Biotech Daily

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Daily news on ASX-listed biotechnology companies

Dr Boreham's Crucible: Pharmaxis

By TIM BOREHAM

ASX code: PXS

Share price: 23 cents

Shares on issue: 394,315,798

Market cap: $90.7 million

Chief executive officer: Gary Phillips

Board: Malcolm McComas (chairman), Gary Phillips, William Delaat, Dr Kathleen Metters, Edward Rayner

Financials (March quarter): receipts $1.4 million, cash burn $6.1 million, cash of $35.1 million, estimated current quarter outflows $7.9 million

Major shareholders: BVF Partners (Biotech Value Fund) 20.6%, Arix Bioscience 11.1%, Australian Ethical 7.6%, D&A Income Ltd 6.9%, Allan Gray Australia 5.2%.

Pharmaxis chief Gary Phillips is keen to differentiate the drug developer from his local peers, noting the company has several potential paths to glory rather than a singular approach.

"A lot of biotechs in Australia are a one-product play, they will either get there or bust," he says. "We have more than one asset coming up to potential valuation points."

Long standing (and long suffering) Pharmaxis holders will be pleased to hear that one of these inflection points is within tantalizing reach.

In early May, the US Food and Drug Administration's pulmonary-allergy drugs advisory committee (Padac) recommended Pharmaxis's Bronchitol should be used to treat adult cystic fibrosis patients in the US.

Bronchitol works by reducing the mucus build up in the lungs that progressively restrict breathing.

After eight hours' deliberation, Padac's 16 esteemed members voted nine to seven in favor, on the question of whether the benefits of the mannitol (dry powder) outweighed the risks.

Ok, it wasn't an overwhelming endorsement but as Scott Morrison would attest, a majority's a majority.

In a complete response letter - the FDA's dictate on what needs to be done to win approval - the authority requested changes to Bronchitol's packaging so that the administration instructions were clearer.

"The letter doesn't ask us to do any more clinical work, just make sure the packaging is up to scratch," Mr Phillips says.

Pharmaxis's distribution partner Chiesi expects to respond to the FDA letter by the end of this year, with approval expected by April 2020.

The likely approval marks the end of a six-year wait for Pharmaxis, given Padac nixed approval in 2013.

Students of the company will recall that in 2011 the European regulatory bigwigs said they would reject the company's marketing application, but in 2012 Pharmaxis won on appeal. In 2015 Chiesi kindly expended $35 million on a further 423-patient US-required study.

"We are confident because the product has been on the market in Australia and Europe for seven years and treated thousands of patients with little by way of adverse events reported," Mr Phillips says.

If Bronchitol is approved, Pharmaxis will receive a $US10 million ($14 million) milestone payment on commercial launch, as well as mid to high teen percentage royalties.

Mr Phillips estimates Bronchitol's peak US market sales at $US50 million a year.

Inflammation is the work of the Devil and can lead to scarring and fibrosis, which is at the core of numerous ailments.

The second leg of the Pharmaxis story

In 2015, Ingelheim, Germany-based drug giant Boehringer Ingelheim acquired the rights to the company's AOC3 inhibitor program, exotically titled BI 1467335.

BI 146 … whatever … is being targeted for the liver disease non-alcoholic steatohepatitis (NASH) and diabetic retinopathy. Characterized by leaky blood vessels, diabetic retinopathy is a leading cause of blindness in type two diabetic patients.

“It’s a very high unmet need,” Mr Phillips says.

Boehringer Ingelheim, which is responsible for the clinical program, is expected to announce the initial results of a 114-patient phase IIa NASH trial in September or October this year.

Mr Phillips notes a number of potential NASH treatments have flopped, highlighting the need for new mechanisms of action. “It was pleasing to see the prominence that this program was given at Boehringer Ingelheim’s annual research update,” he says.

Pharmaxis pocketed a handy $42 million in milestones from the Boehringer Ingelheim transaction in 2017-’18. Since acquiring the program in 2015, Boehringer Ingelheim has paid a total of $83 million in milestones.

Should either program move to phase III, Pharmaxis trousers a further EUR35 million for the first indication and EUR25 million for the second (a total of 95 million Aussie pesos). Then there’s another $200 million or so of potential drug and pricing approval milestones.

All up, Pharmaxis is eligible for up to $625 million more if both the NASH and eye indications are approved.

Wait - there’s more

Management is just as excited - or almost - about its third program based on inhibiting the enzyme LOXL2, which is linked with fostering fibrosis. Current targets are NASH and the fatal lung disease idiopathic pulmonary fibrosis.

Known to its friends as lysyl oxidase-like 2, LOXL2 promotes the linking of collagen fibres, rather like the fibreglass mesh repair on a boat for nautical types.

Manifested as scarring, this process is desirable in the case of wound repair, but not so much in the case of lungs and livers which are meant to be soft and squishy rather than hard and fibrotic.

Pharmaxis’s boffins have developed two molecules that inhibit the enzyme. Both have been through the usual phase I safety stuff.

“The Pharmaxis LOXL2 program is one of the very few truly anti-fibrotic mechanisms in clinical development,” Mr Phillips says.
Initially Pharmaxis partnered with Synairgen, a drug discovery company linked to the University of Southampton.

In late 2017, Pharmaxis in effect bought back the program for a payment of GBP5million ($9 million) although Synairgen remains entitled to 17 percent of any milestones.

Separately, Pharmaxis is carrying out separate programs for ‘pan Lox’, which covers the broader family of LOX1 to LOX4 inhibitors.

The program targets pancreatic cancer and myelofibrosis (which stops the bone marrow from producing cells). In the case of pancreatic cancer, fibrosis prevents effective oncology drug delivery which is probably why it’s one of the most fatal cancers.

Phase I safety trials have been carried out on healthy volunteers - and none of them died. “There’s good evidence the drug could be useful for both indications,” Mr Phillips says.

Don’t forget the Aridol

We shouldn’t forget Pharmaxis’s original product Aridol, an asthma diagnosis tool relaunched by US distributor Methapharm last December.

There’s a bit of history here because the FDA fully approved Aridol in 2011, before Pharmaxis moved its Sydney manufacturing facility, but had to end US Aridol sales temporarily as uneconomic. The new factory in Frenchs Forest is fully approved and it’s game on.

Financials and performance

Pharmaxis managed a flat $1.3 million of Bronchitol sales in the March quarter, $239,000 from Australia, $936,000 from Western Europe and $239,000 from Russia and Eastern Europe.

Nostrovia! [Or formally: Na Zdorovie - Russian Ed]

The company also generated $634,000 of Aridol sales, compared with $421,000 previously.

Overall, Pharmaxis lost $5.7 million, reducing the previous deficit of $8.1 million.

Pharmaxis has cash of $35.1 million, having raised $24 million in a two-tranche placement last year that delivered UK healthcare investment fund Arix Inc to the register.

The company cites assets of $52 million (including cash). But on the liability side it has a $23.4 million financing agreement, repayable only as a percentage of US and European Bronchitol revenue

The company’s overall results have been dragged down by the loss-making status of its manufacturing operation at its Frenchs Forest facility. The factory lost $3 million in the nine months to March 2019, with a likely $4 million full-year loss.

But this is likely to change because the underused facility has big orders for Bronchitol from European customers that just missed the 2018-19 financial year.

Dr Boreham's diagnosis:

Despite the likely US approval, Mr Phillips says the most promising blue sky comes from the drug discovery program, "which is a little bit out of sight".

Pharmaxis has had its fair share of woes since listing in 2006 at 50 cents a share, having raised $25 million. A secondary listing on the Nasdaq was abandoned in 2009 for cost reasons.

The company certainly looks healthier than when Mr Phillips took the top job in March 2013, and oversaw the retrenchment of 100 of the company's 160 workers in an urgent cost cutting drive.

Since then, the company's focus shifted from fully developing drugs in favor of partnering the big stuff and dabbling in the early stage development programs.

The clinical targets of Pharmaxis and its partners are all big dollar prospects, but NASH (which affects obese people in particular) is forecast to be a $US35 billion a year market by 2025.

We're also wary of seeing more NASH repeats - not a reference to the Korean War soapie but to the danger of yet another trial flop for the indication.

When we last covered Pharmaxis in April 2017, the stock traded at 27 cents and a market cap of $88 million. So, despite the tangible process on several fronts, the stock is treading water, having assaulted the 33 cents level in late July last year.

As chairman Malcolm McComas told last November's AGM: "The Pharmaxis share price does not reflect the value created over the years."

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. He doesn't mind NASH, er MASH repeats, but only when he has exhausted all 180 Seinfeld episodes – again.