Biotech Daily

Friday September 22, 2023

Daily news on ASX-listed biotechnology companies

*** ASX EVEN, BIOTECH DOWN: ALCIDION UP 5%; PHARMAXIS DOWN 10.5%**

*** DR BOREHAM'S CRUCIBLE: ARGENICA THERAPEUTICS**

*** NEXT SCIENCE PLANS RAISE $9.5m; TOTAL $21.5m**

*** QUEENSLAND UNI NANOPORE mRNA VACCINE, THERAPY ANALYTIC**

*** PAINCHEK: 'SCOTLAND STUDY - SOFTWARE REDUCES FALLS 75%'**

*** MALAYSIA APPROVES DIMERIX PHASE III DMX-200 FSGS KIDNEY TRIAL**

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*** PYC STARTS PHASE I VP-001 RP11 2nd COHORT**

*** ORTHOCELL LOSES DIRECTOR LARS LIDGREN; LESLIE WISE ON LEAVE**

*** REBECCA THOMPSON REPLACES MACH 7 DIRECTOR PHILIPPE HOUSSIAU**

MARKET REPORT

The Australian stock market edged up 0.05 percent on Friday September 22, 2023 with the ASX200 up 3.6 points to 7,068.8 points. Eleven of the Biotech Daily Top 40 stocks were up, 16 fell, eight traded unchanged and five were untraded.

Alcidion was the best, up 0.5 cents or 4.8 percent to 11 cents, with 1.8 million shares traded. Micro-X climbed 4.35 percent; Cyclopharm and Starpharma were up more than three percent; SDI and Volpara rose more than two percent; Avita, Immutep, Mesoblast and Orthocell were up more than one percent; with Clinuvel and Cochlear up by less than one percent.

Pharmaxis led the falls, down 0.4 cents or 10.5 percent to 3.4 cents, with 315,881 shares traded. Dimerix, Next Science and Opthea fell more than four percent; 4D Medical, Atomo, Emvision and Universal Biosensors lost more than three percent; Medical Developments and Neuren shed more than two percent; Antisense, CSL, Polynovo, Prescient and Pro Medicus were down one percent or more; with Nanosonics, Resmed and Telix down by less than one percent.

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 on from the IPO, the company raised $5.5 million in a placement in May 2022 and a $4 million placement in June this year.

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

The company has just over $9 million of cash.

As well as the Western Australia and Federal grants, the company 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 by Argenica.

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. Also, ASX listed, Micro-X is developing a lightweight stroke imaging tool for use in 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.

NEXT SCIENCE

Next Science says it has raised $8.5 million in an oversubscribed share plan and more than $1 million from a US offer, taking the total with the placement to $21.5 million.
Last month, Next Science said it had raised $12 million in a placement at 42 cents a share and hoped to raise $5 million in an Australian and New Zealand share plan and $1.5 million in a US share plan (BD: Aug 31, 2023).
At that time, the company said it would retire its $10 million Walker Group convertible notes, to be replaced by a share subscription commitment, pending shareholder approval.
Today, Next Science said it received $9.6 million in applications for the share purchase plan but scaled-back the number of applications to $8.5 million.
Next Science said the more than $1 million raised in the US offer included applications from industry participants and members of its management team including managing director Harry Hall, subject to shareholder approval.
The company said the funds would ensure it was “well capitaliZed with a strong balance sheet to deliver on its commercial objectives which include being profitable and cash flow positive by the end of 2024”.
Mr Hall said the funds ensured Next Science was “well placed to fund the promotion of Xperience research, resourcing to service the Healthtrust opportunity, expansion of the [durable medical equipment] sales force, expansion of a second fulfillment site for the [durable medical equipment] and deliver on our commercial objectives”.
Next Science fell two cents or 4.1 percent to 47 cents.

UNIVERSITY OF QUEENSLAND

The University of Queensland says it has developed a nanopore, a nano-sized hole, sequencing-based tool to analyse the quality of mRNA vaccines and therapies.
The University said researchers at its Australian Institute for Bioengineering and Nanotechnology had developed the approach using England’s Oxford Nanopore Technologies’ nanopore sequencing to simplify and ensure the quality of manufactured mRNA-based vaccines and therapeutics.
The University of Queensland said that under a research partnership with Oxford Nanopore, its researchers used nanopore-based sequencing technology to optimise performance and reduce the time needed to measure mRNA vaccine quality attributes.
The University said its Institute was “recognized as the biggest supplier of research-use mRNA in Australia, having bult more than 200 mRNA vaccines and therapies for academic, clinical and industry use”.
The University of Queensland said the research paper, titled ‘mRNA vaccine quality analysis using RNA sequencing’ was published in Nature Communications and the full article was available at https://www.nature.com/articles/s41467-023-41354-y.
University of Queensland mRNA technologies researcher Dr Helen Gunter said mRNA vaccines were currently “analyzed using a range of different methods that are time-consuming, complicated, costly, and often outdated”.
“Nanopore sequencing is the only sensing technology that can read native RNA in real time, making it an essential part of the toolkit supporting the development of mRNA-based therapeutics,” Dr Gunter said.
“By using Oxford Nanopore Technologies sequencing, we can directly analyse each individual mRNA vaccine molecule as it passes through a protein nanopore, providing a real-time measurement of the mRNA sequence identity and integrity,” Dr Gunter said.
“Ultimately, we anticipate the use of nanopore RNA sequencing methods will become central to the development and manufacture of mRNA drugs,” Dr Gunter said.

PAINCHEK

Painchek says Scotland has published the Care Inspectorate finding of a 75 percent reduction in falls following the use of the company's pain assessment software.

The Scottish Government document, titled 'My Health, My Care, My Home - healthcare framework for adults living in care homes: annual progress report September 2023' reported on an 831-pain assessment, first phase study of the Painchek facial recognition software for pain.

Published by Scotland's Cabinet Secretary for National Health Service Recovery, Health and Social Care, Michael Matheson, the document said that Painchek was a software application "that uses artificial intelligence technology and smart automation to assess pain in people who are unable to verbalize pain".

The Government document quoted the Scottish Care Inspectorate finding that following the 831 pain assessments using the Painchek software application "after 12 weeks, falls within the home had reduced by 75 percent and episodes of stress and distress had reduced by 42 percent".

The Scottish Government said that the phase one study had six participating care homes and the project team was looking at the impact and information from this stage.

In a separate document from the Dundee-based Scotland Care Inspectorate, titled 'Quality improvement plan 2023/24' the Inspectorate said the "phase two 'test of change' for the Painchek app … [would be tested] with up to 15 services".

The Inspectorate said that care services in Scotland "must be registered with the Care Inspectorate", it registered more than 11,000 care services in Scotland "and our inspectors visit every one".

The Inspectorate said that it used "a quality improvement approach, … [and] will test out new ways of working and approaches to addressing complex issues and work with partners across the health and care sector to influence policy and practice".

Yesterday, Painchek told an ASX 55.2 percent price query that it was not aware of any information that had not been announced, which, if known, could explain the recent trading in its securities (BD: Sep 21, 2023).

Today, Painchek chief executive officer Philip Daffas told Biotech Daily that while the company was aware of the Scottish Care inspectorate's progress earlier in September, the company was not made aware of the Scottish Government publication citing the pain assessments and 75 percent reduced falls until after the company had responded to yesterday's ASX price query.

Mr Daffas said that the results from the first phase of the Painchek paid pilot program in aged care were initially communicated in April 2023 and a second phase program at 15 care homes in Scotland had begun.

Mr Daffas said that the outcomes of the first phase pilot programs and the inclusion of Painchek as an initiative within the Scottish Care Inspectorate Quality Improvement Plan 2023/24 were disclosed to the ASX in the investor presentations lodged on September 14 and July 27, 2023.

Mr Daffas said the Scottish Care inspectorate published its quality improvement and innovation strategy earlier in September, referencing the 15 care homes that would participate in the phase two program.

"Following a successful phase two, we will move into phase three, potentially national rollout to more than 35,000 beds in care homes across Scotland and phase four could be a potential further rollout to other social care services," Mr Daffas said.

Painchek was up 0.2 cents or five percent to 4.2 cents with 1.5 million shares traded.

DIMERIX

Dimerix says Malaysia has approved its 286-patient, phase III trial of DMX-200 for the kidney disease focal segmental glomerulo-sclerosis (FSGS).

Last year, Dimerix said it had begun recruitment in the pivotal, multi-center, randomized, double-blind, placebo-controlled trial, titled 'Angiotensin II Type 1 Receptor & Chemokine Receptor 2 Targets for Inflammatory Nephrosis' (Action3),' to study the efficacy and safety of its DMX-200 in patients with focal segmental glomerulo-sclerosis (BD: May 31, 2022).

Last month, the company said a data safety monitoring board had recommended that the trial continue unchanged, with the first interim analysis expected to on or about March 15, 2024 (BD: Aug 8, 2023).

Today, Dimerix said that Malaysia's National Pharmaceutical Regulatory Agency had approved the trial and it intended to open sites in additional countries for part two of the trial, following the part one analysis.

Dimerix said the phase III study had two interim analysis points that were designed to capture evidence of proteinuria and kidney function during the trial, aimed at generating evidence to support accelerated marketing approval.

The company said it hoped the first analysis, or part one of the trial, would show the study was on-track for "a clinically and statistical meaningful improvement in proteinuria in patients on DMX-200 versus placebo" and that the trial could continue to part two.

Dimerix chief medical officer Dr Ash Soman said that "expanding the country access and number of sites is an important milestone as we plan progression of the study into part two in 2024, to enable patients globally to participate for our Action3, phase III study in [focal segmental glomerulo-sclerosis] patients".

"Malaysia is one of several key countries we are looking to expand into, and we look forward to reporting on those additional countries as we approach the outcome of our part one analysis in March 2024," Dr Soman said.

Dimerix said that the total focal segmental glomerulo-sclerosis (FSGS) market size was estimated to be "more than $US3 billion by 2032 driven by about 220,000 FSGS sufferers across the seven major markets and premium orphan drug pricing".

Dimerix fell 0.3 cents or 4.6 percent to 6.2 cents.

RECCE PHARMACEUTICALS

Recce says it has completed dosing the male and female cohorts in its phase I/II clinical trial of R327 at faster infusion rates for urinary tract infection and urosepsis.

In July, Recce said it had completed dosing its up-to 16 patient, phase I/II trial of R327 for urinary tract infection and urosepsis ahead of schedule (BD: Jul 28, 2023).

Last month, the company said it had approval to dose the next cohort of the trial with two faster infusion rates of 3,000mg (BD: Aug 28, 2023).

Today, Recce said R327 was shown to be "safe and well tolerated at a faster infusion rate of 30 minutes of 3,000mg, with an independent safety committee reviewing complete cohort dosing data, expected to recommend go ahead, with recruitment well underway".

Chief executive officer James Graham said the company was "pleased to see R327 administered at a faster infusion rate of 3,000mg, reinforcing R327's safety profile among male and female subjects".

"These results further support R327's potential as a treatment option, positioning it as a therapy for patients suffering from urinary tract infection and urosepsis, which is responsible for about 30 percent of all sepsis infections," Mr Graham said.

Recce was up 2.5 cents or 5.4 percent to 49 cents.

PYC THERAPEUTICS

PYC says it has safety review committee approval for a second three-patient cohort in its single-ascending dose phase I trial of VP-001 for retinitis pigmentosa type 11 (RP11).
In June, PYC said it had dosed the first of nine patients in its phase I study of VP-001 for the blinding eye disease retinitis pigmentosa type-11 (BD: Jun 30, 2023).
Today, PYC said the approval came after evaluation of the four-week safety and tolerability data from the first patient cohort and it would begin enrolling and dosing patients in the second cohort evaluating a dose of 10 micrograms of VP-001.
PYC said subject to committee approval it remained on track to complete dosing for patients in cohorts two and three before 2024.
The company said it expected to transition to a phase II, multi-dose study by July 2024, on successful completion of the phase I study.
PYC said on completing the dosing of the second cohort, another four-week safety review will occur before progressing to a third cohort.
PYC said on completing the dosing of cohort three a 24-week safety follow-up assessment would be conducted to assess treatment-emergent serious adverse events.
PYC was up 0.7 cents or 12.3 percent to 6.4 cents with 1.5 million shares traded.

ORTHOCELL

Orthocell says founding director Prof Lars Lidgren will retire, effective from September 30, 2023, and director Leslie Wise has taken a temporary leave of absence from today.
The company said following Prof Lidgren's resignation and Ms Wise's "temporary leave of absence … for personal reasons" the board had six directors.
Orthocell chair John Van Der Wielen thanked Prof Lidgren for "his valuable contributions … [and] pivotal role in the formation of the company, development of its products and setting it up for ongoing success".
Mr Wielen said the company "understand and support [Ms Wise's] need to take a short leave of absence at this time and look forward to her rejoining the Orthocell board".
Orthocell was up half a cent or 1.3 percent to 38 cents.

MACH 7 TECHNOLOGIES

Mach 7 says that Rebecca Thomson will replace non-executive director Philippe Houssiau, effective after the November 16, 2023 annual general meeting.
Mach 7 said Ms Thompson previously worked at JP Morgan and had been a consultant for Mach 7 until her recent appointment as CSR's head of investor relations.
The company said Ms Thompson held a Bachelor of Economics from the University of Sydney.
Mach 7 managing director Mike Lampron thanked Mr Houssiau "for his contribution and strategic guidance".
Mach 7 fell 1.5 cents or 2.05 percent to 71.5 cents.