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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

26 August 2016
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Delivering independent investment research to investors on Australian biotech, pharma and healthcare companies

A Major Setback for Acrux

Acrux (ACR: $0.40) received very disappointing news this week. Its core patents around its Axiron testosterone product in the US were invalidated by a US court (United States District Court for the Southern District of Indiana). The company's share price slumped 42% over the week, with the first generic competitor, Watson (Teva), now able to launch its generic version of Axiron in the US.

Watson has a tentative approval for its generic from the FDA and this will shortly move to a final approval from the regulator. Acrux and its partner Eli Lilly quickly announced that they will appeal the decision. The generic competitors are now likely to launch their products in the US 'at-risk', which means that if the appeal is successful they will have to pay damages to Eli Lilly.

Watson will be the first generic and will have a 180 day exclusivity period before the next generic is able to launch. There are around three other generics expected, with Perrigo also having a tentative approval. Another product on the market, Androgel 1%, has had generic competition for around 18 months with only two competitors on the market. It is not a massive market for generic players, with Axiron sales last financial year reaching US$149 million.

The appeals process is likely to take less than 12 months according to Acrux CEO Michael Kotsanis. Acrux will continue to receive royalties from Axiron sales for the life of the product. Kotasanis said he believes the company has good grounds for appeal. The judgement took four weeks to put together and covers 219 pages. The appeal will be held in Washington which Kotsanis said is a highly experienced court in assessing patent disputes.

Acrux generated Axiron royalty revenue of $25.3 million in FY2016. This income can be expected to reduce substantially in the current year. Acrux finished the year with $29.4 million in cash and as a result of this week's news has halted its dividend program.

Comments

The District Court decision is surprising given that both patents that have been invalidated were approved by the US Patent Office and also in other jurisdictions around the world. The invalidity of the formulation patent, which gave protection out to 2017, is particularly surprising given it is more tangible and specific than the axilla patent (due to expire in 2027) which is less specific and covers the delivery of pharmaceutical products to the armpit.

While the decision is very disappointing for investors, over the last 18 months Acrux has put together an extremely well considered business plan for the next stage of growth for the Acrux business. This includes the development of a suite of topical generic products and a development program in onychomycosis (fungal infection of the toe nail).

Cont'd over

Reproductive Health Science Launches DOPlify

Reproductive Health Science (RHS: $0.092) has launched a new product DOPlify. DOPlify will complement its pre-implantation genetic screening (PGS) EmbryoCellect microrarray kits with a product designed for use with high-throughput instruments, which are often labelled as Next Generation Sequencing (NGS) systems or technologies.

The company's single cell genomic technology is used to determine if embryos intended for IVF implantation have the correct number of chromosomes. Embryos without the correct number of chromosomes represent one of the major sources of a failure to embryos that are transferred to convert to successful clinical pregnancies. This has a failure rate of 70%.

RHS has added an NGS product offering in order to increase its appeal to potential customers, some of whom would be in a position to run tests at the volume associated with NGS testing as well as meet the requirements of customers also seeking a preimplantation genetic diagnostics (PGD).

DOPlify is also not limited to the area of PGS, having the potential for application in other areas where whole genome amplification of a single or small number of cells is required.

The use of RHS's single cell whole genome amplification technology could be extended, for example, into the animal health and pathology sectors.

On an NGS platform, a minimum of 24 embryos are needed.

Progress with EmbryoCellect

The selling of EmbryoCellect and management of customer relationships continues to be refined by RHS. Training constitutes a significant challenge for the company, both in terms of the resources required, and the ability of trainees to learn and follow the protocols required for EmbryoCellect.

The company has developed a new web-based training program. On site training can take up to four days and can be limited to the staff of one lab, with staff from rival labs in the same geographic location generally not welcome over an extended or week long period. Webinars allow RHS staff to access more technical staff requiring training, from rival companies, in the same area.

The company currently completed a web-based program for customers in Israel and has four more in the pipeline.

Summary

The take-home message from RHS's launch of DOPlify is that it can now offer non-IVF and IVF markets with a single cell, whole genome amplification NGS offering, thus bringing it into competition with Rubicon Genomics, Sigma, Qiagen and Yikon Genomics.

Reproductive Health Science is capitalised at $5 million.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

– Acrux cont'd

The formulation of the company's first three topical generic products has been completed. These three products have an addressable market worth in excess of US$500 million in the US. The development of these first three generics remains unaltered at this point with the first product expected to be launched in the US in 2019 with all three to reach the market by 2021.

The onychomycosis program will cost around $30 million to bring to market. This program combines an existing antifungal drug with an improved delivery profile.

The outcome of the patent decision means there may be a curtailment of the R&D program. In 12 months time Acrux had expected to have between five to seven generics in development. So it is possible that the rate of topical generic development may need to be slowed.

Acrux may also need to partner the onychomycosis program earlier, or alternatively discontinue the program, if a reappraisal of its budget and ROI analysis of programs results in a downwards re-rating. These are the options that the company has to reduce its cash expenditure. We also believe that Acrux also has the option to return to capital markets in the future, provided it can offer a coherent investment proposition.

Acrux has previously stated that it believes the revenue from the generic products in development could match last year's Axiron royalty revenue by the early part of next decade.

The attraction of the generic *topical* market is a lower level of competition. Acrux is applying its experience in topical drug development to this market opportunity.

Bioshares recommendation: **Speculative Hold Class B**

(The stock has been removed from the Bioshares Model Portfolio)

Bioshares

Full Year Results Wrap: SOM, NAN, IPD, CGS

Somnomed – Sales to Exceed 70,000 Devices in FY17

Somnomed (SOM: $3.48) increased revenue by 28% to $44 million in FY2016. Net profit for the year fell by $0.4 million to $0.16 million. Overall unit sales growth of the company's mandibular splints (used for the treatment of sleep disordered breathing) increased by 15% for the year to 58,983 devices. However, growth in devices through the company's direct distribution channels increased by 29% for the year.

There has been very good take-up of the company's new products in the US, with the Somnodent Herbst Advance product now making up 22% of direct sales. The Somnodent Air and Somnodent Air+, which are budget versions of other similar Somnodent products, made up 7.9% of direct sales in the US.

Somnomed is forecasting a 20% growth in unit sales this year to over 70,000 devices. Revenue is forecast to grow by 23% to over $54 million. The company is expecting EBITDA to double to $4 million in the year.

In May this year Somnomed announced that it would roll out five sleep treatment centres in the US under a new entity called Sleep Centres America Inc (SCA). That business is expected to treat over 1,000 patients this year (with Somnomed products), generate revenue of over $2 million, producing an EBITDA loss of $4 million. By the end of FY2018, SCA expects to have 18 centres operational in the US.

Somnomed owns 84% of SCA, with the balance owned by operators of a similar sleep treatment business in Texas. Somnomed expects to invest around $500,000 in each new centre, with each centre expected to reach breakeven within 12 months.

Somnomed finished the year with $17.6 million in cash. It is trading at a price-sales ratio (less cash) of 3.3 times based on forecast FY2017 sales.

Bioshares recommendation: **Buy**

Nanosonics – 22% Market Penetration in Nth America

Over FY2016, Nanosonics (NAN: $3.00) increased its installed base in North America by 74% to over 8,700 systems (22% market penetration) and 10,000 units globally (8.3% market penetration).

For the 2016 financial year sales increased by 93% over the previous year to $42.8 million. The company made a full year profit of only $0.12 million. However it moved through an important inflexion point during the year delivering a net profit of $3.4 million in the second half of FY2016.

Nanosonics increased its R&D expenditure by 50% to $7.3 million last year. It has increased its sales staff by 18% over the year to 150 employees.

The company has not made forecasts for FY2017. However, it has indicated that the global addressable market for Nanosonics' Trophon EPR ultrasound probe disinfection systems is 120,000 units, with the potential market in North America alone being around 40,0000 systems.

Nanosonics generates sales from Trophon systems, from accessories, service, and consumables. Consumables make up around 35% - 40% of revenue at this point. At its current trajectory, we estimate sales over FY2017 will reach $90 million.

Nanosonics is capitalised at $888 million. The company finished the year with $49 million in cash.

Bioshares recommendation: **Hold**

Impedimed – Stronger Sales Growth Anticipated

Impedimed (IPD: $1.53) increased its revenue over the year by 21% to $5.8 million. After spending much of 2015 preparing for the full commercial launch of the company's L-Dex product in the oncology area, the company set a target of gaining entry of its product into 50 leading centres in the US over calendar year 2016. By mid year the company was well on track, having secured entry to 33 leading cancer centres.

Over 2017, Impedimed is aiming to have its L-Dex product installed and integrated at an additional 50 major cancer centres in the US. It is seeking to have its technology adopted as the standard-of-care in the management of patients who have undergone cancer surgery to prevent the occurrence and progression of lymphedema.

Earlier this month the company surprised investors by announcing that its next product, SOZO, had been launched for use in the health and wellness markets. The new product will allow users to monitor fluid build up in the body at home to track per-

Selected FY2016 Results Summary

Company	Sales	PCP change	NPAT ($M)	Forecast FY2017	Cap'n ($M)
Cogstate	$27.1	69%	$2.6	20% growth in sales contracts (US$33.5M)	$85
Somnomed	$44.1	28%	$0.2	$4.0 million EBITDA	$197
Nanosonics	$42.8	93%	$0.1	$90 million in sales*	$888
Impedimed	$5.8	21%	-$26.0	Stronger sales growth*	$572

** Bioshares estimate*

Cont'd over

– Impedimed cont'd

sonal performance. SOZO will also be used by Scripps Health in a validation study in monitoring patients with heart failure as a lead up into a pivotal study for this new application of the company's bioimpedance technology.

Data from Impedimed's long term study in preventing lymphedema following locoregional treatment for breast cancers should start to emerge in early 2017. This data is expected to support reimbursement of the technology across private payors, with CMS reimbursement in the public health system already in place in the US.

Impedimed finished the year with $82.3 million in cash. Stronger sales growth can be expected in this financial year. Impedimed is capitalised at $572 million. Impedimed continues to position itself very well for widespread adoption of its products into multiple markets. We view the stock as a takeover target, a factor supporting a continuation of a Speculative Buy Class A recommendation.

Bioshares recommendation: **Speculative Buy Class A**

Cogstate – Boosts Staff by 47% to 129

Cogstate (CGS: $0.76) has delivered an EBIT result of $1.0 million for the year (NPAT of $2.6 million which included a $1.6 million tax benefit). The EBIT result was a $4 million turnaround after the $3.0 million loss in the previous year.

While the headline figure was within our forecast sales of between $27 - $28 million, the EBIT was lower than our pre-tax profit forecast of between $2.1 - $3.8 million. For the year, revenue increased by 69% to $27 million. Contracts signed increased by 20% to US$28.5 million.

For the year ahead, Cogstate expects contract signings to increase at a similar rate (which would see new contracts signed worth around US$33.5 million). The company also has contracted revenue to date for FY2017 worth $17.5 million. Based on these numbers, we estimate revenue for the current financial year of between $37 - $40 million.

Costs for new product development were $3.29 million in FY2016. This is expected to increase to between $5.5 - $6.0 million this year. R&D has focused on upgrading the company's software platforms. Our estimate for profit before tax for FY2017 is between $3.0 - $4.8 million.

Cogstate has increased its employee count by 47% over the last year to 129 staff.

Bioshares recommendation: **Speculative Buy Class A**

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).

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.

Cont'd over

Bioshares Model Portfolio (26 August 2016)

Company	Price (current)	Price added to portfolio	Recommend-ation	Cap'n ($M)	Date added
GI Dynamics	$0.029	$0.024	Spec Buy B	$14	May 2016
Adherium	$0.480	$0.495	Spec Buy A	$80	March 2015
Bionomics	$0.245	$0.295	Spec Buy A	$118	March 2016
Reproductive Health Science	$0.092	$0.150	Spec Buy B	$5	December 2015
Rhinomed	$0.021	$0.032	Spec Hold B	$17	December 2015
AirXpanders	$1.120	$0.745	Spec Hold A	$264	September 2015
Osprey Medical	$0.360	$0.695	Spec Buy B	$69	September 2015
Atcor Medical	$0.130	$0.20	Spec Buy A	$26	June 2015
Clinuvel Pharmaceuticals	$5.15	$4.15	Spec Buy A	$246	December 2014
Innate Immunotherapeutics	$0.415	$0.190	Spec Buy A	$82	November 2014
Opthea	$0.550	$0.160	Spec Buy A	$83	November 2014
pSivida	$5.100	$3.800	Spec Buy A	$174	May 2014
Impedimed	$1.530	$0.245	Spec Buy A	$571	December 2013
IDT Australia	$0.220	$0.260	Spec Buy B	$54	August 2013
Viralytics	$0.915	$0.300	Spec Buy B	$220	August 2013
Somnomed	$3.48	$0.94	Buy	$192	January 2011
Cogstate	$0.760	$0.13	Spec Buy A	$90	November 2007

Portfolio Changes – 26 August 2016

IN:
No changes

OUT:
Acrux removed

– Adalta cont'd

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