Biotech Daily

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Daily news on ASX-listed biotechnology companies

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 Invex 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 monkier 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