



# Biotech Daily

Friday May 22, 2020

*Daily news on ASX-listed biotechnology companies*

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- \* **CARDIEX APPOINTS CFO, CO SEC JARROD WHITE DIRECTOR**

## MARKET REPORT

The Australian stock market fell 0.96 percent on Friday May 22, with the ASX200 down 53.4 points to 5,497.0 points. Eleven of the Biotech Daily Top 40 stocks were up, 22 fell, five traded unchanged and three were untraded.

Antisense was the best, up 1.9 cents or 39.6 percent to 6.7 cents with 69.5 million shares traded. Amplia, Impedimed and Patrys climbed more than seven percent; Kazia was up 5.3 percent; Optiscan improved 4.9 percent; Neuren and Resonance were both up three percent; Dimerix and Ellex rose two percent or more; with Pharmaxis up 1.1 percent.

Immutep led the falls, down one cent or 6.1 percent to 15.5 cents, with 2.9 million shares traded. Actinogen fell five percent; Compumedics, LBT, Medical Developments, Mesoblast, Polynovo and Volpara were down more than three percent; Avita, CSL, Genetic Signatures, Next Science, Opthea, Paradigm, Proteomics, Starpharma, Universal Biosensors and Uscom shed more than two percent; Cochlear, Orthocell, Resmed and Telix were down more than one percent; with Nanosonics and Pro Medicus down by less than one percent.

## DR BOREHAM'S CRUCIBLE: INVEX THERAPEUTICS

**By TIM BOREHAM**

**ASX code:** IXC

**Share price:** \$1.665

**Market cap:** \$91.6 million\*

**Shares on issue:** 55,000,001\* (of which 21,069,220 are in escrow until July 3, 2021)

\* pre today's \$26 million capital raising

**Chairman:** Dr Jason Loveridge

**Board:** Prof Alexandra Sinclair (executive director and chief scientific officer), David McAuliffe, Narelle Warren

**Financials (March quarter 2020):** revenue nil, net cash outflows \$416,000, cash \$10.42 million, quarters of available funding: 24

**Identifiable major shareholders:** (directors and management 20%), Dr Jason Loveridge 9.3%, Minderoo Pty Ltd (Forrest Family) 9.1%, JK Nominees Pty Ltd\*\* 7.3%, Tisia Nominees\*\* 7.3%, Oakton Nominees 7.3%, David McAuliffe 6.1%, University of Birmingham 3.6%.

\*\* Tisia and JK Nominees are linked with Forrest Capital

From the bulging file of Nasty Obscure Diseases we present idiopathic intracranial hypertension (IIH), a condition characterized by debilitating chronic daily headaches and in some cases severe vision impairment.

It's a poorly treated condition because as "idiopathic" implies, no-one has been able to glean the exact cause. But it results from undue pressure in the brain.

Happily, for sufferers, Invex is on the case with its quest to repurpose a diabetes drug to treat the condition, which largely affects younger obese women.

Classed an "orphan" disease in Europe and the US, IIH is rare but growing in line with the Western world's waistline.

"There are no approved drugs, patients have no option," says Invex chairman Dr Jason Loveridge.

However, this sorry state of affairs may change after the company this week reported positive phase II results – and today joined the conga line of biotechs raising funds with a \$26 million placement.

## **The exena-tide is high**

The drug in question is exenatide; a treatment for type-2 diabetes marketed by Astrazeneca under two variants.

Exenatide is a small peptide that binds to the GLP-1 receptor, in the brain's choroid plexus. One action is to decrease the fluid secretions, hence the diabetes application.

Astrazeneca markets the drug under the names of Byetta and Bydureon to treat diabetes, with combined annual sales of \$US659 million (\$A1.03 billion).

Invex has named its reformulated version Presendin - as in presenden' of the Unitin' States - and why not? We've heard stranger concocted drug names.

As with other 'repurposers', Invex claims the benefit of a safety track record from past use.

A key aspect to the Invex story is the company's "novel and patented" formulation of the drug, via subcutaneous delivery and able to transcend the so-called blood-brain-barrier that keeps foreign agents out of the noggin.

## **The experts behind Invex**

Invex was founded on the back of fundamental work done by its chief scientific officer and undisputed IIH guru, Prof Alex Sinclair of England's University of Birmingham.

Invex also acquired the relevant intellectual property from these halls of learning and listed on the ASX in July last year, after raising \$12 million at 40 cents apiece.

A neurology consultant and clinician scientist, Prof Sinclair has devoted years to understanding how pressure is regulated in the brain.

She authored the European treatment guidelines and is on the board of the International Headache Society, the prime organization devoted to mitigating the curse of cephalalgia (look it up).

A biotech investor and seasoned CEO, Dr Loveridge headed the listed German oncology outfit 4SC AG - an outfit with sound prospects but in need of a snazzy moniker such as Presendin.

He was also involved in big transactions, including the sale of Genable Technologies to the Nasdaq-listed Spark Therapeutics and Anaconda Pharma to Aviragen (also Nasdaq listed).

Dr Loveridge was also a director and interim chairman of Actinogen, pursuing another neurological indication with its Xanamem treatment for Alzheimer's disease.

He retired as a director from the Perth-based Resonance Health to take up the gig with 4SC AG.

## **IIH explained**

Nine out of 10 IIH sufferers are child bearing age women and are almost always obese.

“The disease can last for many years, even a lifetime,” Dr Loveridge says.

“Around 25 percent of patients with IIH can lose their vision completely, so it is a very serious disease.”

At least diagnosing the disease is relatively straightforward.

Typically, patients present to an emergency ward with a chronic headache, or to an eye doctor with impaired vision. Other symptoms are tinnitus (ringing in the ears) and back pain.

The IIH is diagnosed after other usual suspects such as a brain haemorrhage or meningitis have been discounted.

Ultimately the patients end up in the hands of neuro-ophthalmologists, the clinicians who Invex ultimately will target.

Dr Loveridge says sufferers at no immediate risk of vision loss are told to lose weight, which of course is easier said than done (especially in ‘iso’).

More urgent cases might involve a lumbar drain (a spinal injection), an optic nerve fenestration (cutting a hole) or a stent in the brain to reduce the pressure over a longer period.

“The problem with stents ... is they tend to get blocked and infected and half are removed pretty rapidly,” Dr Loveridge says.

Patients do have off-label access to a drug called acetazolamide, which was first used in the 1950s.

Marketed as Diamox and Diacarb, but also available as a generic, acetazolamide is used for glaucoma, epilepsy and altitude sickness.

But there’s only anecdotal evidence as to its efficacy with IIH and patients suffer side effects such as nausea.

## **Rare disease, big market**

Invex estimates that 93,000 people live with IIH but this number is probably understated because 40 percent of cases are believed to be undiagnosed.

The incidence of the ailment has risen 350 percent over the last decade.

The company estimates 40,000 new diagnosed cases annually, with about half of them treatable with Presendin.

“We can increase the number of patients seeking treatment if we can provide an effective treatment,” Dr Loveridge says.

Currently, about 90 percent of the diagnosed patients are prescribed the aforementioned acetazolamide.

Given the high rate of IIH hospitalization, the ailment is projected to cost the British health system 400 million quid (\$745 million) by 2023, with a similar burden in the US.

## **Clinical progress**

This week’s “statistically significant and clinically meaningful” trial results pave the way for Invox to launch a phase III trial aimed at US and European registration.

Enrolling 16 patients aged 18 to 60 years, the randomized, double-blinded, placebo-controlled study had a primary endpoint of change in intracranial pressure (ICP) in 2.5 hours, 24 hours and 12 weeks.

The changes were measured in real time, via a sensor in the brain. And conspiracy theorists can relax: it’s got nothing to do with Bill Gates, 5G, grassy knolls or the Covidsafe app.

The results showed an ICP reduction of 18.1 percent to 20.8 percent, relative to the hurdle of more than 10 percent.

On secondary endpoints, the trial showed a reduction in monthly headache days of 7.7 days (37 percent) and improved visual acuity at 12 weeks.

“For too long, no progress has been made to treat the devastating effects of raised ICP,” says Prof Sinclair, the trial’s lead investigator.

“This study provides the first clear evidence that a drug - exenatide - can significantly reduce ICP in IIH patients.”

The data will be used for a planned phase III registration trial aimed at winning US and European approval, slated to begin by July 2021.

This trial is envisaged to enrol 250 patients across multiple sites, on a randomized one to one basis (half of them take the placebo, that is).

The primary endpoints are a measure of either headache or visual function. Secondary endpoints are expected to include quality of life measures - designed to support pricing and reimbursement following regulatory clearance (if successful).

“One of the key advantages of being an orphan indication is we don’t need to run two phase III studies to get the drug approved,” Dr Loveridge says.

“We can run a single phase III based on the outcomes of the phase II study. This reduces [our] cost of getting to market and time to get to market very substantially.

“The other key advantage is seven years of marketing exclusivity in the US and 10 years in Europe.”

### **A bargain at double the price**

Invex’s early work on pricing revolves around the drug selling for \$1,500 a month, compared with \$600 to \$800 for the diabetic version.

Price gouging? Far from it, says Dr Loveridge.

“We have chosen a conservative multiple, given most repurposed orphan indication can result in pricing changes of up to 100-fold and on average 60-fold.

“Here we are talking about doubling of the price.”

On these metrics, Dr Loveridge estimates a market size \$400 million to \$1.5 billion.

### **Finances and performance**

At the time of writing, Invex shares were in trading halt ahead of the capital raising due to be announced today (Friday May 22, 2020).

Ahead of the raising Invex had cash of just over \$10 million - enough to complete the phase II analysis and the phase III “lead in activities”.

The extra \$26 million - raised at \$1.30 a share, a 13 percent discount to the previous closing price - should take care of the phase III stuff. The raise included a further \$5 million from Andrew Forrest’s Minderoo Group, under the new moniker of Tattarang.

Earlier, Dr Loveridge said he was just as keen as the next investor to avoid a dilutive share raising – and by definition any equity raising is dilutive.

“I’m also keen to move things forward as quickly as possible because at the end of the day that’s how value is created,” he says.

“If we get good phase II data at some point it would be sensible ... to get the company right through to market.”

Unusually Invex acquired - rather than licenced - the relevant intellectual property from the University of Birmingham, so no royalties or milestones are payable.

“It is the company’s alone to exploit,” Dr Loveridge says.

Invex shares lost more than half their value during the initial Covid-19 rout, plumbing a record low of 54 cents. The shares jumped as much as 37 percent to \$2.05 after emerging from the trading halt.

A notable inclusion on the register is Minderoo, iron ore magnate Andrew Forrest’s family company. The unrelated Forrest Capital was lead manager for the company’s initial public offer.

### **Dr Boreham’s diagnosis:**

At the risk of sounding glib, Invex will either get there or it won’t.

Apart from an expanded indication, there’s no plan B but the company is no orphan in that sense.

At least it’s got the funds to live the dream.

If the clinical news remains positive, there’s a good chance Invex will end up in someone else’s hands (bearing in mind Dr Loveridge’s experience in wheeling and dealing companies).

“Our goal for Invex is to develop exenatide for IIH and then look at least one other indication,” Dr Loveridge says.

“We would then look for a partner or potentially a buyer of the company who can commercialize the drug over the longer term.”

When it comes to comparative companies, Invex’s own material avers to the ASX-listed Paradigm Biopharmaceuticals and Clinuvel.

Paradigm also repurposes a blood-thinning drug for osteoarthritis pain. Paradigm is also phase II stage and has a \$500 million-plus market valuation.

Clinuvel had orphan drug status and has achieved the holy grail of US approval for its treatment for a rare sunlight intolerance disorder. The company is now valued at more than \$1 billion.

“If we can develop an effective drug, there will be large demand not only from clinicians but the patient groups themselves,” Dr Loveridge says.

***Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. While his brain occasionally hurts, he attributes this to lifestyle - rather than unknown - reasons***

## ANTISENSE THERAPEUTICS

Antisense says its nine-patient trial of ATL1102 for Duchenne muscular dystrophy met its safety primary endpoint and indicated some efficacy, supporting a phase IIb trial.

Antisense said the non-ambulant boys, treated at Melbourne's Royal Children's Hospital, received 25mg of ATL1102 once weekly by sub-cutaneous injection for 24 weeks.

The company said that no serious adverse events were reported with the most common adverse events, injections site erythema and skin discoloration which were mild and either resolved or close to resolution at the end of the monitoring period.

Last year, Antisense said that function capacity and upper limb strength was evaluated through the performance of upper limb test (PUL2.0) and the Myogrip and Myopinch tests and the PUL2.0 data showed that seven of the nine participants showed either increases or no change in their PUL2.0 scores from baseline "suggestive of an overall improvement with a positive mean change of 0.9 in this key parameter" (BD: Dec 17, 2019).

The company said at that time the Myogrip and Myopinch assessments showed "a distinct improvement in muscle strength based on the observed mean changes from baseline".

Today, Antisense said the results "confirmed the drug's positive effects on the secondary trial endpoints that assessed the drug's activity and efficacy including measuring the effects on immune cell numbers in the blood and measuring the participants' functional capacity as evaluated via Performance of Upper Limb Test, grip and pinch strength and distal mobility".

The company said that magnetic resonance imaging (MRI) assessment of the upper limb muscles dystrophy showed the drug's apparent beneficial effects in stabilizing the fat fraction percentage within the muscles of the forearm, with increased fat levels a "key marker of disease progression in non-ambulant [Duchenne muscular dystrophy] boys. Antisense said that an increase or maintenance of functional muscle mass, was "both outstanding and unexpected for a drug treating the inflammation and not the muscle dystrophin loss".

The company said that European Medicines Agency scientific advice was due "mid-year" and was the next milestone for submission of an application for a phase IIb trial in Europe and UK, and it was in the process of preparing submissions for orphan drug designation for ATL1102 for Duchenne muscular dystrophy in the US and the EU.

Antisense was up 1.9 cents or 39.6 percent to 6.7 cents with 69.5 million shares traded.

## INVEX THERAPEUTICS

Invex says it has raised \$26.2 million through a placement to institutional, professional and sophisticated investors at \$1.30 a share.

Invex said the placement was in two tranches, with tranche one raising \$16.25 million and tranche two raising \$9.95 million.

The company said it had received \$10.5 million in cornerstone commitments from existing investors, including \$5 million from Tattarang, formerly Minderoo Group and from Dr Jason Loveridge, who participated in tranche two of the placement.

The company said the issue price was at a four percent discount to the 15-day volume weighted average price to May 15, 2020 and a 13 percent discount to the closing price before its May 18, 2020 trading halt.

Invex said the funds would be used to complete a phase III study of Presendin, for the manufacture and supply for trials, and to commence a phase II study by July 2021.

The company said Bell Potter Securities was lead manager and book runner for the placement and Forrest Capital and CPS Securities were co-managers.

Invex climbed 17 cents or 11.4 percent to \$1.665 with 1.3 million shares traded.



## VICTORIA GOVERNMENT

The Victoria Government says applications have opened for the Victoria Prize for Science and Innovation and the Victoria Fellowships, worth \$50,000 each.

A media release from the Victorian Endowment for Science, Knowledge and Innovation (Veski), on behalf of the Victoria Government, said the prize would allow leading Victorian scientific researchers to continue their work, especially in helping to stop the spread of Covid-19.

The Victoria Government said it was offering 12 Victoria Fellowships of up to \$18,000 each “to assist early career scientists to undertake a short-term study mission overseas to develop and foster their networks and collaborations with international centres of science research”.

The Government said the Fellowship travel period had been extended to between January 1, 2021 and March 31, 2022 due to Covid-19 disruptions.

To nominate for the Victoria Prize or for information on how to apply for a Victoria Fellowship, go to: [https://veski.org.au/VicPrizeFellow\\_howtogetstarted](https://veski.org.au/VicPrizeFellow_howtogetstarted).

## BOTANIX PHARMACEUTICALS

Botanix says it will vote to issue chairman Vince Ippolito and directors Dr Michael Thurn, Dr Bill Bosch and Dr Stewart Washer a total of 38,907,922 “inventive” options.

Botanix said the extraordinary general meeting would vote to issue 17,994,914 options to Mr Ippolito, 11,186,028 options to Dr Thurn, and 4,863,490 options each to Dr Bosch and Dr Washer, exercisable at 5.51 cents each within two years.

The company said the options were priced at a 34 percent premium to the seven-day volume weighed average price to April 15, 2020 and were to acknowledge “the additional workload taken on by each of the participating directors and the reduction in their cash-based compensation in order to retain key resources”.

Last year, Botanix said its 368-patient phase II trial of BTX1503 for acne did not meet its inflammatory lesion reduction primary endpoint and this year, said its 200-patient phase II trial of BTX1204 for atopic dermatitis, or eczema, did not meet its primary or secondary endpoints (BD: Oct 23, 2019, Mar 25, 2020).

Today, the company said it would also vote to amend its constitution.

The meeting will be held at the Duxton Hotel, 1 St Georges Terrace, Perth, on June 24, 2020 at 9am (AWST).

Botanix was up 0.2 cents or 4.65 percent to 4.5 cents with 6.5 million shares traded.

## CELLMID

Cellmid says its extraordinary general meeting passed all resolutions but with 13.33 percent dissent against the issue of broker options.

Cellmid said 2,986,770 votes (13.33%) opposed the issue of 1,000,000 broker options to Evolution Capital Advisors, with 19,425,407 votes (86.67%) in favor.

The company said shareholders approved the issue of 227,273 shares to director Maria Halasz, 4,318,182 shares to director Dennis Eck and ratified the prior issue of 14,489,529 placement shares, with more than 88 percent of votes in favor.

According to Cellmid’s most recent Appendix 2A application for quotation of securities, the company had 120,701,411 shares on issue, meaning the 2,986,770 votes against the issue of broker shares amounted to 2.47 percent of the company, not sufficient to requisition extraordinary general meetings.

Cellmid was in a voluntary suspension and last traded at 18.5 cents.

### IMPEDIMED

Impedimed has told the ASX that it is not aware of any information it has not announced which, if known, could explain recent trading in its securities.

The ASX said the company's share price rose 36.6 percent from 4.1 cents to 5.6 cents yesterday May 21, 2020 and noted a significant increase in the trading volume.

Impedimed said that "each of the analysts that cover the company, Canaccord Genuity Australia, Wilsons HTM Equities Research and Morgans Financial, have recent price targets in excess of currently traded prices".

Impedimed climbed a further 0.4 cents or seven percent to 6.1 cents with 22.1 million shares traded.

### G (GEVA) MEDICAL INNOVATIONS

G Medical says it has a \$US880,000 (\$A1,345,844) loan from the Bank of America under the US Paycheck Protection Program for Covid-19 relief.

G Medical said it would be eligible for loan forgiveness for funds used for payroll, interest on mortgages, rent, leases and utilities.

G Medical fell 0.1 cents or 1.3 percent to 7.6 cents with 5.7 million shares traded.

### CARDIEX

The Sydney-based Paul Cozzi says he has increased his substantial shareholding in Cardiex from 97,615,392 shares (12.96%) to 109,515,392 shares (14.54%).

Mr Cozzi said he bought and sold shares between January 31 and May 7, 2020 for a total acquisition of 11,900,000 shares for \$250,329 or 2.1 cents a share.

Cardiex was up 0.2 cents or 9.1 percent to 2.4 cents with 1.6 million shares traded.

### OPYL

Opyl has requested a voluntary suspension following the trading halt requested on Wednesday pending "the commercial details of two contracts" (BD: May 20, 2020).

The company said the suspension would last until May 26, 2020 or until the release of an earlier announcement

Opyl last traded at 10 cents.

### PROBIOTEC

Probiotec says it has appointed Jonathan Wenig as a non-executive director effective from June 1, 2020 and Sandy Beard as chairman from July 1, 2020.

Last month, Probiotec said that current chairman Geoff Pearce would retire effective from June 30, 2020 due to "the additional workload arising from the current and unprecedented business landscape" (BD: Apr 9, 2020).

Today, the company said Mr Wenig would join the board on a casual vacancy and it would continue to search for an additional non-executive director.

Probiotec said Mr Wenig was a corporate and mergers and acquisitions lawyer and a partner at law firm Arnold Block Leibler.

Probiotec was up two cents or 1.1 percent to \$1.87.

## CARDIEX

Cardiex says it has appointed chief financial officer and company secretary Jarrod White as a director.

Cardiex said Mr White had been with the company since early 2018.