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Daily news on ASX-listed biotechnology companies

Dr Boreham's Crucible: Pharmaxis

By TIM BOREHAM

ASX code: PXS

Share price: 8.7 cents

Shares on issue: 452,249,264

Market cap: $39.3 million

Chief executive officer: Gary Phillips

Board: Malcolm McComas (chairman), Gary Phillips, William Delaat, Dr Kathleen Metters, Neil Graham

Financials (December half 2020): revenue from sale of goods $3.086m (down 5%), total revenue $13.69m (up 240%), net profit $46,000 (previous $10.32m loss), cash of $18.24m (up 23%)

Major shareholders: BVF Partners (Biotech Value Fund) 19%, Karst Peak Capital 8.9%, D & A Income 7%

The inflammatory diseases company this month welcomed a familiar biotech name to the register: Karst Peak Capital.

The Hong Kong and Sydney based 'contrarian' fund manager is also a major holder in Neuren and Cyclopharm, and earlier made a motzah out of Avita Medical and Viralytics.

After approaching Pharmaxis, Karst Peak committed $3.3 million to the $4.4 million placement at eight cents a share, a slight premium on the prevailing price.

Pharmaxis chief Gary Phillips says the fund took its due diligence seriously, having spoken to six of the world's top 10 experts in myelofibrosis, one of the company's key targets (see below).

In casting such a strong vote of faith in Pharmaxis, Karst Peak is cognizant of what Mr Phillips dubs the "pitiful" valuation of the company.

In a separate deal, Pharmaxis pockets $2 million upfront in a Russian distributor deal with a Turkish party we will know only as GEN (only because we don't have Turkish characters on our keyboard).

Given Pharmaxis now has more than $20 million in the bank, the market, in effect, values the company's approved drug Bronchitol and its two key clinical programs at a mere $18 million.

"We have had our challenges, but that's what makes us an opportunity for investors," Mr Phillips says.

Unsung hero of drug development

Pharmaxis has always stressed the company's multi-pronged approach to drug development, on the grounds that one failed program won't torpedo the company.

In hindsight, that strategy was wise, as shown by the decision of German drug giant Boehringer Ingelheim to walk away from its liver disease and diabetic retinopathy partnerships with Pharmaxis.

Mr Phillips says Pharmaxis has been "remarkably successful" in taking no fewer than five drugs from invention to at least phase I trials.

"We have done that because we are global leaders in amine oxidase chemistry which is the backbone of several enzymes involved in inflammation and fibrosis," he says.

Mr Phillips has more than 30 years' experience in big pharma, including two senior roles at Novartis.

The Bronchitol story

Pharmaxis is one of a handful of Australian biotechs to win US Food and Drug Administration (FDA) approval for Bronchitol, its home-grown therapy for cystic fibrosis.

But it was not an easy journey, with the agency in 2013 ordering the company to do a third phase III study.

At that stage, management sagely concluded that someone else should bear the costs and the risks, striking a global distribution deal with the Italian based Chiesi.

An inhaled dry mannitol powder, Bronchitol is produced at the company's Frenchs Forest facility in northern Sydney.

Pharmaxis also sells Aridol, an asthma diagnosis tool that is relatively small beer to Bronchitol.

Bronchitol has also been approved by authorities in Europe, Australia, Brazil, South Korea and Russia as a treatment for cystic fibrosis.

The most common inherited disease, cystic fibrosis results in the build-up of dry mucus in the lungs, which inhibits breathing and causes infection. While life expectancy is improving, sufferers can only expect to live to their forties.

It's not as if there aren't other treatments, which range from low tech (physio), saline solutions (inhaled via nebulizer) and pulmozone (a drug that breaks up the protein strains in the mucus and makes it less viscous).

But one advantage of Bronchitol is that it is portable and does not require a nebulizer.

Company 'lox' in myelofibrosis as a key target

On the drug discovery side Pharmaxis is targeting myelofibrosis, a rare bone cancer suffered by one in 500,000 citizens.

Myelofibrosis is a scarring of the bone marrow that interrupts the normal production of white and red blood cells and platelets.

This leads to fatigue, reduced immunity, clotting and bruising and bleeding.

Myelofibrosis sufferers typically are aged 50 to 80 years and can expect to live an average of only five years. About 10 percent will go on to develop leukemia.

"Myelofibrosis is a very attractive area with very high valuations," Mr Philips says.

Currently, myelofibrosis is treated by a class of drugs called JAK (Janus kinase) inhibitors that provide symptomatic relief but do not ameliorate the disease. They also cause unpleasant side effects.

Pharmaxis's proposed therapy is a compound calls PXS-5505, which aims to inhibit pan-lysyl oxidase (LOX), an enzyme closely implicated in inflammation and fibrosis.

PXS-5505 last year was granted 'orphan drug'; designation by the US Food and Drug Administration.

"The mode of action in our drug is different to anything on the market or in the clinic," Mr Phillips says.

“It targets the matrix [inflammation] formation in the bone marrow and has disease modifying potential.”

In February, Pharmaxis recruited the first patient for its next stage of clinical development, a phase Ic/IIa trial looking at both the safety and efficacy of the molecule.

The trial is being carried out at sites in Australia and South Korea - two countries relatively unscathed by Covid-19.

The dose escalation trial aims to recruit up to 18 patients in its initial stage. A further dose expansion stage will enrol up to 24 patients.

Work to date consists of a six-month safety study on healthy volunteers, as well as preclinical animal modelling that showed increased blood production and reduced spleen size.

(When the bone marrow is damaged, the spleen tries to take over production and is enlarged, causing fevers and bone pain).

First results are expected in the second half of 2021, with full results due a year later.

Success will be measured by reduction in bone marrow fibrosis as measured by a biopsy, reduced anaemia and lessened spleen size.

“They are not soft endpoints,” Mr Phillips says. “It’s not a half-hearted study that we are looking to fudge.”

Anything else?

The company is also targeting burns-related scarring, in league with Perth burns legend Prof Fiona Wood and other esteemed researchers at the Fiona Stanley Hospital.

It’s hoped that Pharmaxis’s compound PXS-6302, which it discovered in its own labs, will suppress the enzymes responsible for such scarring.

Following positive animal results, the plan is to test the topical (cream) treatment on healthy volunteers.

To date, Mr Phillips says, scarring has been measured by aesthetics more than anything.

“Scarring is subjective,” he says. “We are attempting to bring some science into this.”

In collaboration with various parties, the company is also undertaking earlier stage work on variant LOX inhibitors for other hard-to-treat cancers.

These include other blood cancers, liver carcinoma, pancreatic cancer and glioblastoma (brain cancer).

Bye, bye to B.I.

In 2015, Germany-based drug giant Boehringer Ingelheim acquired the rights to the company's so-called AOC3 inhibitor program, which was targeted for the liver disease non-alcoholic steatohepatitis (NASH) and diabetic retinopathy.

Boehringer handed back the NASH program in December 2019 and then returned the eye program in September last year.

"I can understand why Boehringer didn't want to go ahead with our drug." Mr Phillips says. "It worked in NASH and met primary endpoints, but there was an issue in terms of potential interaction with other drugs."

The program potentially was worth up to $625 million to Pharmaxis. But as management likes to remind anyone who will listen, the company did pocket $83 million in milestone payments before Boehringer pulled the pin.

Finances and performance

Pharmaxis achieved a financial breakthrough in the 2019-'20 year, when the mannitol business became cash flow positive to the tune of $2.1 million having burned through $4 million the previous year.

In the December (first) half of the 2020-'21 year, the company recorded a slender $46,000 profit on Bronchitol sales of just over $3 million.

The Russian deal not only injects $2 million into the company, but removes $1 million of costs because GEN bears responsibilities including regulatory and compliance costs.

So, if you want to know about Russian progress from now on, do what (Prime Minister) Scott Morrison does and ask GEN.

Under the Chiesi compact, the Italian company bears all clinical and most regulatory costs. Pharmaxis is entitled to double digit royalties and a manufacturing margin and is pocketing a $US10 million ($A13 million) milestone triggered by FDA approval.

With Bronchitol, the US accounts for about 30,000 to 35,000 of the global market of 80,000 patients, which reflects not just the number of patients per se, but the higher reimbursement available. Chiesi expected to post first sales in the March quarter.

"[FDA approval] more than doubles the patient opportunity and there is very attractive pricing in the US," Mr Phillips says. "We expect a significant price premium on the rest of the world."

All up, Pharmaxis expects to earn 20 percent of the value of Chiesi's sales, which equates to $US50 million over five years based on Chiesi's forecast of peak Bronchitol sales of $US50 million annually.

Mr Phillips notes that costs at Frenchs Forest are largely fixed and the company could double or triple output with the only extra cost being consumables such as cartons and foils.

Over the last 12 months Pharmaxis shares have perambulated between seven cents (June 23, 2020) and 12 cents (August 19, 2020). Once upon a time they were worth as much as $4.18 (November 2007).

Dr Boreham's diagnosis:

Pharmaxis has had its fair share of woes since listing in 2006 at 50 cents a share to raise $25 million (a secondary listing on the Nasdaq was abandoned in 2009 for cost reasons).

When we last applied the metaphorical Bunsen burner to Pharmaxis in July 2019, the shares traded at 23 cents and the company was valued at $90 million.

With a current $38 million market cap, arguably the company is suffering the baffling market syndrome that values blue-sky drug developers (or resource explorers) more highly than the established stocks.

"I think the market is confused that we have this manufacturing business on the side [mannitol] that is also producing cash," Mr Phillips says.

A drug developer producing cash? That's indeed baffling.

Mr Phillips urges investors to hold tight for the fruits of the company's prolonged labors: "The company is at a really interesting stage for potential investors with a lot of news flow coming."

Indeed! Just as Karst Peak. Or GEN.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. He briefly owned a keyboard with Turkish characters, having ordered an offshore-sourced Apple laptop from a well-known online electronics retailer. Buyer beware!