Biotech Daily

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Daily news on ASX-listed biotechnology companies

Dr Boreham's Crucible: Argenica Therapeutics

By TIM BOREHAM

ASX code: AGN

Share price: 41 cents

Shares on issue: 99,150,822

Market cap: $40.7 million

Chief executive: Dr Liz Dallimore

Board: Geoff Pocock (chair), Dr Dallimore, Dr Samantha South, Terry Budge, Liddy McCall

Finances (year to June 2023): revenue nil, net loss $4.81 million (previously a $4.09 million deficit), cash of $9.29 million (up 4%).

Identifiable major holders: Oofy Prosser (Drones family) 4.47%, Neil Donald Delroy 4.24%, Perron Institute 3.58%, University of WA 3.45%, Litis Super 2.82%

For such a common and debilitating disease, strokes haven't garnered their fair share of attention but this is changing as more drug developers turn their attention to the underserved condition that affects one in four adults.

"One in four people will suffer a stroke in their lifetime and of those only 10 percent will recover completely," says Argenica chief Dr Liz Dallimore.

"There are no neuro-protective drugs to prevent cell death, post-event."

While 15 million people globally suffer a stroke each year, five million of them fatally, there's no effective treatment for front-line responders (usually paramedics) to administer.

Victims of the most common ischaemic (vessel blockage) strokes are usually delivered anti-clotting medication, but this can only be administered up to four hours after the event.

Argenica's lead candidate is ARG-007, a cationic arginine-rich peptide.

Arginines are not denizens of a populous South American nation but are amino acids derived from one's diet and essential for producing proteins.

ARG-007 has multiple mechanisms of action which prevent cascading cell deaths.

In effect, if used as a front-line therapy it buys time for the patient. Hopefully.

Potted history

Argenica and ARG-007 are based on research carried out by the University of Western Australia (UWA) and the Perron Neuroscience Institute.

This effort was headed up by the UWA's Prof Bruno Meloni and Prof Neville Knuckey, head of stroke research at Perron.

Argenica listed on June 11, 2021 after raising $7 million at 20 cents a share.

The compound has been assessed in 25 peer-reviewed publications, mainly in relation to ischaemic stroke but also traumatic brain injury (TBI) and infant stroke.

Dr Dallimore started out in stroke research at the Australian Neuromuscular Research Institute, now the Perron Institute.

After completing a Doctor of Philosophy in neuroplasticity - jointly at the University of WA and at Oxford - Dr Dallimore then picked up a Masters of Business Administration from the Australian Graduate School of Management.

She changed tack and worked for some of the big accounting firms for 15 years.

But she remained a board member of the Perron Institute where Prof Meloni, now Argenica's chief scientific officer, worked.

Hailing from a scientific Perth family, Dr Dallimore says her interest in brain regeneration developed after a friend developed quadriplegia from rugby.

"The brain is mostly fat and water [but] is a complex organ that cannot be understood like other organs," she says.

Different strokes for different folks

About 85 percent of strokes are ischaemic, which means a clot in an artery is cutting off blood supply to the brain.

Brain cells that are deprived of blood - therefore oxygen - die and they won't regenerate.

The remainder of cases are haemorrhagic and result from arterial bleeding.

The stroke treatment mantra is 'time is brain' in that every minute counts (especially in the first hour, dubbed the Golden Hour).

Currently, a patient is whisked away by ambulance but there is little triaging or treatment on board (except for Victoria and Australia's single specialist stroke ambulance).

The reason for the on-board inertia is that the type of stroke needs to be determined with an in-hospital scan.

Administering a clot dissolver to a haemorrhagic patient could cause fatal bleeding.

But that all takes time and in the interim the patient is losing brain cells - fast.

"The aim is to get to hospital ASAP," Dr Dallimore says.

ARG-007 – Licence to Cure

ARG 007 can be administered for either type of stroke, and alongside a clot dissolver.

ARG-007 works in several ways to reduce cell deaths, including reducing oxidative stress and calcium influx.

When a vessel is blocked, the reduction in the blood flow affects the neurons around the vessels - with all kinds of nasty flow-on effects.

For instance, an influx of calcium into the cell can activate cell death pathways.

ARG-007 also appears to overcome the blood-brain-barrier, the body's natural defence against foreign agents. (So do python roundworms.)

"The drug down-regulates neurons for 12 hours, so it's a pretty good window to get to hospital," Dr Dallimore says.

Animal modelling showed ARG-007 could reduce the total volume of cell death by 66 percent, 24 hours after the stroke.

With only one intravenous injection, the drug's effect was still evident 28 days later.

Off to the clinic

In September, the company won ethics approval from Melbourne's St Vincent's Hospital to undertake a 92-patient, phase II, proof-of-concept trial of ARG-007, for acute ischaemia patients.

This assent covers 10 hospitals, with other takers including the Royal Melbourne and Royal Adelaide hospitals, Melbourne's Monash Medical Centre, Perth's Sir Charles Gardiner Hospital and Fiona Stanley Hospital and Queensland's Princess Alexandra Hospital.

These patients will have been wheeled into an emergency department with confirmed acute ischaemic strokes.

A patient is scanned and assessed and - if referred to the trial - will receive either a single intravenous dose of ARG-007 or saline placebo prior to undergoing a thrombectomy (removing a blood clot).

"It takes a bit of time for the interventional procedure, which hopefully gives time for our drug to work," Dr Dallimore says.

The primary safety endpoint aside, the trial measures the impact of ARG-007 on secondary brain cell death volumes (reperfusion) as blood rushed back to the brain post-thrombectomy.

Meanwhile, in August this year the company received "extremely encouraging" feedback from the US Food and Drug Administration, in a pre-IND (investigational new drug) meeting.

In essence, the regulator is happy with Argenica's trial design, drug manufacturing protocols and such.

If the local phase II trial is successful, this feedback could support a phase III study in the US.

Dr Dallimore says a phase III trial endpoint would be functional outcomes, although surrogate endpoints (such as imaging) could be deemed acceptable to the FDA.

Can't say no

Not surprisingly, enrolment for trials of acute conditions such as stroke needs to be more immediate than for studies in, say, oncology.

When the ambulance arrives at the hospital, the suspected stroke victim is assessed and scanned for stroke severity, with eligibility screening for the trial done at the same time.

Patient consent is not required and most are not able to give it.

The consulting neurologist will usually give the nod, with protocols varying from state to state.

“We are expecting about 18 months to get those 92 patients through the door,” Dr Dallimore says.

“The limiting factor is not the flow of patients, but getting the clinicians to refer the patients to the trial.”

On that note, the company is not averse to stirring up competition between the neurologists by providing the site-by-site recruitment numbers.

Great! Now it’s ARG-008

While Argenica’s starting point is stroke, the company is working on the notion that its drug is just as relevant for other types of brain injury related to neuro-inflammation.

These include hypoxic ischaemic encephalopathy, Parkinson’s disease, Alzheimer’s disease and moderate traumatic brain injury.

The idea is to reformulate ARG-007 into oral or nasal form to treat such conditions.

Aiding this quest, Argenica has received a $419,000 grant from Western Australia’s Innovation Seed Fund Program: a.k.a ‘let’s do something as a state, other than dig up iron ore’.

Specifically, the dollars will support a reformulated dosage for Alzheimer’s research.

Such a reformulation into a distinct new drug would be referred to as - you guessed it - ARG-008.

Ferreting out the truth

The company has also received a $1.2 million grant under the Federal Cooperative Research Centres Program, to carry out early-stage work in traumatic brain injury and concussion.

A rat study showed reduced protein aggregation and inflammation down to normal levels, once administered following a moderate traumatic brain injury.

“We are repeating that study in a ferret model, because a ferret brain is more akin to a human brain; it’s always best to do these studies in two different animal models,” Dr Dallimore says.

The study is being carried out at the University of Adelaide, under the auspices of esteemed neuroscientist Prof Melinda (Lindy) Fitzgerald.

Finances and performance

Following the IPO, the company raised $5.5 million in a placement in May 2022 and a $4 million placement in June this year. The company has just over $9 million of cash.

“It is tough going but there is still money out there for the right company,” Dr Dallimore says.

As well as the Western Australia and Federal grants, Argenica was awarded $350,000 from the McCusker Charitable Foundation and Jim Litis for further in-vivo studies to assess ARG-007 for Alzheimer’s disease.

Dr Dallimore says these resources are adequate for the time being, but running the phase II trial will cost $10 million to $15 million.

“We are looking at grants but anticipate having to do another raise,” Dr Dallimore says.

Since listing, Argenica shares have traded between 20 cents (early August 2021) and 94 cents (mid-January 2022).

On August 15, the company copped an ASX ‘speeding ticket’ in relation to a positive write-up in the Biomedicines journal on an ARG-007 mechanism of action. The article was published on July 25 but the company did not announce the fact until August 1. In its response, the company conceded it should have announced the existence of the article - co-authored by Prof Meloni - when it was published.

What the rivals are up to

Argenica’s nearest rival appears to be Canadian company Nono Inc, which has completed a second phase III trial for its neuro-protective drug.

Helpfully for Argenica, some of Nono’s trial sites were in Australia, which means these hospitals are au-fait with carrying out neuro-protective trials and could be reactivated.

On the ASX, Nyrada Inc is focused on cholesterol-lowering drugs but also has a compound aimed at traumatic brain injury and strokes.

Skin disorders house Clinuvel is evaluating the effect of its approved lead drug afamelanotide (Penumbra) in a wee 12-patient, phase II stroke study carried out at Melbourne’s Alfred Hospital.

Emvision (EMV) is developing a helmet-type device aimed for early stroke detection in ambulances. Micro-X is developing a lightweight stroke imaging tool for ambulances.

In 2016, Neuren dropped NNZ-2566 (an oral, modified, synthetic analog of Glypromate) for traumatic brain injury but finally had it approved by the FDA as trofinetide, also known as Acadia’s Daybue, for Rett syndrome. NNZ-2566 had originally been tested in an animal model for stroke.

Dr Boreham's diagnosis:

So far, Dr Dallimore she is happy with Argenica's progress and investors appear to share the sentiment.

"We are a little over two years post-IPO and we have managed to take the company from pre-clinical stage to a phase II trial," she says.

"We feel like we are kicking goals despite the challenge of the market."

A self-confessed whiz at assembling Ikea furniture, Dr Dallimore will be deploying these 'construction skills' to build Argenica into a commercial-stage venture.

Her skills with an Alley key aside, Dr Dallimore's experience with capital markets and US regulatory approval processes should help the company achieve its aim.

The prize is a stroke market expected to be worth some $US180 billion a year by 2030, even with the paucity of current treatments.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. His recent Ikea desk construction went swimmingly - until he found the end panel which actually should have been the first panel, and he had to start all over again.