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In this edition...
We begin coverage of the 12th Bioshares Biotech Summit with commentary on Opthea's discussion of results from its Phase I dose escalation trial of OPT-302.

In the next few editions of Bioshares we will present coverage of other sessions of the Summit.

The regular 'Survival Index' analysis of ASX-listed life science companies rounds out this edition.

Companies covered: OPT, Cash Analysis

	Bioshares Portfolio
Year 1 (May '01 - May '02)	21.2%
Year 2 (May '02 - May '03)	-9.4%
Year 3 (May '03 - May '04)	70.6%
Year 4 (May '04 - May '05)	-16.3%
Year 5 (May '05 - May '06)	77.8%
Year 6 (May '06 - May '07)	17.4%
Year 7 (May '07 - May '08)	-36%
Year 8 (May '08 - May '09)	-7.4%
Year 9 (May '09 - May '10)	50.2%
Year 10 (May '10 - May'11)	45.4%
Year 11 (May '11 - May '12)	-18.0%
Year 12 (May '12 - May '13)	3.1%
Year 13 (May '13 - May '14)	26.6%
Year 14 (May '14 - May '15)	23.0%
Year 15 (May '15 - May '16)	33.0%
Year 16 (May '16 - current)	13.8%
Cumulative Gain	**739%**

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Bioshares

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Extract from Bioshares –

Early Signs of Efficacy and Clinical Relevance for Opthea's OPT-302

Opthea (OPT: $0.645) has released results from its Phase Ib study with its drug candidate OPT-302, treating patients with wet AMD (age-related macular degeneration). Although it was a small trial with only 20 patients, early signs of efficacy were evident. These signs indicate that the company may have a drug candidate with commercial appeal as a combination treatment for this condition.

The appeal of Opthea is that it is working in market that is valued at over US$10 billion that is served by only two existing compounds, branded as Lucentis (and Avastin) and Eylea, which generate over US$10 billion a year of revenue. Also appealing is that there are only eight other clinical programs in development in this field that are working on novel targets according to Opthea CEO Megan Baldwin.

Safety

The safety profile of OPT-302 appears to be excellent. In the 20 patients who received the drug candidate for up to three months of treatment, there were no signs of increases in intra-ocular pressure, no infection issues, no immune reactions, and no dose limiting toxicity at the highest dose.

Efficacy

The efficacy results require some explanation and analysis for relevance. This is because with only 20 patients there were three dose groups (0.3mg, 1.0mg and 2.0mg), there was a combination arm with Lucentis and a monotherapy arm with OPT-302 alone, and there were patients who had received Lucentis or a similar treatment previously and stopped responding, and treatment naïve patients who had not received VEGF therapy.

Another consideration is what the results mean with respect to clinical benefit. At this year's *Bioshares* Biotech Summit, Baldwin provided further explanation of the results.

In the table on the next page, we have provided visual representation to help clarify the results and the potential clinical relevance of this early clinical trial data.

Monotherapy

As a monotherapy, OPT-302 achieved a 3.3 letter gain on the standard eye chart. This was in both treatment naïve and previously treated patients and included only those (three patients) who did not require rescue therapy with Lucentis treatment.

In a Phase III registration trial (MARINA) in what Baldwin said was a similar patient population with similar lesions to patients in Opthea's trial, Genentech (Roche) showed that Lucentis achieved an average 5.9 letter visual acuity improvement after 12 weeks of treatment (which was the length of the Opthea trial).

Cont'd over

Opthea Phase Ib Trial Patient Population

Dose	Previously failed VEGF therapy	Naïve patients	Letter gain (av)
0.3mg OPT-302 plus Lucentis	3	2	16.5
1.0mg OPT-302 plus Lucentis	5	0	
2.0mg OPT-302 plus Lucentis	3**	2	4.0
2.0mg OPT-302	3	2	3.3*
Total	**14**	**6**	

Results with Competing Compounds

Lucentis Phase III study results (letter gain) in naïve patients	Fovista Phase IIb trial result in combination w ith Lucentis (in naïve patients)
5.9	8.7 (5.1 w ith Lucentis alone)
5.9	

** Includes only 3 of 5 patients who did not require rescue therapy with Lucentis*
*** One pt died during the trial because of ovarian cancer complications*

In that same trial, patients who received a sham injection experienced a 3.7 letter average decline in vision.

Combination Therapy in Naïve Patients

Other than the safety data reported, effects of treatment in the combination arm in naïve patients are of most interest from this trial. Lucentis achieves a 5.9 letter improvement in visual acuity at three months as indicated above. In the four treatment naïve patients who received OPT-302 plus Lucentis, the average improvement in visual acuity was 16.5 letters. Whilst this is only in four patients, there is an implied benefit of 10.6 letters. This will obviously need to be supported with larger patient trial data but it is an encouraging result.

Previously VEGF Failed Therapy

In the 10 patients who had failed previous treatment with VEGF inhibitors, the vision gain was 4.0 letters when treated with OPT-302 and Lucentis. (Note, one patient died in the trial from an existing cancer related condition and did not complete treatment.) This is a meaningful result, with the improvement just under the 5.9 letter visual gain achieved with Lucentis in a Phase III study in treatment naive patients.

Comparison with Fovista

The leading combination therapy drug in development is Fovista from Ophthotech Corporation. Ophthotech listed in 2013 at a market value of US$662 million on the back of its Phase II trial results in 449 patients.

That trial showed that after three months of therapy, Fovista plus Lucentis achieved a visual gain of 8.7 letters compared to 5.1 letters with Lucentis alone (a 3.6 letter gain). Opthea achieved an average gain of 16.5 letters in the four naïve patients, however this should be tempered due to the small patient group, and one patient in this group achieved a very high result (in the lower dose group). In the two patients of the four in the higher dose, a lower improvement in visual gain of 9.5 letters was achieved. As indicated above, these are very early results but once again encouraging.

Most of the gain is traditionally experienced in the first three months of treatment. In the Ophthotech Phase IIb trial, at six months, the visual gain was 10.6 letters in the combination arm compared to 6.5 letters with Lucentis alone (4.1 letter gain).

Ophthotech has completed enrolment into three Phase III studies involving 1866 patients. Results from the first two of those trials are expected in Q4 this year.

Ophthotech has a current market value of US$2.3 billion.

OPT-302 Trials Timeline

Opthea has progressed to a Phase IIa study, effectively extending the patient numbers in two of the groups in the Phase Ib trial. This will give the company trial data in 20 patients in the monotherapy arm, and 20 patients in the 2.0mg OPT-302 (highest dose) plus Lucentis arm. Results from this Phase IIa trial will be released in Q1 2017.

The next step after that is to conduct a Phase IIb study which is scheduled to start in 2017. Baldwin expects that Opthea's Phase IIb trial may only require 200 patients and take 18 months to conduct.

Opthea is capitalised at $97 million (US$73 million) and held cash of $17.7 million at the end of last year.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

How Bioshares Rates Stocks

For the purpose of valuation, Bioshares divides biotech stocks into two categories. The first group are stocks with existing positive cash flows or close to producing positive cash flows. The second group are stocks without near term positive cash flows, history of losses, or at early stages of commercialisation. In this second group, which are essentially speculative propositions, Bioshares grades them according to relative risk within that group, to better reflect the very large spread of risk within those stocks. For both groups, the rating "Take Profits" means that investors may re-weight their holding by selling between 25%-75% of a stock.

Group A

Stocks with existing positive cash flows or close to producing positive cash flows.

Buy	CMP is 20% < Fair Value
Accumulate	CMP is 10% < Fair Value
Hold	Value = CMP
Lighten	CMP is 10% > Fair Value
Sell	CMP is 20% > Fair Value

(CMP–Current Market Price)

Group B

Stocks without near term positive cash flows, history of losses, or at early stages commercialisation.

Speculative Buy – Class A
These stocks will have more than one technology, product or investment in development, with perhaps those same technologies offering multiple opportunities. These features, coupled to the presence of alliances, partnerships and scientific advisory boards, indicate the stock is relative less risky than other biotech stocks.

Speculative Buy – Class B
These stocks may have more than one product or opportunity, and may even be close to market. However, they are likely to be lacking in several key areas. For example, their cash position is weak, or management or board may need strengthening.

Speculative Buy – Class C
These stocks generally have one product in development and lack many external validation features.

Speculative Hold – Class A or B or C

Sell

Corporate Subscribers: Cogstate, Bionomics, Impedimed, LBT Innovations, Viralytics, Phylogica, pSivida, Benitec BioPharma, Analytica, Opthea, Reproductive Health Science, Regeneus, Innate Immunotherapeutics, Anatara Life Sciences, ResApp, Pharmaxis, Starpharma, Antisense Therapeutics, Atcor Medical, Dimerix