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*Daily news on ASX-listed biotechnology companies*

# Dr Boreham's Crucible: Phylogica

**By TIM BOREHAM**

**ASX code:** PYC

**Share price:** 6.2 cents

**Shares on issue:** 2,931,427,990*****

**Market cap:** $181.75 million*****

**Chief executive officer:** Dr Rohan Hockings

**Board:** Alan Tribe (chairman), Dr Bernard Hockings, Dr Rohan Hockings

**Financials (September quarter 2019):** Revenue nil, cash burn $2.1 million, cash of $30.9 million*****, estimated current quarter outflows $2.6 million

***** Including $26.8 million capital raising, completed yesterday

**Major identifiable holders:** Alan Tribe/Australian Land Holdings 27.4%, Dr Bernard Hockings 13.0%, Sietsma Holdings 9.7%, Anthony Barton 5.0%.

Phylogica CEO Dr Rohan Hockings is blunt about the drug delivery outfit's erratic development path since listing 14 years ago.

"We were chasing all the rabbits and catching none," he says. "Investors were saying: 'You have this nice delivery system but what are you going to do with it?'"

Having applied its platform of "cell penetrating peptides" (formerly known as "phylomers") to multiple diseases over the years, Phylogica is confident that it has found its ideal bunny: a rare eye disease called retinosa pigmentosa.

“Things are coming together after a hard slog,” Dr Hockings says.

The hard slog has indeed been rewarded in the most tangible of ways: investor support for a $26.8 million rights offer that has replenished the company’s coffers.

Phylogica’s business has always been based on the same platform: a ‘library’ of peptides that are hooked-up with known drug ‘cargoes’ to improve the reach and efficacy of the molecules.

The key philosophy is that the highest value drug targets (including DNA) are inside the cells, but the clever cell membranes have evolved to keep out foreign matter.

“The company’s techniques have always been the same; it’s just that the [cell penetrating peptides] have improved,” Dr Hockings says. “They are much higher performing and less toxic.”

A spin off from the not-for profit medical research body Telethon Kids Institute, the Perth-based Phylogica listed a decade ago - on March 23, 2005 to be exact - raising $5 million at 20 cents apiece.

The company’s premise was to build a library of hundreds of billions of phylomers, which are protein fragments with active molecules that can fight diseases.

Quirkily, the genetic material that gives rise to these phylomers derives from extreme environments such as volcanoes, geysers and deep-sea vents.

Initially the company tackled inflammatory diseases, led by biotech man-about-town Dr Stewart Washer. Dr Washer was joined on the board by future medical marijuana mover-and-shaker Harry Karelis.

As it transpired, Dr Washer became the first of a revolving door of five CEOs, but to be fair Australia has had six PMs during that time (not counting Kevin Rudd’s brief return bout).

Perth cardiologist Dr Bernard Hockings first appeared on the register in August 2012, initially with a 6.8 percent stake. If you haven’t guessed it already, Bernard is Rohan’s old man.

Phylogica is following the old marketing playbook of rebadging itself to PYC Therapeutics, probably to forget the past 15 years.

**Not Lion around**

Over time, a slew of impressive sounding collaborations with Pfizer (up to $136 million), Medimmune ($110 million plus), Johnson & Johnson and Astrazeneca went absolutely nowhere and the company struggled to disseminate its message in user-friendly terms.

Phylogica needed a lucky break and respite came in the guise of a drug candidate developed by Murdoch University molecular biologist, Prof Sue Fletcher.

Prof Fletcher is Phylogica's research and development chief. "She is like a national living treasure," Dr Hockings says.

Prof Fletcher and fellow Prof Steve Wilson invented eteplirsen (Exondys-51) which eventually became a blockbuster drug to treat Duchenne's muscular dystrophy (Exondys-51 is owned by Sarepta Therapeutics of the US).

Phylogica formed a joint venture called Vision Pharma with Lion's Eye Institute, a Perth not-for-profit research body.

In effect, Phylogica delivered the vehicle (the penetrating peptides) and Lion's Eye provided the molecule, known as an anti-sense oligonucleotide.

Phylogica had a 50 percent share of the joint venture, but has committed $15 million to take its ownership to 90 percent. Of this amount, the institutional component of the rights offer will provide $14.3 million.

"Up to now we were reliant on someone else," Dr Hockings says: "We now have our own molecule and we can keep taking it forward in the clinic."

**Seeing you asked …**

Because you're dying to know, anti-sense oligonucleotides are a class of precision medicine.

The beauty of them is that they are made up of the same 'building blocks' (nucleotides) as DNA and the 'anti-sense' strand is the exact opposite sequence of the 'sense' strand of nucleotides in the DNA.

Over to you, Rohan: "This means that the anti-sense oligonucleotide is a perfect match for its target inside the cell and can 'silence' or 'knock down' a genetic defect represented by an error in the human genetic code in the DNA".

"The potent and precise nature of the anti-sense oligonucleotides has led to multiple new drug approvals over the past couple of years for this class of therapeutic."

**About retinosa pigmentosa**

Retinosa pigmentosa is a specific mutation that affects about 0.03 percent of children, or about 30 in 100,000. There are about 300,000 known sufferers.

The kids first lose their night vision, then their peripheral vision and eventually go completely blind.

Phylogica is addressing a sub-type which is only two to three percent of total cases, or 4,000 to 8,000 people in the Western world.

Dr Hockings said the company chose retinosa pigmentosa because there was no existing treatment and nothing upcoming in the clinic, either.

“It occurs in cells in the deepest layer of the retina,” he says. “We are addressing a condition that others can't because of the depth of the target cell that we are pursuing in the eye.”

He cites retinosa pigmentosa as a $1 billion target market.

“Our patient population is equivalent to the Duchenne’s muscular dystrophy population,” he says. As alert readers of this organ would be aware, Duchenne’s muscular dystrophy is being targeted by fellow ASX-listee Antisense Therapeutics.

“Exondys-51 is a $500 million a year drug and that’s only approved in the US and not Europe,” Mr Hockings says.

**In the lab**

The company says mouse models delivered the drug four times more effectively than the “nearest competitor”.

We presume this to be a reference to Sarepta’s cell-penetrating peptide called RXR4, which should not be confused with a Wankel rotary engine Mazda model favored by 1970s hoons.

The company then turned to a novel ‘retina in a dish’ technique, by which a human eyeball was created on a bench top using 3-D techniques.

Skin samples were turned back into a stem cell and then organized in the same cell layers of the retina.

The experiment reversed the disease, showing “more than 90 percent efficacy from a single dose”.

“It was done with remarkable fidelity,” Dr Hockings says. “It was a very good simulation.”

Repeat studies (and variations) are planned ahead of a planned visit to the US Food and Drug Administration with an investigational new drug application by July 2020.

If the FDA accedes, the company will launch a phase I trial with 10 patients whose tissues were used to grow the eyeballs in a dish.

This is scheduled for the first half of 2021.

“We believe we can also progress to a combined pivotal [phase II/III] study in the second half of 2021,” Dr Hockings says.

**Can’t win ‘em all**

In 2014, Phylogica extended a collaboration with existing partner Genentech (a subsidiary of Roche) to discover novel antibiotics. As followers of fellow ASX dweller Recce will know, this is an increasingly urgent quest given growing resistance to current treatments.

Genentech delivered a $US2 million ($A2.9 million) milestone payment to Phylogica last quarter, with the promise of $US140 million more. But fairytales rarely come true in biotech land and in November Phylogica reported the program has “concluded”, which is a nice way of saying it did not achieve what Genentech wanted.

**Finances and performance**

Post the underwritten one-for-five rights issue, Phylogica will have about $30 million in the bank and also expects to pocket a $2.5 million Federal R&D Tax Incentive.

This will be more than enough to cover the planned trial. “You only need 40 to 50 patients for a pivotal trial, so it’s really cheap,” Dr Hockings says.

The company last raised $9.5 million 18 months ago, with chairman Alan Tribe and Dr Bernard Hockings stumping up seven-figure amounts.

The former owner of Ikea’s Perth franchise, Mr Tribe accounts for 23 percent of the register. As well as being a handy funding source, Alan can assemble a board room table from scratch with an Allen key if needs be.

Over the last 12 months, Phylogica shares have traded between 2.2 cents (March 2019) and 6.6 cents (mid-October). A decade ago, they traded at 10 cents and have been as low as 1.2 cents. In early 2006, Phylogica peaked at 58 cents.

**Dr Boreham’s diagnosis:**

It’s self-evident, but worth stressing, that the retinosa pigmentosa program is in pre-clinical studies, only.

Phylogica has other programs bubbling away for other indications including neuro-degenerative (brain) and genetic liver disorders, as well as oncology.

“We will have more for inherited retinal disease, in effect swapping one anti-sense oligonucleotide for another,” Mr Hockings says.

Phylogica’s original oncology program, Imyc, is still bubbling away. But the company has learned its lesson about past premature hyperventilation and will only communicate about the lead programs, so as not confuse investors.

On the ASX, Phylogica is roughly comparable with Opthea, but only because they are tracking eye diseases (but with different technologies).

On the Nasdaq, Stoke Therapeutics is developing anti-sense oligonucleotides for rare diseases and has a $US1 billion market cap.

Dr Hockings says Stoke Therapeutics is at a similar stage of progress to Phylogica.

Dutch company Proqr, also listed on the Nasdaq, is also developing anti-sense oligonucleotides for retinal diseases and is at pivotal trial stage.

Proqr has a $US500 million market cap. “But a minority of patients are responding, so they have some issues,” Dr Hockings says.

On his frank assessment, Phylogica has been “in discovery stage for far too long and we have been very lucky to survive”.

In reality, the odds are still stacked against the company getting anything commercialized.

But naysayers were also saying that about $1.5 billion market cap Clinuvel, which is tackling a similar patient population for a rare skin disorder.

So hang on! Magic can happen in biotech land after all.

***Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. He once assembled an Ikea table from scratch and it stayed upright, which was just like magic.***