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*Daily news on ASX-listed biotechnology companies*

# Dr Boreham's Crucible: Arovella Therapeutics

**By TIM BOREHAM**

**ASX code:** ALA

**Share price:** 4.7 cents; **Shares on issue:** 899,149,698; **Market cap:** $42.3 million

**Chief executive officer:** Dr Michael Baker

**Board:** Dr Tom Duthy (chair), Dr Baker, David Simmonds, Dr Debora Barton, Dr Elizabeth Stoner, Gary Phillips

**Financials (March quarter 2023):** receipts $19,000, net cash outflows $1.83 million, cash on hand - about $8 million post-raising.

**Identifiable major shareholders:** Merchant Funds Management 11.3%, Richard Mann (Mann Beef Pty Ltd) 6.4%

Little by little, investor purse strings are re-opening and biotechs are raising capital again. But their efforts are in dribs and drabs and no-one is aiming too high.

An exemplar is Arovella, the cancer immunotherapy play that raised $4.1 million and strived for an additional $1 million by way of a share purchase plan (SPP).

As it happened, on Tuesday the company announced the SPP had raised $2.2 million and - yes - the company would keep the over-subscription bestowed by the biotech gods.

Formerly the oral drug delivery developer Suda, Arovella has re-invented itself with a singular focus on the sexy immunotherapy discipline of Car-T therapies.

The Monty Python catchphrase - “and now for something completely different” - comes to mind. Put another way, the company is like grandpa’s axe with a new management, new board and a new raison d’etre within the old entity.

With a long-time interest in immunotherapies, Paul Hopper took over as chair of the then Suda in 2019. The country’s busiest biotech entrepreneur declared the company was pursuing too many small programs without a commercial focus.

Still, little did we know that Suda/Arovella would pitch its spray mist delivery program completely, in favour of the Car-T program. But it did.

But one must angle where the fish are biting and investors have been lured by the pre-clinical results pertaining to Arovella’s lead compound, called ALA-101, which targets a cancer marker called CD19 (see below).

**Don’t quiver, it’s Arovella**

The name Arovella derives from arrow (as in targeted drug delivery) and novel (as in new therapies).

Arovella plays in Car-T therapies alongside the ASX-listed Chimeric Therapeutics, Imugene and Prescient Therapeutics. (All of which just happen to be, or were, Paul Hopper-related companies.)

‘Car’ stands for chimeric antigen receptor and T refers to T-cells.

Arovella’s program revolves around invariant natural killer T-cells (iNKT) assets, acquired from Imperial College London.

The company also has technology that targets a cancer marker called DKK1, acquired from the Houston, Texas-based MD Anderson Cancer Centre. The idea is eventually to use this in conjunction with the iNKT platform.

Arovella was initially known as Eastland Medical, which was incorporated in 1999 and listed in 2001, developing the sublingual Artimist as a treatment for malaria.

The troubled Eastland changed its name to Suda in 2012, with a remit to develop spray-based oral delivery Oromist platform.

Mr Hopper’s appointment resulted in the departure of chief executive Stephen Carter after nine years at the helm, to be replaced by Dr Michael Baker.

Dr Baker was an investment manager with Bioscience Managers and is on the board of the Mr Hopper-chaired nuclear medicine play Radiopharm Theranostics.

In October 2021, Suda changed its name to Arovella.

A year later, the company said it would cease development of Oromist and close its Perth facility.

Mr Hopper quit the board in June 2022, with Dr Thomas Duthy eventually taking his place as chair.

Mr Hopper continues to chair Chimeric Therapeutics, which is also Car-T driven.

With about five staff, Arovella operates on a pure virtual model by which trials and pre-clinical work are outsourced.

**Fighting the scourge of cancer - and acronyms**

In June 2021, Arovella signed a deal with Imperial College London to acquire a cell therapy platform called invariant natural killer T-cells, or iNKT.

The body's strongest immune cells, iNKTs are a rare variant of T-cells.

Dr Baker said the program appealed because of Imperial College's lofty status and the laboratory-ready nature of the asset.

Separately, the MD Anderson Cancer Centre delivered a poetically monikered asset called DKK1-Car/mAb. This peptide is the first to target DKK1, a biomarker of several forms of blood and solid cancers.

Dr Baker describes iNKT cells as "one of the most potent, naturally occurring immune cells." (A mAb is a monoclonal antibody.)

**Tackling blood cancers**

Arovella's lead program, ALA-101, is showing early promise as a treatment for CD19-expressing blood cancers.

In April this year, the company's shares went on a mini-run after pre-clinical data was aired at the American Association of Cancer Research (AACR) in April.

In the mouse study, the rodents were infused with CD19-expressing, aggressive B-cell acute lymphoblastic leukemia cells. At the 90-day mark, only the 38 mice treated with ALA-101 (Car19-iNKT cells) and other Car-T therapies survived.

Of the 19 mice treated with ALA-101, the 90-day rate was 1.5 times better than the other Car-T mice and 90 percent of them were still squeaking.

An interesting twist is that four of the ALA-101 mice developed subsequent brain tumors, but they cleared up without further treatment. This suggests the effect of ALA-101 is enduring and that the molecule can cross the blood-brain barrier.

Crucially, the studies have shown the iNKT cells can be expanded by a factor of 5,000 without losing their potency.

“The data has given us great comfort that our proprietary manufacturing process allows for sufficient expansion of the iNKT cells that retain their functionality,” Dr Baker says.

He adds that the first-generation Car-T therapies have resulted in significant relapses and safety risks such as cytokine release syndrome, neurotoxicity and infection.

“We believe there is a significant unmet need and ALA-101 is well placed to fill that need by having an off-the-shelf strategy to treat B cell lymphomas and leukaemia.”

**… and solid cancers**

Arovella also has a joint program with the ASX-listed Imugene, which combines ALA-101 with Imugene’s Oncarlytics therapy (more formally known as CF33-CD19).

This effort is relevant for solid cancers which - unlike blood cancers - do not exhibit the CD19 marker.

As Dr Baker says the Oncarlytic virus infects the cancer cells and forces them to express CD19. “Our iNKT cells will come along like heat-seeking missiles and find and destroy them,” Dr Baker says.

The Imugene therapy also aims to kill the tumor cells. So, like Harpic Flushmatic dual action cistern blocks, there is a two-fold efficacy by combining both therapies.

This collaboration is in proof-of-study, in-vitro stage, with animal data expected in the second half of 2023.

**Bespoke versus off-the-shelf**

The usual Car-T manufacturing process involves blood being taken from a patient’s arm. The T-cells are collected and are genetically reprogrammed to produce millions of chimeric antigen receptors.

The souped-up cells are infused back into the patient, where they define the cancer cells and trigger their destruction.

A point of (polite) debate in the Car-T community is whether the cells should be acquired from the patient (the autologous approach) or derived from healthy people and prepared as off -the-shelf therapy (allogeneic). All six Car-T approved therapies to date are autologous.

Dr Baker says the pharmaceutical industry is not set-up for the bespoke (autologous) approach, resulting in high manufacturing costs and supply chain issues.

“As the starter cells come from a diseased patient, there are problems with immune compromise,” he says.

“It also takes about four to six weeks to prepare the therapies and not all cancer centres are able to get access to them. Patients might succumb to the diseases while waiting for the treatment.”

Arovella also has an option with the University of North Carolina, which involves licencing cytokine technology for the company’s iNKT program.

The cell therapy sector’s answer to Viagra, the program could result in potent and longer-lasting iNKT cells.

**Finances and performance**

Given the ratty market, Arovella has been a dab hand at raising capital under new management.

In January, the company raised $4.57 million in a placement at 3.8 cents a share, with biggest shareholder Merchant Funds chipping in $3 million. An underwritten, oversubscribed share purchase plan raised a further $1.5 million.

The latest placement secured $4.1 million at 4.5 cents, a 10 percent discount to the then prevailing price, followed by a share purchase plan that raised an additional $2.2 million.

As at the end of the March, the company had cash of $3.25 million, so the raising means it should be well endowed to meet its short-term goals.

Arovella shares were trading at a record low of two cents at the start of 2023, peaking at 10.5 cents in mid-April after the AACR prezzo.

**Hits and misses**

Arovella is the only Australian company working on an iNKT therapy - and only one of three or four globally.

In May, the Buffalo, New York based Athenex Inc entered voluntary bankruptcy protection after the US Food and Drug Administration placed its phase I program on clinical hold (after a patient died). Athenex bought its relevant asset for $US185 million two years previously and already owed $US250 million to Oaktree Capital (as with Arovella, the company reinvented itself).

Others are the Nasdaq-listed, $US76 million market cap Mink Therapeutics (in phase I stage) and the private, pre-clinical Appia Biotech. In 2021, Appia signed a $US875 million partnership with cell therapy leader Kite Pharma, so its shareholders could not have been ‘appier.

In the broader Car-T space, there are dozens of drug developers and no shortage of big-ticket deals.

In May this year, Janssen and Cellular Biomedicines Group announced a phase IIb collaboration involving a $US245 million upfront.

In January, Astrazeneca acquired Neogene Therapies for $US200 million of upfront payments and $US120 million of milestones.

In phase I stage, the same-but-different Neogene dabbles in a variant called T-cell receptor therapies that recognise intracellular targets such as mutations.

**Dr Boreham's diagnosis:**

Dr Baker says Car-T therapies have revolutionised blood cancer treatment, "to the point where are using 'cure' and 'cancer' in the one sentence".

He adds that patient experience elsewhere shows that patients who took the treatment 10 years ago are still cancer-free.

In the short term, Arovella will focus on optimizing its cell manufacturing process and scaling it up, in view of gaining regulatory approval for a phase I Hodgkinson's lymphoma trial.

This background work does not sound especially exciting, but the acquisitive action in the Car-T sector shows that things can happen at an early development stage.

For those who last the arduous journey, the value of the Car-T drug market is expected to exceed $US60 billion by 2030.

The two earliest-approved drugs - Yescarta and Kyriah - last year turned over $US1.1 billion and $US500 million, respectively. Approved in 2021, Abecma achieved more than $US400 million in revenue.

"It's a very promising sector that is set to get a lot bigger," Dr Baker says.

***Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. He is in a very promising sector that is set to get a lot bigger – or so he has been told all his life.***