Biotech Daily

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Daily news on ASX-listed biotechnology companies

Dr Boreham's Crucible: Opthea

By TIM BOREHAM

ASX and Nasdaq code: OPT (eight ASX shares = 1 American depositary share)

Share price: 62.5 cents

Shares on issue: 662,808,634

Market cap: $414.3 million

Chief executive officer: Dr Frederic Guerard

Board: Dr Jeremy Levin (chair), Dr Megan Baldwin (founder and executive director), Lawrence Gozlan, Dr Julia Haller, Dr Susan Orr, Quinton Oswald, Sujal Shah, Anshul Thakral

Financials (half year to December 31, 2023): revenue $US60,798 ($A93,200) (up 17%), loss of $US96.1 million (previous deficit $US79.1 million), cash $US157 million (up 76%).

Identifiable major shareholders: Regal Funds Management 22.96%

One doesn't have to be a Madison Avenue 'Mad Man' to know that it's more effective to have a credible third party spruik a product or service, rather than the advertiser itself.

Back-of-the eye treatment company Opthea has taken this lore to heart, having rolled out three key opinion leaders - eye clinicians - to spread the message about the company's proposed drug to treat wet age-related macular degeneration (wet AMD).

Wet AMD is the leading cause of blindness in the over 50s.

In a recent online clinical seminar, investors were told the company's proposed treatment for wet AMD would be the first new one in 15 years.

"This is the only program in late-stage development designed to have better visual acuity outcomes for patients and that is what matters," said Dr Arshad M Khanani, founder of Sierra Eye Associates.

Indeed!

University of Illinois retinal specialist Dr Veeral Sheth chimed in: "this program has the potential to transform how we treat wet AMD in our daily clinical practice."

After years of development, D-day is approaching as the company carries out two pivotal phase III combination trials for its drug candidate sozinibercept - OPT-302 to friends.

Eye-catching history

Opthea's corporate history goes back to the days of Circadian Technologies, which toyed with melatonin for jet lag.

Founded by biotech doyen Leon Serry, Circadian incubated companies including the Victoria state-founded Amrad, (later renamed Zenyth and sold to CSL).

Other companies in its portfolio were Metabolic (which became Calzada before morphing into Polynovo), Antisense and Optiscan.

Circadian acquired the eye portfolio - based on vascular endothelial growth factor (VEGF) inhibitors - from the University of Helsinki in 2008. The company changed its name to Opthea in December 2015.

With a Doctor of Philosophy in VEGF, Dr Megan Baldwin joined the company in 2008 and was anointed CEO in February 2014.

In October last year, the company appointed Dr Guerard as CEO and Peter Lang as chief financial officer, both US-based.

Dr Baldwin assumes a new role of executive director and chief innovation officer, responsible for 'forward looking' programs such as co-formulation and pre-filled syringe development and clinical studies beyond wet AMD.

Dr Guerard was CEO of the clinical stage Graybug Vision Inc, where he led the development of a late-stage wet AMD candidate.

Before that, he was worldwide business franchise head of ophthalmology for Novartis.

In October 2020, the company raised $US128 million by way of American depositary shares and listed on the Nasdaq Global Select Exchange.

Opthea's vision statement

The leading cause of vision impairment in people over the age of 50 years, wet age-related macular degeneration is linked with blood vessel dysfunction in the macular region.

Blood vessels grow abnormally under the retina, resulting in leakage of fluids, lipids and blood from the vessel. Patients can lose vision in as little as 10 weeks.

A so-called 'trap inhibitor', OPT-302 is a fusion protein that blocks the activity of two VEGF proteins: VEGF-C and VEGF-D.

Opthea is developing OPT-302 as a wet AMD combination therapy with the existing drugs Lucentis (ranibizumab) and Eylea (aflibercept), which only block VEGF-A.

Currently about 60 percent of patients have sub-optimal results, because the disease process is more complex than just blocking VEGF-A.

About half the market is treated off-label with Avastin, an old cancer drug.

Eye see more letters

In August 2019, Opthea released "statistically significant and clinically meaningful" results of its keenly-awaited phase IIb trial that enrolled 366 previously-untreated patients across 110 sites.

The study tested a combination of Opthea's OPT-302 with the standard-of-care Lucentis.

The primary endpoint was the ability of patients to read more letters on an eye chart after 24 weeks of treatment. Aged on average in their mid-70s, the 'combo' group read 14.2 letters, a mean 3.4 more than those on the standard-of-care therapy alone.

Coast and Shore trials launched, but company not at 'see'

The market's attention is now focused on the two phase III wet AMD trials, nautically dubbed Coast and Shore, in combination with Lucentis and Eylea respectively.

The company recently enrolled its last patient in Coast, while Shore is 96 percent enrolled. Both trials each enrol 990 treatment-naïve patients, with one-third allocated to a sham (placebo) group.

The primary endpoint is the mean change in the eye chart reading at week 52, with the secondary endpoints of an improvement of either more than 15 letters (three lines), or ten letters (two lines). There are also "anatomical" endpoints, including fluid measures at the back of the eye.

As of December 2023, Shore had 198 active trial sites in 22 countries, while Coast had 219 sites in 30 nations.

Enrolment had been challenging because of the pandemic, inflation, supply chain issues and the old railways excuse of “lack of qualified staff”.

Trial recruits include patients with a form of hard-to-treat wet AMD called polypoidal choroidal vasculopathy (PCV), by which fluid leaks and bleeds from abnormal blood vessels. PCV is common in people with Asian background.

In the phase IIb trial,18 percent of the 366 treatment-naïve patients had PCV and the results for this cohort were impressive.

Dr Baldwin says some of the phase III patients have completed the 100th week of treatment, well beyond the week-52 milestone for the top-line data.

“Of course, the company hasn’t seen the data because it is masked and they will only get a look see when all patients have completed week-52,” she says.

Opthea will move swiftly to file a US Food and Drug Administration application - if the 2025 trial read-out is positive - and probably within six to 12 months of the results.

The company has fast-track approval, which enables it to submit a biologics licence application (BLA) on a module-by-module approach.

Eyeballing the competition

Some changes to the wet AMD competitive landscape have unfolded since we last covered Opthea in May 2022.

Last October, the FDA approved a Roche drug, Vabysmo (faricimab). The subsequent launch was spectacular and the drug now outsells previous market leader Lucentis.

Vabysmo is a bi-specific molecule targeting ANG2 and VEGF-A. But Dr Baldwin says there’s no efficacy benefits over the other anti VEGF-A drugs (Eylea and Lucentis).

“We view it as another standard-of-care molecule, with a view that we would be able to add on it to just in the same way as we plan to with Lucentis, Eylea, Avastin or a biosimilar.” (A biosimilar is a cheaper copy of an existing drug).

“The fact the uptake has been so fast shows the clinicians are willing to try new drugs,” Dr Baldwin says.

Meanwhile, Regeneron recently won approval for a high-dose form of Eylea, which is likely to be more competitive with Vabysmo.

In 2019, the FDA approved a Novartis wet AMD drug called Beovu (brolucizumab).

The subsequent launch flopped after evidence emerged of side effects including retinal vasculitis, which can cause profound vision loss.

Talk about the cure being worse than the disease!

Glory or bust

In August 2022, Opthea unveiled a share placement and a novel non-dilutive deal with US outfit Launch Therapeutics (an offshoot of global investment giant Carlyle and its acquired life sciences franchise, Abingworth).

Launch agreed to provide $US120 million over three unconditional instalments, with an option to tip in a further $US50 million.

If OPT-302 is approved in a major market, Opthea repays Launch through a quasi-royalty of 7.0 percent on annual net sales.

The unusual aspect is that these payments are capped at four times the invested amount: a tidy $US510 million profit.

But if OPT-302 is not approved Launch gets yada, zip and a donut.

Opthea keeps the full rights to the drug and is only obliged to repay the funding - let's call it quasi debt - if successful.

Technically, the arrangement is called a structured financing royalty deal, which are common in the US but not here.

The deal was accompanied by a $US90 million placement - a prerequisite for Launch's involvement - struck at $1.15 a share (a 12.5 percent discount).

Finances and performance

In December 2023, Opthea pocketed the last scheduled $US35 million from the deal, with Launch chucking in another $US50 million with a co-investor.

In August 2023, the company again replenished its coffers with a $73 million placement and rights issue at 46 cents apiece, followed by a rights offer that raised $16.3 million for a total $90 million.

Opthea recorded an ugly-sounding $96 million loss in the December 2023 half, reflecting the cost of rolling out more trial sites.

The (very) modest revenue of $60,798 came from royalty and licencing income.

Opthea has $US157 million in cash, but phase III trials don't come cheaply. According to Opthea's annual report, the company is funded to the third quarter of calendar 2024.

Opthea still has access to an at-the-market equity program, by which the company can issue up to $US75 million of its American depositary shares at a time of its choosing.

Opthea shares peaked at $3.45 in September 2019 and troughed to 20 cents in June 2015.

Dr Boreham's diagnosis:

Despite the stiffening wet AMD drug competition, Dr Baldwin says OPT-302 is still the most advanced product in development that has shown superiority over standard-of-care therapy, as opposed to showing better treatment durability (extended efficacy between injections).

"Only a couple of very early-stage companies are looking at new mechanisms of action so we have a clear runway in terms of that development path," Dr Baldwin says.

"We are going to have a lot of commercial interest in our readout and there's huge potential because of that."

By entering phase III, Opthea is in a rare pantheon of ASX-listed biotechs that includes Dimerix, Mesoblast and Paradigm.

Opthea cites the size of the prize as a $US15 billion market: $US9 billion for Lucentis and Eylea and $US5 billion for the off-label Avastin and other biosimilars.

"Any way you cut and dice the market, it is a multi-billion-dollar opportunity even on conservative estimates of the proportion of clinicians administering it initially," Dr Baldwin says.

Disclosure: Any way you cut and dice it, Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. His vision is to get one eventually.