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Daily news on ASX-listed biotechnology companies

Dr Boreham's Crucible: Clinuvel Pharmaceuticals

By TIM BOREHAM

ASX code: CUV

Share price: $31.85

Shares on issue: 48,960,633

Market cap: $1.56 billion

Chief executive officer: Dr Philippe Wolgen

Board: Stan McLiesh (chairman)*****, Dr Wolgen, Brenda Shanahan, Willem Blijdorp, Dr Karen Agersborg, Susan Smith

***** Retiring at the AGM, expected in November

Financials (year to June 30, 2019): revenue $31.05 million (up 22%), net profit $18.1 million (up 37%), earnings per share 36.6c (up 37%), cash balance $54.3 million (up 50%), dividend per share 2.5 cents (up 25%).

Major identifiable holders: Dr Wolgen 6.73%, Fidelity Investment Management 5.45%, Ender1 LLC (Sean Parker) 5.4%.

While proclaiming the US Food and Drug Administration's approval of Clinuvel's rare skin disorders drug Scenesse as a "momentous occasion for an Australian biotech company" CEO Dr Philippe Wolgen avoids any hubris.

"I'm very careful about using the word success because the minute you proclaim success, the next day the house falls down," he says.

Dr Wolgen's reticence is understandable, given Clinuvel's quest for the FDA's stamp of approval as a 'serious' drug took more than 14 years.

But he's happy to highlight that not only has Clinuvel become one of the few Australian biotechs to obtain fully-fledged FDA approval, it did so while beating the key financial metrics outlined in a 2006 business plan.

At the time, management decreed the drug needed to be developed for under $200 million, compared with the typical $400 million to $600 million for a phase III drug.

It also needed to be done with a maximum 250 percent share dilution, costs not exceeding $12 million a year, a cost of capital of under 10 percent and a return on equity of more than six percent.

The company was also to become dividend-paying when it achieved profits within 10 years.

As things transpired, the drug cost $129 million with only a 165 percent share dilution and a return on equity of more than 20 percent.

The company posted its first meaningful profit in 2016-'17 and paid a maiden 2.0 cents a share dividend a year later.

Okay, so a slight miss on the 10-year deadline.

Average annual costs over the period were $12.75 million and not $12 million as targeted.

But investors who pushed Clinuvel shares 60 percent higher after the October 9 news were hardly going to quibble about these slippages.

Out of the shadows

After two years of pontification, the FDA czars approved Scenesse as an adult treatment for the rare condition erythropoietic protoporphyria, or EPP.

EPP is an inherited metabolic disorder that causes a severe reaction to sunlight because of a dearth of the compound protoporphyrin nine (PPIX) in blood and tissues.

PPIX is activated by visible light and ultraviolet radiation, causing tissue damage and howling pain.

Scenesse binds to the melanocortin 1 receptor on skill cells and sets in motion a "cascade of cellular events" to activate melanin and create a prophylactic barrier.

In other words, the drug tans the skin - a side effect that has been both a boon and a bane for the company's development (more on that later).

Scenesse is a formulation of the peptide afamelanotide. About the size of a rice grain, the Scenesse shots are injected subcutaneously in a 16mg dose and ooze their goodness for two months (after which the patients have another one).

EPP affects about one in 140,000 people, equating to about 5,000 to 10,000 sufferers.

Life is hell for these folk, a.k.a. shadow chasers, who are confined indoors all day.

If at first you don't succeed …

While Clinuvel flies the Australian flag, Scenesse evolved from lab work by four scientists at the University of Arizona in 1987.

In 1995, the owners applied for investigational new drug status with the FDA, based on marketing claims of a "tanning solution by chemical induction".

The FDA demurred.

Epitan was incorporated in 1999 and back-door listed on the ASX in 2000, before changing its name to Clinuvel in 2006.

In 2003, the molecule was out-licenced to an Australian team, which fronted the FDA again. "The FDA labeled it as the next injectable Botox," Dr Wolgen rues.

In 2004, the company tried yet again and the agency's rejection was more pointed.

"The FDA said they would not allow it ever to come to market for reasons of efficacy, tolerability and lifestyle use," Dr Wolgen says.

A former facio-cranial surgeon and almost professional soccer player, Dr Wolgen joined the company in 2005 and set it on a new direction: a Europe-focused and strict medical agenda.

Changing course to Europe

Management was spurred by the breakthrough results of a five-person Swiss trial that showed the patients increased their tolerance to sunlight 11-fold.

"The [Clinuvel] board was quite strict and said the technology was quite promising but there is no guarantee it is going to generate returns," Dr Wolgen says.

In pursuit of "financial proof-of-concept" the company zeroed-in on Italy, where the government formally supported drugs addressing an unmet need (as long as they had the support of the relevant medical community).

Rome agreed to subsidize 23 percent of the cost of the users, which then was EUR5,375 ($A8,810) per injection (up to six per year are required).

Swiss insurers then said they were willing to subsidize the drug.

“So, we went back to Australia and said ‘we think there are people willing to write a cheque for it’,” Dr Wolgen said.

After a “hefty” board debate, the company decided to offer Scenesse for compassionate use (that is, free) to needy patients.

“There are pros and cons to do doing this,” Dr Wolgen says. “If you start incurring costs and distribute free of charge, it also sets a precedent for insurers to delay and not pay.”

“That was a difficult and pivotal decision, but for two years we did it across Europe and in Australia.”

In 2012 the company sought European marketing approval, with management fronting a presentation at London’s Canary Wharf where regulators from all 28 European Union member states were represented (we’re talking pre-Brexit times, of course).

“We thought if the Europeans had the audacity to approve the drug that certainty would count in the US as they would not need to take regulatory leadership,” Dr Wolgen says.

The European Medicines Agency approved Scenesse for EPP in late 2014 and the company launched the drug in Europe in 2016.

The secrets of Clinuvel’s success

Clinuvel has done a couple of things differently to attain the holy grail of FDA approval.

Firstly, it stayed headquartered in Melbourne Australia. “In 2005 there was a tendency to go to the US and Europe because that is where notionally there is the talent to develop it,” Dr Wolgen says.

“But we went the other way. We said we have a base here and tax incentives and there is a good infrastructure.”

Secondly, Clinuvel retained control of distribution in-house.

“We said if you built this knowledge in-house you would be mad to give it out of your hands and let others determine the destiny of your best molecule.”

The in-house approach - which relates to functions over and above distribution - was a key factor in helping the company to contain costs.

Finances and performance

Clinuvel generated its first meaningful revenue in 2015-'16 - $6.4 million - and then turned its first profit of $7.1 million in 2016-'17.

For the year to June 30, 2019, the company reported an $18.1 million net profit, up 37 percent on revenue of $31 million (up 22 percent).

Clinuvel is coy about likely US revenue, given big pharma has been roughed up by both sides of US politics, with price-gouging accusations. To ameliorate these concerns, the company has adopted a policy of uniform global pricing.

In Europe, the treatment costs EUR55,000 to EUR85,000 ($A90,000 to $A140,000) a year, depending on the number of injections required. At the midpoint, treating a mere 1,000 patients implies annual revenue of $A115 million.

Of course, much depends on the availability of reimbursement, but Dr Wolgen notes that US insurers are already stumping up for US patients to be treated in Europe.

(In the UK, the company is struggling to win reimbursement from the National Institute for Health and Care Excellence - NICE – which isn't being so nice about the matter).

Dr Wolgen says the company has taken a selective approach to pursuing supportive shareholders with deep pockets and a longer-term view. The register includes Fidelity and billionaire Napster-founder Sean Parker.

"We wanted to build a registry of investors that fitted the way we go about our business," Dr Wolgen says.

"We have consciously kept the share register clean and tidy."

As of June 30, Clinuvel had $54 million of cash and given its revenue generating status it won't be bothering holders for more of the folding stuff in the foreseeable future.

Clinuvel shares have traded as low as $1.13 (December 2013) and as high as $45.88 (after the October 9 news).

Dr Boreham's diagnosis:

Clinuvel's home-spun success makes the failed $2.17 a share, $95 million takeover offer from Retrophin in 2014 look like pure larceny. In hindsight, of course.

Clinuvel certainly has done a sterling job of generating revenue from such a low patient base, but Dr Wolgen agrees that investors are expecting wider applications.

"Will the company grow only on this technology or does it need more," he asks, rhetorically. "The answer is there has to be more."

“We have an organic strategy [labs in Singapore developing next molecules] and we are going to grow inorganically by [acquisitions] and licencing other technologies.”

Clinuvel is targeting a pigmentation disorder called vitiligo, which affects about 45 million people. Known as the Michael Jackson disease in some circles, vitiligo causes the skin to go pale, generally in blotches.

Since 2010, Clinuvel has carried out two vitiligo trials in Singapore and the US, with “significant” results.

But there have been unexpected obstacles unrelated to efficacy.

“We went to Singapore and discovered … it was culturally unacceptable to become so dark. But African-Americans were delighted to [get] back their pigmentation.”

Clinuvel’s criterion for the next indication is simple: “there has to be a high unmet need and no alternative in sight”.

This, we assume, precludes safe tanning but we did hear something about an over-the-counter sunscreen in development.

In the meantime, Clinuvel has a five to seven-year window to make hay from the EPP indication before rivals wake-up to the enormous potential that even an obscure disease can present.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. He admittedly was sceptical about the company’s chances but has now seen the light.