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Companies covered: IPD, OPT, PNV

	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 - current)	18.9%
Cumulative Gain	**559%**
Av. Annual gain (14 yrs)	**17.8%**

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Bioshares

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Extract from Bioshares –

Results Time Approaching for Opthea

Ophthalmology drug development company Opthea (OPT: $0.375) is due to report initial results from its Phase Ib/IIa trial in patients with wet AMD with its drug candidate OPT-302. This trial is firstly a safety study. With the trial continuing on track to release results at the end of next month, it can be assumed that the safety profile of the drug, used both alone and in combination with another ophthalmology drug, Lucentis, is positive.

There are also several efficacy measures that will be examined as secondary endpoints. There are three different doses being assessed in four cohorts. However, being such an early stage study, results should not be considered as a whole, but rather be about looking for signs of improved efficacy at different doses, as a solo treatment and as a combination treatment, and whether the treatment favours patients who have not been on the VEGF-A inhibitors such as Lucentis previously, or whether treatment is more effective in those patients who have been previously treated with these drugs.

Any hint of efficacy in this trial will cause a dramatic uplift of interest in this company, given the very large market opportunity for eye drugs alongside limited treatment options, both from investors and from pharmaceutical companies operating in this space.

This trial should not be considered as a binary event given that its aim is to ascertain safety first, but also ascertain early signs in individual patients to help guide how additional trials should be structured. There is no placebo arm and the study is not blinded. However, differences in responses from patients in the four separate cohorts will be of interest, any signs of a dose response will be very well received, as will the compound's effect as a monotherapy.

In the Phase Ib part of the trial, patients in the four cohorts receive an injection every month for three months. The first three cohorts are in combination with Lucentis, increasing the dose from 0.3mg to 1.0mg and 2.0mg of OPT-302. At the highest dose (2.0mg) there will also be a cohort of patients receiving only OPT-302.

Interim results to be released towards the end of March will include data from the four cohorts, including 28 data from Cohorts 3 and 4, the highest dose. Longer use data, up to three months, will be available from patients in Cohorts 1 and 2. And there may be longer use data from the first patients to enrol in the highest dose cohorts.

The company will move into a Phase IIa dose expansion study (Cohorts 5 and 6) once patients Cohorts 3 and 4 have passed the 28 day mark.

Cohort 5 will involve 15 patients who will receive similar injections monthly of Lucentis and OPT-302 (highest does from Phase Ib). Cohort 6 will see 15 patients treated monthly for three months with OPT-302 only (highest does from Phase Ib).

Remaining data from the trial is expected to be released towards the end of this year, with the company able to release more progressive data as it is received, such as three month treatment data and six month follow-up data.

Patients in this Phase Ib/IIa trial are either treatment naïve patients or patients who have plateaued on other VEGF-A treatments.

Benefit to Existing Treatments

At an investor presentation this week, Opthea CEO, Megan Baldwin, spelled out the three potential benefits of using its drug candidate and appeared very confident and optimistic about the company's lead drug program. As a combination therapy, the potential benefit is to (a) increase the number of patients who may benefit from treatment with more than half of patients on Lucentis or Eylea not achieving significant vision gain (b) to increase the level of benefit with two thirds of patients still having fluid at the back of the eye after treatment with these drugs (c) and extend the length of response, reducing the frequency of injections which is current between four to eight weeks.

In a mouse model in wet AMD, OPT-302 achieved a 70% reduction in the wet AMD lesion, Eylea achieved a 78% reduction in area, and combined (Eylea and OPT-302), a 91% reduction in lesion area was achieved.

Market Size and Potential in DME

In 2015 global sales of Lucentis and Eylea were over $7 billion, and this excludes the sales of Avastin (same active biologic as Lucentis but used in oncology) which is used in 60% of cases off-label. Combined the market is estimated at over $10 billion a year.

This market size and the limitations of these existing therapies explains the interest in improving the existing products on the market.

An aging global population is another appealing factor for this market segment. Baldwin said that the prevalence of wet AMD is expected to double by 2020. In the US there are 1.8 million people with wet AMD.

The rationale for combining OPT-302 with Lucentis or Eylea is that the current drugs only block one of the channels of new (excessive) blood vessel formation in the eye, that being VEGF-A. Baldwin said that OPT-302 'addresses the responsiveness to VEGF-A inhibitors'. However, OPT-302 blocks VEGF-C and D proteins involved in blood vessel formation.

VEGF-C also increases vascular permeability. Inhibiting this protein may also help reduce fluid build up in the eye, which may give it potential in treating diabetic macular edema, which occurs as a result of fluid leakage from blood vessels within the macula. This is a feature that the drug candidate Fovista, in Phase III development by Ophthotech Corporation, does not have, and is unlikely to have utility in DME. Ophthotech is capitalised at US$1.8 billion.

Summary

Opthea is capitalised $56 million (or $75 million on a fully diluted basis). It has cash sufficient to complete the current Phase Ib/IIa study and the Phase IIb trial, by 2017.

The Phase IIb study will be a randomised control study comparing a combination treatment with Lucentis versus Lucentis alone. The trial design will be set following the results of the Phase Ib/IIa trial, expected in 2017. However, the Phase IIb trial may look at treatment naïve patients or patients who have responded poorly to Lucentis treatment.

Patients in this study will be treated for six months versus only three months of treatment in the Phase Ib/IIa study. It will likely recruit 180 patients, half in the control and half in the treatment arm, with the study likely to start next 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, Tissue Therapies, Viralytics, Phylogica, pSivida, Benitec BioPharma, Invion, Imugene, Analytica, Circadian Technologies, Reproductive Health Science, Regeneus, Innate Immunotherapeutics, Anatara Life Sciences, ResApp, Pharmaxis, Starpharma, Antisense Therapeutics, Atcor Medical