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Daily news on ASX-listed biotechnology companies

Dr Boreham's Crucible: Syntara

(Formerly Pharmaxis)

By TIM BOREHAM

ASX code: SNT

Share price: 7.8 cents; **Shares on issue:** 1,623,327,805; **Market cap:** $126.6 million

Chief executive officer: Gary Phillips

Board: Dr Kathleen Metters (chair), Mr Phillips, Dr Simon Green, Hashan DeSilva

Financials (December half 2024): revenue nil, loss of $2.7 million (previous deficit $5.95 million), cash of $18.1 million (up 217%).

Major shareholders: D & A Income 18%, Platinum Investment Management 14%, BVF Partners 6%, HB Technology 3.5%

While the myelofibrosis drug landscape has become more crowded since Syntara (then Pharmaxis) decided to focus on that disease in 2020, CEO Gary Phillips has no qualms about the company's 'strategy about-face' that turned the rare blood disease into its lead program.

Syntara is all about amine oxidase chemistry, the basis of several enzymes involved in inflammation and fibrosis.

Pharmaxis's reason for being was its approved Bronchitol treatment for cystic fibrosis, but in 2023 the company sold the program and slashed its cost base.

“The ramifications of the change rumbles on,” Mr Phillips says. “We reduced our staff from 65 to 25 and saved $14 million in annual expenditure.

“Once we realized the underlying [Bronchitol] sales in the US weren’t going to materially change, it was a no-brainer to get rid of it. It was a relief just to be able to focus on that lead program and it makes us easier to understand as well.”

Now, new myelofibrosis drugs have entered the market, notably the home-grown Glaxosmithkline-Cytopia Ojjaara. Two more are at phase III.

But Mr Phillips says the Devil’s in the detail and these ‘rival’ drugs may help Syntara’s efforts to bring its lead drug to market. Details below.

Bronchitol took its toll

In its Pharmaxis days, the company’s business revolved around Bronchitol, an inhaled dry mannitol powder for cystic fibrosis.

While European, Australian, Brazilian and even Russian health regulators were quick to the party, the US Food and Drug Administration held out and did not approve the therapy until 2020.

By then, the pandemic was upon us and the treatment landscape had moved on anyway.

In October 2023, Pharmaxis sold its loss-making Bronchitol business to Arna Pharma for nil consideration (but with adjustments, see below). Pharmaxis also closed its Frenchs Forest headquarters in Sydney and moved to smaller digs.

Luckily, Pharmaxis was partnered with the Italian-based Chiesi for Bronchitol, with Chiesi bearing all clinical - and most regulatory - costs of developing Bronchitol.

Pharmaxis listed on the ASX in 2006, raising $25 million at 50 cents a share. A secondary listing on the Nasdaq was abandoned in 2009 for cost reasons.

In 2019, long-time German partner Boehringer Ingelheim handed back the rights to a non-mannitol drug PXS4728A for the liver disease non-alcoholic steato-hepatitis (NASH or fatty liver disease), having generated $83 million of milestone payments for Pharmaxis along the way.

Syntara’s ‘gelati’ flavors

The company’s compound comes in three ‘flavors’: SNT-4728 (for Parkinson’s disease), SNT-6302 (scarring) and SNT-5505 (myelofibrosis and hepatocellular carcinomas).

The target is pan-lysyl oxidase (LOX), an enzyme closely implicated in inflammation and fibrosis.

Investors are focused on Syntara's current phase I/IIa trial for the rare blood cancer, myelofibrosis, a scarring of the bone marrow that interrupts the normal production of white and red blood cells and platelets.

Globally there are about half a million sufferers, generally aged between 50 and 80 with an average five-year life expectancy.

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

Granted orphan drug status by the FDA in in 2020, SNT-5505 targets the matrix [inflammation] formation in the bone marrow and thus modifies the disease.

"Our drug does something about the underlying disease, so we have quite a different approach," Mr Phillips says.

My oh my! Decent trial results

On December 12, 2024, Syntara reported the first interim results from its 16-patient, phase I/IIa myelofibrosis trial, showing "excellent" tolerability and improvements in symptoms, including spleen volume reduction (a good thing).

The open-label study, at 19 sites in Australia, South Korea, Taiwan and the US, combined SNT-5505 with ruxolitinib (branded Jakafi), and enrolled 16 patients with intermediate or high-risk myelofibrosis, with average ruxolitinib use of 3.2 years.

At 12 weeks of treatment, 46 percent of the evaluable patients (six of 13) had achieved a 50 percent improvement in their total symptom score, a standard primary endpoint for myelofibrosis trials.

This improved to 80 percent (four of five patients) who reached 38 weeks of treatment. Also, 30 percent of patients achieved a "clinically meaningful" spleen volume reduction of 25 percent, with one-quarter of them having a reduction of at least 35 percent.

The company is analyzing 52-week results, which it expects by July, and then meet the FDA to discuss a pivotal study aimed at US (and European) marketing approval.

Mr Philips hopes the study can be an adaptive phase IIc/III trial, which uses the current trial candidates as the base for expanded enrolment.

No drug program is an island

John Donne said that no man is an island – and a drug development program also can't be viewed in isolation.

As we said, there's a lot going on in the myelofibrosis space. For a start, Jakafi - a $US17,000 per bottle drug - comes off-patent in 2028.

"When that is genericized, it will significantly impact the market for JAK inhibitors," Mr Phillips says.

In September 2023, the FDA approved Glaxosmithkline's Ojjaara, developed by local lads Prof Andrew Wilks and Dr Chris Burns (CEO of the listed Amplia).

Good job!

Meanwhile, two myelofibrosis drugs are in phase III, but Mr Phillips claims they are beset with problems.

Abbvie's Navitoclax did not show a significant difference in symptom score when combined with ruxolitinib.

"It didn't raise much hope within the myelofibrosis community it was going to offer much different."

The phase III trial of another candidate, pelabresib, showed improved symptoms - but maybe not enough.

Novartis acquired Morphosis, owner the program for $US2.9 billion in April 2024.

But some patients on the treatment arm developed leukaemia - a salient case of the cure being worse than the disease.

Novartis' plans for an FDA approval application have been delayed.

Meanwhile, Kartos Therapeutics plans a phase III trial of Navtemadlin (KRT-232), which puts the program about a year ahead of Syntara's.

Mr Phillips says while Syntara's trial numbers were small, SNT-5505 had a superior symptom rating with similar spleen reduction stats.

Parkinson's program a good show

Syntara's secondary programs are for myelodysplastic syndrome (MDS), a Parkinson's disease precursor condition and a skin scarring program.

Another haematological malignancy, MDS is a high unmet need which Mr Phillips dubs a $US3 billion-plus market opportunity.

Pending a successful phase I effort, the company envisages a phase II dose escalation and expansion trial.

The program is backed by leukaemia groups locally and in Germany but ultimately funded by government grants.

SNT-4728 targets a precursor condition called idiopathic rapid eye movement sleep behavior disorder (IRBD).

IRBD sufferers thrash about and cry out in their sleep as they live out their dreams.

The disorder can precede motor cognition dysfunction by up to 20 years, with 70 percent of sufferers going on to develop neuro-degenerative diseases such as Parkinson's.

The problem with Parkinson's is by the time IRBD is diagnosed, about 80 percent of the dopaminergic neurons are gone.

The charity Parkinson's UK is funding a phase II trial, with clinical proof-of-concept data is expected in the December half year.

Scarring: a burning, unresolved issue

The company is also targeting burns-related scarring, in an investigator-led trial with Perth burns legend Prof Fiona Wood.

This one is all about using the company's pan-LOX inhibitors to prevent scarring after burns surgery.

In 2023, a 42-patient, phase Ic trial met its primary safety objective and two secondary biomarker endpoints in patients with established scars.

"We are still working with Prof Wood and her team on the next topic study, which is likely to be in keloid or hypertrophic scars," Mr Phillips says.

Some of the funds from the recent placement were earmarked for a follow-on company-sponsored study.

Finances and performances

In December 2024, the company launched a $15 million capital raising, in a two-tranche placement at six cents a share.

At the end of December, the company had $18.1 million of cash and no debt, before banking the second tranche $2.6 million.

This should last the company until mid-2026.

In the December 2024 quarter, the company reported $300,000 of net cash inflow, courtesy of a $4.6 million research and development tax incentive payment.

Still, the performance is a turnaround from the September quarter deficit of $4.2 million and average $3.4 million of outflows over four quarters.

Over the last 12 months, Syntara shares have JAK-knifed between 1.5 cents (May 2, 2024) and 8.7 cents (February 19, 2025).

The stock had a five-year peak of 14.5 cents in September 2021 – a long way from the $4.07 in 2007.

Arna you gonna pay up?

While the Pharmaxis/Bronchitol separation is complete, there is the wee matter of money owed to the company by Sydney's Arna as part of the deal.

Suffice to say, payments have been slow because Arna has disputed certain amounts.

So far, Arna has paid $3.5 million of the $7.5 million owed, while a "large chunk" of the remaining $4 million has been agreed to and is being recovered "steadily and surely".

The $4 million is not recognized as cash in the December quarter statement.

We take it the matter didn't get to court, but some stern correspondence has been entered into and Syntara is confident of full recovery.

"Slowly, slowly catchee monkey," Mr Phillips says.

Dr Boreham's diagnosis:

Despite the flurry of activity in the sector, Mr Phillips says the song remains the same for the myelofibrosis program.

The lyrics are that about 60 percent of myelofibrosis cases are not well controlled with JAK inhibitors, and the remaining patients deteriorate over time.

Mr Phillips is long in the tooth enough to know that taking the myelofibrosis drug to market - and even to next clinical trial phase - is a bridge too far for the company.

"We will talk to potential acquirors and investors in the first half of this year, as we wait for the FDA response to our application," he says.

"Our register is stuffed with specialist healthcare investors who understand the myelofibrosis space specifically," he says.

"It's conceivable we could raise a significant amount of money in the second half of this year to do a phase III study."

Cutting through the noise from the myelofibrosis drug landscape, Mr Phillips says: “Our mechanism of action is very different from almost all the other drugs in the myelofibrosis pipeline.”

He had better be right - and other challengers had best not emerge in the tortuous juncture between promising trials and approval.

In the words of Pat Benatar - sort of - the company should hit investors with its best shot with the myelofibrosis program.

The promise of the secondary programs aside, that’s why they are shareholders.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. But he will give it his best shot.