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Bioshares

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Delivering independent investment research to investors on Australian biotech, pharma and healthcare companies

Companies covered: IDT, OPT, Adalta IPO Profile

	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)	6.6%
Cumulative Gain	**686%**
Av. Annual gain (14 yrs)	**18.0%**

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Extract from Bioshares –

Opthea Approaches Important Trial Outcome

Opthea (OPT: $0.545) this week presented at an investor event. The key milestone ahead this quarter is the efficacy readout from a Phase Ib trial with its biologic drug candidate OPT-302. While Phase I results generally only provide safety data, this result should provide important details with respect to evidence of efficacy. Any hint of efficacy, particularly at the higher doses, will likely provide a trigger for a stock re-rating.

Evidence for the approach Opthea is taking is firming. The standard-of-care in the treatment of wet AMD are two drugs, Lucentis and Eylea, which both block the VEGF-A pathway. But these drugs do not block the VEGF-C and –D pathways which OPT-302 does. In fact anyone who tries to block these other pathways infringes on Opthea's patents.

What was also revealed at the investor briefing was new data that shows VEGF-C protein levels have been found to increase by 66% when patients take a VEGF-A inhibitor, supporting the idea that blocking the VEGF-C pathway as well will improve patient outcomes. OPT-302 is a soluble VEGF trap compound that soaks up VEGF-C and VEGF-D proteins in the eye. This process inhibits unwanted blood vessel formation in the eye and fluid leakage in the eye.

Opthea is aiming to provide three benefits by using its drug candidate in conjunction with Lucentis or Eylea. The first is that the magnitude in vision gain should be increased; the duration of response may be extended, therefore less frequent injections into the eye would be required; and the number of patients who would benefit from treatment would be enlarged.

Currently more than 50% of patients do not experience vision gain from Lucentis or Eylea. Two thirds will continue to have fluid build up in the back of the eye when on treatment. And a quarter of patients will have continued vision loss at 12 months.

When Opthea reports efficacy results from the 20 patients in the Phase Ib trial, what will be most interesting to observe will be the effect in the five patients on treatment at the highest dose in the monotherapy arm, and the five at the highest dose in the combination arm with Lucentis.

In response to a question as to why the company has not released some of the data from the current open label Phase Ib study, CEO Megan Baldwin, indicated that there is generally a strong improvement after the first month of therapy, so the company wanted to provide full three month treatment data from the trial. The trial data is sent from the trial sites to a central data facility, from which the company has yet to retrieve efficacy data.

Eylea and Lucentis generated sales of US$7 billion last year, but this is only 40% of the market, with Avastin (a cancer drug but the same active as Lucentis) being used in 60% of cases because it is considerably cheaper.

Phase IIa Data Late This Year

Opthea has started the Phase IIa part of the above trial, which is recruiting an additional 15 patients in the monotherapy and combination therapy at the highest dose. This will give the company results from 20 patients at the highest dose on monotherapy and 20 patients with combination therapy (with Lucentis) at the highest OPT-302 dose at the end of the year. The Phase Ib/IIa trial is being conducted in the US with 13 trial sites currently recruiting patients.

Competition

With respect to competition, the filed is narrowing not widening according to Baldwin, with a gene therapy approach falling over because of the difficulty in getting the vector to transfect the retina fully. Delivering drugs directly to the retina is very difficult compared to delivery of VEGF inhibitors to the vitreous fluid in the eye.

The most advanced competitor is Ophthotech Corporation in the US. Ophthotech is combining its drug candidate Fovista with Eylea or Avastin and has recently completed recruitment into its third Phase III trial, with recruitment of 1866 patients now complete in three Phase III studies.

Ophthotech has a market value of US$1.95 billion. It listed in 2013 and started its Phase III program that year. In 2014, it signed a deal with Novartis Pharmaceuticals for Fovista. For non-US rights only, Novartis will pay up to US$1 billion in upfront and milestone payments plus royalties. It was one of the largest ex-US partnering deals ever conducted.

Ophthotech Corporation conducted a 449 Phase IIb trial which took two and a half years to complete. Baldwin said that Opthea will conduct a Phase IIb trial that will recruit 200 patients and take 18 months to conduct. Completion is expected in 1H 2018. Baldwin said the time to execute a deal would be once the large randomized Phase IIb study had been completed.

Global Investor Base

Opthea's investor base is now evenly distributed across the world, with one third of investors based in Australia, one third in the US and one third in Europe. Major investors include Baker Brothers and Biotechnology Value Fund in the US. The interest of these funds is a significant investment factor, both from experienced US investor validation and the potential access for future funding.

Appeal of Working in Ophthalmic Ondications for Drug Development

There are a number of appealing features with working in the development of ophthalmic drug candidates. Firstly, by direct injection of the compound into the vitreous, 100% of the drug is delivered to the target site. Trials are short, with efficacy measures assessed in three months. And efficacy endpoints are easy to measure and are unambiguous.

The current trial is being used to assess safety foremost, and initial safety data has been clear. The main efficacy measure for investors to judge function of OPT-202 in this trial is changes in visual acuity, as assessed using a standard eye chart test. Other supporting endpoints will be fluid build up in the eye, as measured by central retinal thickness or macula volume.

Summary

Opthea raised $17.4 million in 2014 at 17.5 cents a share. Its share price has climbed over 200% in that time due to the anticipation of clinical results, said Baldwin.

Opthea has a strong patent position. It has granted composition of matter patents granted in major jurisdictions, including Europe, Japan, Canada and the US. These patents expire in the US in 2026 and in Europe and Japan in 2022. There is the potential for extended protection for between eight to 12 years in major markets because OPT-302 is a biologic drug. It has a granted US 'use' patent and has recently filed a new composition of matter patent, that if granted, would extend protection out to around 2034.

If positive efficacy results start to emerge for Opthea, then considerable share price appreciation can be expected. Opthea currently is valued at $82 million (US$62 million) with $17.7 million in cash 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