penn but the engine is from Oxford."

**The old programs explained**

Coming back to the old stuff on the company's books, Mr Yatomi-Clarke says Ras was the first oncogene discovered, but remains an elusive target. While rival developers are looking at very specific mutations, Prescient targets a range of them (when patients have a Ras mutation, they have more than one).

With PTX100, Prescient is in the midst of a Melbourne-based phase I dose escalation trial, targeting a "basket" of solid and blood cancers.

In an update this month, the company said it would proceed to the third dosing level (2000 milligrams) after the second level of 1000 milligrams proved to be safe. Also, two of the three patients in the first cohort (500 milligrams) showed disease stability or better.

"We saw a clinical signal in the first cohort in addition to safety, which we didn't expect to see," Mr Yatomi-Clarke says.

PTX-200 is currently in early stage trials, focusing on blood and solid cancers that display these mutations. Novel in action, PTX-200 inhibits a tumor pathway called Akt, which plays a key role in breast and ovarian cancers as well as leukaemia.

The therapy is claimed to be safer than existing Akt inhibitors, which have toxicity problems.

This compound has produced “encouraging” phase IIa data in HER2-negative breast cancer; and phase Ib/II results in relapsed and refractory acute myeloid leukaemia.

The proof-of-principle breast cancer study saw a 91 percent response in the HER2-negative cohort.

In a key change of tack, the company is now looking at hormone therapy and has dropped the chemotherapy drug paclitaxel as the combination therapy.

**Finances and performance**

Prescient initially extended the closing date of its share purchase plan from July 7 to August 20, in order to give investors time to absorb the news flow. Pitched at 5.5 cents a share, a then 15 percent discount, the $6.5 million raising was heavily oversubscribed and it closed ‘early’, on August 18.

The company this week snaffled a further $7 million in a placement, also at 5.5 cents apiece. Given the company already had a healthy cash balance of $7.3 million, Mr Yatomi-Clarke says the raising was an “opportunistic top-up from a position of strength.”

But as any investment banker would attest, you don’t wait until the petrol tank is empty before pulling into the servo.

Prescient shares have snapped back strongly from the Covid nadir (and record low) of 2.4 cents in mid-March. The shares peaked at 14 cents in June 2018.

**Dr Boreham’s diagnosis:**

We won’t pretend that the Prescient yarn is easy to comprehend, or that it’s on to a certain winner.

It’s well known that only one in 100 drugs or so will ever get to market, so the imperative is to enhance clinical data in view of a partnering deal.

As the enthused reaction to the share purchase plan shows, at least the company is winning the ear of investors.

The company is undertaking a strategic review to decide exactly what it should be chasing.

In the shorter term, investors should expect further articulation of the Omnicar strategy; and an update on PTX-100.

There’s also potentially some Covid-19 news with Prescient joining the long conga line of claimants for a treatment.

Mr Yatomi-Clarke notes that Prescient is the only ASX-listed Car-T developer*****.

“We are also ahead of the next wave, with very little competition,” he says. “It doesn’t get sexier than that”.

Still, with its complex science, Prescient is more a story of patient seduction rather than an airport bodice ripper.

***** The private Adelaide-based Carina Biotech is developing Car-T therapies for solid cancers and is led by former Bionomics chief Dr Deborah Rathjen.

***Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort – or a licence to kill.***