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Science 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 - May '17)	16.8%
Year 17 (May '17 - May '18)	-7.1%
Year 18 (May '18 - current)	-11.0%
<b>Cumulative Gain</b>	<b>609%</b>
<b>Av. Annual gain (17 yrs)</b>	<b>17.1%</b>

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# Bioshares

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

Extract from *Bioshares* –

## **Biogen & Eisai Stop Two Phase III Studies; Start Another Phase III Trial in Alzheimer's Disease**

Last week Biogen and Eisai announced that they were stopping two Phase III trials in early stage Alzheimer's disease with aducanumab, a monoclonal antibody that removes accumulated beta amyloid plaque in the brain. Results from the ENGAGE and EMERGE studies were expected early next year. However, an interim futility analysis indicated that the trials were unlikely to yield a positive result.

There was some optimism for aducanumab, based on the following of 143 patients for four years from a Phase Ib study. That trial had yielded positive signals, including complete removal of plaque in the brain at the highest dose and significant slowing in cognitive decline. The cessation of the Phase III trials follows a myriad of Phase III studies that have ended prematurely over the last 18 months, mostly of BACE inhibitor drugs that prevent the production of beta amyloid. Biogen and Eisai are now reassessing whether another Phase III disease prevention trial with aducanumab will go ahead.

However, on the same day as announcing the cessation of the aducanumab studies, Biogen and Eisai announced that they would start a 1,566 patient Phase III study with another drug candidate, BAN2401, also in early Alzheimer's disease. Like aducanumab, BAN2401 targets aggregated forms of beta amyloid in the brain. One of the differences between the two programs is that a Phase II study with BAN2401 in 856 patients has been completed.

That study found that a statistically significant reduction in beta amyloid was achieved at 18 months and a statistically significant slowing of cognitive decline, by 30%, was achieved compared to placebo at 18 months. There was a strong correlation (84%) between beta amyloid clearance and slowing of cognitive decline in patients.

Biogen and Eisai appear to remain committed to the Alzheimer's disease space. In December last year Eisai announced the start of a Phase I study of an anti-tau monoclonal antibody, E2814.

While most late stage trials over the last decade have focussed on tackling Alzheimer's disease based on the theory that the disease is caused by the accumulation of beta amyloid, this series of setbacks is promoting the development of alternative approaches.

### **A Local Investment Perspective**

Three companies in Australia that are working on such alternative mechanisms are Actinogen Medical (ACW: \$0.055), Bionomics (BNO: \$0.17) and NeuroScientific Biopharmaceuticals (NSB: \$0.185)

Actinogen is the most advanced of these companies. It has a Phase II study underway of Xanamem, a small molecule inhibitor of 11B-HSD1. Xanamem works by reducing the levels of cortisol in the body. High cortisol levels have been shown to accelerate the

*Continued over*

effect of beta amyloid in Alzheimer's disease and also improve the cognition in healthy elderly men and in people with type 2 diabetes.

A Phase II study with Xanamem in 186 subjects has completed recruitment with results due mid year.

A Phase I study in healthy elderly volunteers started last month to explore higher doses of Xanamem at 20mg and 30mg per day (for 12 weeks) compared to the 10mg dose being investigated in the Phase II study. Changes in cognition will be measured in this study, with results expected to be released around the same time as the Phase II study results.

Bionomics has an Alzheimer's disease program that was licensed to Merck Sharp Dohme in June 2014. Bionomics has received US\$30 million in upfront and milestone payments in connection to the program. In February last year the program moved into a Phase I study. The compound licensed is a positive allosteric modulator of the alpha-7 nicotinic acetylcholine receptor.

NeuroScientific Biopharmaceuticals is expecting to start two Phase I trials this year with its drug candidate, EmtinB. EmtinB is a 14 amino acid peptide that is part of the sequence found on the neuroprotective protein, Metallothionein.

In preclinical studies, EmtinB has shown to promote neurite outgrowth from neurons and to have neuroprotective properties, including protection from the toxic beta amyloid protein.

The company will be assessing the compound initially in healthy volunteers, both for delivery into the eye for ophthalmic applications and as a systemic injection for the treatment of Alzheimer's disease.

A limitation with this treatment is the need to inject the compound, as well as the short three hour half-life.

Cogstate (CGS: \$0.26) has built a clinical trials services business with the majority of its work in the Alzheimer's disease area. The cancellation of multiple Phase III studies over the last 18 months has seen a slow down in the level of new contracts signed by the company.

*Bioshares* recommendations:

Actinogen Medical: **Speculative Buy Class B**

Bionomics: **Speculative Hold Class B**

NeuroScientific Biopharmaceuticals: **Not formally covered**

Cogstate: **Speculative Hold Class B**

**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 Some 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, LBT Innovations, Opthea, ResApp Health, Pharmaxis, Dimerix, Adalta, Actinogen Medical, Patrys, Cyclopharm, Emvision, Antisense Therapeutics

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