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Companies covered: 1AD, ACR, CGS, IPD, NAN, RHS, SOM

	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)	9.3%
Cumulative Gain	**705%**
Av. Annual gain (14 yrs)	**18.2%**

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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 –

Adalta Raises $10 Million from IPO

Adalta (1AD; $0.22) listed on the ASX on Monday, August 22, after completing an oversubscribed IPO. The company raised $10 million from the issue of 40 million shares at $0.25.

The company is developing a novel therapeutic protein, AD-114, for the treatment of lung fibrosis (idiopathic lung fibrosis). Adalta will also investigate AD-114 as a treatment for scarring in the eye.

The funds raised by Adalta will allow it to progress AD-114 into a Phase I clinical trial, expand its pipeline and also build the business development capabilities of the firm.

Adalta intends to seek a partner for the further development of AD-114 once it has confirmed the safety and efficacy of AD-114 in lung fibrosis.

Why IPF?

Idiopathic pulmonary fibrosis is a condition characterised by shortness of breath and worsening lung function. The condition's exact causes are not known i.e. there does not appear be one single cause.

What is known is that fibrosis (hardening) of lung tissue takes place because of abnormal functioning and signalling of alveoloar epithelial cells and interstitial fibroblasts (within the lungs). Fibroblasts are cells which form part of connective tissue.

Lung biopsies, radiography and CT scans are used in the diagnosis of the condition.

Idiopathic pulmonary fibrosis is an attractive market opportunity because there are few medicines available to treat the disease. These treatments only work to halt the progression of the disease, and do so poorly.

Patients diagnosed with IPF survive for an average of four years post diagnosis. The small number of patients with the condition means that it qualifies for Orphan Drug Disease status (<200,000).

Current drug treatments include steroids such as prednisone, immunosuppressants such as azathiorone and cyclophosphamide, the tyrosine kinase inhibitor nintedanib, and the antifibrotic agent pirfenidone.

Nintedanib (marketed by Boehringer Ingelheim) is a small molecule drug which inhibits multiple kinase receptors, including the platelet-derived growth factor receptors (PDGFR-alpha and -beta), the vascular endothelial growth factor receptors (VEGFR1, -2 and -3) and fibroblast growth factor receptors (FGFR1 and -2).

Cont'd over

Nintidanib, along with pirfenidone, became the first drugs approved by the FDA for IPF in October 2014. The US brand name for nintidanib is OFEV and for pirfenidone, Esbriet.

Roche completed its acquisition of Intermune, the developer of pirfenidone for US$8.3 billion, in September 2014.

Pirfenidone has a different mode of action to that of nintidanib, influencing or modulating TGF-beta, TNF, IL-10, p38-alpha and MRC5.

Impact on FVC

Nintedanib showed in two Phase III trials (n=1066) that it could arrest the decline of lung function as measured by the annual rate of decline in forced vital capacity (FVC).

The adjusted annual rate of change in FVC was 112.7 ml for nintedanib compared to 239.9 ml for the placebo group ($p<0.001$), or a 52.1% relative reduction. (These trials required the administration of drug over 52 weeks.)

In the 555 patient, ASCEND study, pirfenidone delivered a change in absolute FVC of 116ml, a relative difference of 41.5% ($p<0.0001$).

Impact on Mortality

From results combined from the ASCEND study and the 692 patients from the CAPACITY studies, pirfenidone reduced the risk of death at one year by 48% compared to placebo.

In the Phase III studies of nintedanib, there was no difference in the treatment groups and the placebo groups in death from any cause or death from respiratory cause.

AD-114 Mode of Action

Adalta's AD-114 has a different mode of action. It is designed to bind very selectively to the chemokine receptor CXCR4. This receptor is elevated in what are called 'fast progressing' IPF patients. The company has shown in an animal model that AD-114 can inhibit fibrocyte migration to the lungs and it has also shown that AD-114 does not inhibit normal, as opposed to progressor, fibroblast cells. This would appear to confer an advantage over nintidanib, which cannot distinguish between either groups of fibroblast cells, and pirfenidone which does not affect normal fibroblast cells but is not able to affect progressor fibroblast cells.

Investment Thesis

The investment thesis pertaining to Adalta begins with the fact that there are now two drugs on the market for IPF. These two drugs supply a clinical and regulatory road map, as well as benefits and safety profiles that competitors can aim to better. Such features will be relevant to the companies with whom Adalta will seek to partner AD-114.

A second point is that deal flow in the IPF area has proved that large pharmaceutical companies have an appetite for new approaches in the field, including in the protein drug technology space.

In September 2015, Roche acquired Adheron Therapeutics, for up to US$550 million, for its antibody, SDP051, which targets the cell surface protein cadherin-11. The upfront payment was US$105 million. SDP051 had completed a Phase I safety study.

In August 2015, Bristol-Myers Squibb paid an upfront of US$150 million for Promedior for the right to acquire the company, with US$1.25 billion in milestone and other payments to follow. The object of the deal was PRM-151, a recombinant form of human pentraxin-2 protein. This protein targets monocytes and macrophages in areas of tissue damage and also, according to a company statement, "prevent and reverse fibrosis". PRM-151 is currently being evaluated in Phase II trials for IPF and myelofibrosis.

Adalta's workplan for the remainder of 2016 and throughout 2017 includes manufacturing drug material for toxicology studies followed by a Phase I trial in 2018.

In parallel, however, the company will be releasing more pre-clinical data that will hopefully strengthen the scientific basis for the AD-114 role in IPF as well as in its ability to influence hypertrophic scarring (scarring related to skin damage).

The appeal of Adalta is that it is a company that has the potential to cut one, maybe more, very large deals and do this at an early stage in the development process. This is because of the largely uncontested, or historically unsuccessful, field of IPF drug development and the fact that current treatments, including pirfenidone and nintidanib, do not have a game-changing impact on the disease.

Another attraction with the company's protein drug technology is that it can potentially give rise to protein drugs that could be administered orally or inhaled, unlike many protein drugs which must be injected. However, this multiple-routes-of-administration feature will have to be thoroughly tested and proven in humans before it is to be of any value to the company.

Adalta is capitalised at $22 million.

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, Opthea, Reproductive Health Science, Regeneus, Innate Immunotherapeutics, Anatara Life Sciences, ResApp, Pharmaxis, Starpharma, Antisense Therapeutics, Atcor Medical, Dimerix, Cyclopharm, Adalta