ISSN 1443-850X

Companies covered: ALT, CGS, CIR, PYC, RNO

	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 14 (May '15 - current)	2.8%
Cumulative Gain	**470%**
Av. Annual gain (14 yrs)	**16.7%**

Bioshares is published by Blake Industry & Market Analysis Pty Ltd.

Blake Industry & Market Analysis Pty Ltd
ACN 085 334 292
PO Box 193
Richmond Vic 3121
AFS Licence
No. 258032

Enquiries for *Bioshares*
Ph: (03) 9326 5382
Fax: (03) 9329 3350
Email: info@bioshares.com.au

David Blake - Editor
Ph: (03) 9326 5382
Email: blake@bioshares.com.au
Mark Pachacz - Research Principal
Ph: 0403 850 425
Email: pachacz@bioshares.com.au

Individual Subscriptions (48 issues/year)
$440 (Inc.GST)
Edition Number 608 (10 July 2015)

Bioshares

10 July 2015
Edition 608

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

Clarus Ventures Eyes Circadian Technologies

This week Circadian Technologies (CIR: $0.20) CEO, Megan Baldwin met with investors and analysts in Sydney and Melbourne. Dr Emmett Cunningham, a partner with San Francisco-based life sciences venture capital firm, Clarus Ventures, also spoke.

Dr Cunningham is an eye specialist who for the last 20 years has been involved in the development of ophthalmic drugs, either directly through pharmaceutical companies or as a venture capital investor. He has contributed to more than 300 publications. He led the team which developed and commercialised the first VEGF-A inhibitor for the eye, Macugen, at Eyetech Pharmaceuticals, for which Pfizer acquired US rights. That drug has since been followed by the VEGF-A inhibitor, Lucentis (ranibizumab), developed by Genentech and the VEGF-A and VEGF-B trap molecule Eylea (aflibercept), developed by Regeneron.

Clarus Ventures has US$1.7 billion in funds under management. Clarus invests around 10% of its funds in ophthalmic programs, having invested in five ophthalmic companies, including Ophthotech Corporation, which is currently capitalised at US$1.85 billion.

Ophthotech's lead program is a Phase III drug candidate, Fovista (a novel aptamer technology), that is being tested in combination use with Lucentis in wet age-related macular degeneration. The first of three Phase III trial has completed recruitment. (*A table listing selected wet AMD drugs in development can be found on the next page*.) Ophthotech is a very relevant company for Circadian, because Circadian is also looking to develop a combination therapy with existing VEGF-A inhibitors.

This month Circadian started a Phase I study OPT-302, in combination with Lucentis. OPT-302 is a soluble receptor protein i.e. a soluble version of the Vascular Endothelial Growth Factor (VEGF) receptor R3. It works as a trap molecule, or sponge, for the circulating growth factors (cytokines) VEGF-C and VEGF-D.

Preclinical studies have shown that combining OPT-302 with Eylea improves on Eylea alone. While sales of Lucentis and Eylea generate billions of dollars in sales each year (Eylea sales in 2014 were US$1.74 billion, up 23%), the drugs need to be injected every four to eight weeks, and more than half of the patients receiving these drugs do no achieve significant vision gain. However Dr Cunningham said these drugs are still very potent therapies.

Market Opportunity Lies With Non Responders to Lucentis and Eylea

This leaves a large market opportunity for a combination therapy approach with the existing standard-of-care (Lucentis and Eylea) that can potentially increase the number of responders to treatment, increase the magnitude of response, and extend the response time, reducing the frequency of injections into the eye.

Dr Cunningham has been advising Circadian since its last capital raising in October last year, when the company raised $17.4 million. Although Cunningham is not an investor

(through Clarus) at this stage in Circadian, he has been advising the company on its clinical trial design and is following the company's progress as well as two or three other companies in the same space.

The implication for investors is that if the Phase I and Phase II trials deliver a positive result, then Clarus Ventures is a potential investor in the company, either after Phase I or Phase II studies.

Circadian is currently fully funded to the end of Phase IIb study results, which are expected by the end of 2017. The Phase I trial is recruiting patients with wet AMD who have shown a sub-optimal response to existing VEGF-A therapies as well as treatment naïve patients. It can be expected that more treatment naïve patients will be recruited into the study as the safety of the combination therapy is better understood, once what are expected to be efficacious doses are reached. The benefit of recruiting treatment naïve patients, according to Dr Cunningham, is that a clearer result with drug treatment can be achieved than with patients who have what he termed 'end-stage eyes'.

Results from the Phase I study are expected toward the end of the first quarter of 2016. Depending on when sufficient data is available, Dr Cunningham said that if the data was right then Clarus Ventures will invest in Circadian. Even though Circadian is fully funded until the end of the Phase IIb trial, if the data is promising, then there may be a push (from Clarus) for the company to raise additional funds earlier to conduct larger Phase II studies.

Dr Cunningham believes that there is investor fatigue with Circadian, with the valuation being part of the attraction with the company. There is a very favourable risk-reward profile with the stock. The chance for clinical success with a biologic drug at the Phase I stage of development he believes is between 40%-60% for a validated target; the potential upside is a 50-fold gain for investors.

Aside from valuation, the appealing aspects of OPT-302 for Dr Cunningham are that it works in a known pathway, with evidence of the role that VEGF-C and VEGF-D play in wet AMD now known.

So what results should investors be monitoring with Circadian's trial? According to Cunningham, retinal thickness is one endpoint to follow. However, the most important measure is a gain in vision. Achieving five letters or more improvement in visual acuity (which is what Ophthotech achieved with Fovista) would be a value creating result, he said.

Circadian is capitalised at $30 million.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Selected Phase II and Phase III Trials, Wet Aged Related Macular Degeneration Therapies

Sponsor/Collaborators	Interventions	MOA	Combination Agents or Controls	Phase	Enrollment
Ophthotech Corporation	Fovista (E10030)	anti PGDF aptamer (nucleic acid)	bevacizumab or aflibercept E10030 sham intravitreal injection	Phase III	622
Ophthotech Corporation	Fovista (E10030)	anti PGDF aptamer (nucleic acid)	ranibizumab E10030 sham intravitreal injection	Phase III	622
Allergan	abicipar pegol	anti VEGF DARPin	ranibizumab sham procedure	Phase III	900
Allergan	abicipar pegol	anti VEGF DARPin	ranibizumab sham procedure	Phase III	900
Alcon (Novartis)	RTH258 solution for IVT injection	High-potency scFV VEGFi	Aflibercept solution for IVT injection	Phase III	1600
Alcon (Novartis)	RTH258 solution for IVT injection	High-potency scFV VEGFi	Aflibercept solution for IVT injection	Phase III	1200
Santen	DE-120 (TRC-105)	anti-endoglin antibody	Aflibercept	Phase II	30
Ophthotech Corporation	Fovista	anti PGDF aptamer (nucleic acid)	bevacizumab ranibizumab aflibercept	Phase II	60
Maturi, Raj K., M.D., P.C.	Sirolimus (rapamycin)	mTor pathway inihibitor	Standard of Care intravitreal injections of anti-VEGF	Phase II	30
Tyrogenex	X-82	VEGF and PDGF inhibitor, small mol	Aflibercept Placebo	Phase II	132
Iconic Therapeutics	hL-con1	factor VII-IgGFc chimeric protein targeting tissue factor	ranibizumab Sham injection	Phase II	90
Alcon (Novartis)	LHA510 ophthalmic suspension	Topical VEGFi	LHA510 vehicle Ranibizumab ophthalmic solution	Phase II	60
Allergan	abicipar pegol	anti VEGF DARPin	ranibizumab sham procedure	Phase II	25
Bayer	Regorafenib, ophthalmic oily suspension (BAY73-4506)	small molecule inhibitor of VEGFR2 and TIE2	Sham IVT Ranibizumab Placebo	Phase II	350
Roche	RG7716	cross mab binding to VEGF-A and ANG-2	Ranibizumab	Phase II	271
Regeneron Pharmaceuticals	REGN2176-3	PDGFbeta receptor antbody combined with Elyea (aflibercept)	Intravitreal Aflibercept Injection (IAI)	Phase II	500
Alcon (Novartis)	LMG324	Long-acting anti-VEGF Ab	Ranibizumab 0.5 mg Sham	Phase I/II	106
Neurotech Pharmaceuticals	NT-503-3 ECT implantation	Implant: encapsulation of a human RPE cell line transfected to produce VEGF-R	Eylea injected intravitreally administered every 8 weeks	Phase I/II	170

Source: clinicaltrials.gov; company reports, filings and websites

Rhinomed – It's Not About The Bike

Rhinomed (RNO: $0.030) has signed on 2013 Tour de France winner and the current leader of the Tour de France, Chris Froome, as its Global Ambassador of the Turbine, a nasal stent that is used in sports to increase airflow through the nose and into the lungs.

Froome wore the Turbine in the first stage of the Tour and has even worn the Turbine during interviews with media. His official comments about the device in the media release by Rhinomed were: "It's a great piece of equipment. Less energy and distraction with breathing means I can use more energy in other important parts of my riding, like focusing on power, cadence and keeping my head in the game."

But for Rhinomed, the cycling market for its nasal stents is not the primary market. CEO Michael Johnson said the application of the technology in the sleep area is expected to dwarf sales into the sports market. The first sleep product is called Mute.

That is not to say that the sports application does not play a crucial role for the company. Getting the Turbine adopted by elite sports people such as Froome builds what Johnson refers to as the socialisation of the device. As customers see people such as Chris Froome using the device in the Tour de France, then people will be more disposed to wearing the device during sleep.

Seattle Sleep Conference

Last month Rhinomed attended the Seattle Sleep conference. Johnson was surprised at the level of interest the company received. He said the company receive good interest from multiple channels, including dentists, sleep specialists, ENT specialists, hospitals and sleep clinics, from using the device not just on its own, but as an adjunct therapy to CPAP and oral devices, such as Somnomed's mandibular advancement splints. "They instantly got it!"

Johnson said there was 'extreme interest' in the company's latest sleep product in development, INPEAP, which is an acronym for Intra Nasal Positive Expiratory Airway Pressure. This device stents the nose, but includes a one way valve that restricts the air leaving the nose. The aim is to achieve a similar effect to the CPAP device, which is a positive airway pressure during sleep to prevent sleep apneas.

Last month Rhinomed received approval to commence a Phase I study with the INPEAP device in Melbourne in 20 patients with moderate obstructive sleep apnea (OSA). The primary outcome of the study, being conducted at the Monash Lung and Sleep Department, is seeking to determine if the INPEAP device can attenuate OSA. Results are expected at the end of this year.

An enormous market opportunity exists in the sleep space. CPAP targets those with severe sleep apnea, which represents around 30% of the market. People with moderate OSA make up 70% of the market. The existing market is poorly served with CPAP with compliance rates below 40%. And oral stents represent only a small percentage of the market in the US at present.

Rhinomed sells its products on-line (www.theturbine.com and www.mutesnoring.com) as well as through distributors. It has also been testing an affiliate sales approach, where third parties with large customer bases offer the company's products for a split of initial sales only.

Rhinomed is capitalised at $16 million.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

Innate Immunotherapeutics Flags Oral Formulation For MIS416

In its annual report released last month, Innate Immunotherapeutics (IIL: $0.175) announced that it was close to half way through with its enrolment into its 90 patient Phase IIb study in secondary progressive multiple sclerosis (SPMS). At the time of the report, 45 patients had either been enrolled, were being screened for enrolment, or were coming off previous medications to allow commencement in the study.

The study is taking around a year longer to complete than originally expected, with full enrolment now expected around October/ November this year. One reason for the delay is that it has been easier to recruit patients in New Zealand. This is because in Australia patients remain on medications longer for relapsing-remitting MS even though they have moved on to SPMS (when RRMS medications are not effective).

Innate originally had four trial sites in Australia in Melbourne, Brisbane, Perth and Adelaide. It added a site in Wellington, New Zealand, which hit its target recruitment within three months. Brisbane is another site recruiting well, with additional patients to be potentially recruited in Wellington and Brisbane.

CEO of Innate, Simon Wilkinson, said he believes the company's drug candidate makes a fundamental difference to patients with SPMS, for which there are no treatment options.

Innate also indicated that in the year ahead it intends to carry out preclinical work on oral formulations of MIS416. MIS416 is dosed weekly through an intravenous infusion. Some patients taking the drug on compassionate use in New Zealand have found that the frequency of delivery of the drug could be lowered after six months of treatment, to once every two, three of four weeks. It is possible that an oral version of the drug could be used as a maintenance therapy after six months or so of treatment in the future.

Innate is capitalised at $29 million. The company had $4.1 million in cash at the end of March. We expect the company will need to raise additional funds in the next six months to get the company to the end of the Phase IIb study, which should occur towards the end of 2016.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Phylogica to Raise $10 Million

Phylogica (PYC: $0.013) has announced that it is raising $10 million in a fully underwritten entitlement issue. The offer is fully underwritten by Paterson Securities, with the offer sub-underwritten by the company's largest shareholder, Dr Bernard Hockings. After costs, the capital raise will deliver Phylogica an additional $8.8 million in funds to develop its cell penetrating peptide technology.

It is a noteworthy capital raise by the company for several reasons. The issue price will be 1 cent per share, which represents a 56.5% discount to the company's closing price before the capital raise was announced. It is Phylogica's largest capital raise and gives the company an estimated two to three years of funding. At the same time there is significant dilution, with the company doubling the number of shares on issue.

Of interest is that the company's largest shareholder is sub-underwriting most raise (952 million shares), for a fee of $1.1 million. Dr Hockings is showing a very strong commitment to the company. Currently he has a 25% share (255 million shares) in Phylogica. Under the underwriting agreement, Dr Hockings will take up the first 400 million shortfall shares in capital raising.

In order to reduce his control in the company, Dr Hockings has entered into an agreement to sell 142 million of his shares in Phylogica in a block sale prior to the closing date of the offer. Phylogica has received commitments from other large shareholders for 91 million shares in the offer.

The capital raise places the company in a considerably stronger financial position. At the end of March the company had $3.1 million in funds. On a pro-forma basis, the company had $10.7 million in cash at the end of May, taking into account this capital raising.

The majority of the funds raised will be used to conduct lead optimisation, confirm effectiveness of its leads in in-house animal models, and conduct preclinical studies. This will potentially be enough to gain the interest from pharmaceutical partners.

Getting good animal data (across a number of models) is a tipping point for Big Pharma believes CEO Richard Hopkins. Hopkins believes the value of the company's platform should rise immeasurably when it can deliver lead compounds, and convince potential partners that it can turn its platform into drugs.

Around 50% of all deals done are with companies at the preclinical or discovery stage according to Hopkins. This early stage deal interest is supported by acquisitions in the last 12 months of Fibrotech for an initial US$75 million and Pharmaxis' $39 million upfront sale of its NASH compound to Boehringer Ingelheim.

Phylogica is capitalised at $26 million following the raise. Entitlement date for the offer is 9 July and the offer closes on 23 July.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

Cogstate Grows Contracts

In a recent investor update, Cogstate (CGS: $0.215) revealed that it expects to move into profitability in this financial year. The company now employs more than 90 staff across four countries. Its main revenue (97%) is from providing its cognitive test for use in clinical trials, with an emphasis in Alzheimer's disease drug trials. Its test is provided in 45 countries with over 22,000 patients having being assessed with the test to date.

The company signed at least US$23 million ($30 million) in sales contracts in the last financial year. This is up substantially on the contracts signed in FY2014, which totaled only US$9 million.

The increase in sales can be attributed to a new and well resourced sales team in the US, provision of additional services in clinical trials (rater training in Alzheimer's disease trials), an escalation in early stage clinical studies in Alzheimer's disease, new regulatory requirements for cognition measurement in pediatric clinical studies, and increased activity in schizophrenia and depression drug trials.

For the year ahead, Cogstate already has around $11 million of contracted revenue that is expected to be generated from existing contracts in this financial year.

Further upside can be expected to come from signing of new contracts, as well as high margin revenue from the company's Precision Recruitment product.

Precision Recruitment is a service whereby Cogstate helps screen patients into Alzheimer's disease studies. Currently the screening failure rate for Alzheimer's trials is around 95%.

If Cogstate can improve the enrolment rate into these studies, even by only a small amount, by correctly identifying those with Alzheimer's disease, then it will become an important revenue stream for the company. If that occurs then its service can be expected to be in strong demand from other pharmaceutical and biotech companies conducting Alzheimer's disease drug trials.

In the first nine months of FY2015, Cogstate generated receipts from customers of $11.7 million, with a net cash outflow of $3.3 million. Cogstate is expected to report a stronger second half of FY2015, with a positive EBITDA for the second half as a result of a significant increase in clinical trial sales.

Cogstate had $3.2 million cash at the end of March, with an additional $2 million from a placement to Alan Finkel in May, who has joined the board of the company.

Cogstate is capitalised at $23 million.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Bioshares Model Portfolio (10 July 2015)

Company	Price (current)	Price added to portfolio	Recommend-ation	Cap'n ($M)	Date added
Atcor Medical	$0.18	$0.20	Spec Buy A	$33	June 15
Clinuvel Pharmaceuticals	$2.85	$4.15	Spec Buy A	$127	December 14
Innate Immunotherapeutics	$0.175	$0.190	Spec Buy A	$30	November 14
Circadian Technologies	$0.200	$0.160	Spec Buy A	$30	November 14
Actinogen	$0.076	$0.050	Spec Buy A	$46	September 14
pSivida	$5.120	$3.800	Spec Buy A	$151	May 14
Impedimed	$0.830	$0.245	Spec Buy A	$243	December 13
IDT Australia	$0.225	$0.260	Spec Buy B	$43	August 13
Viralytics	$0.725	$0.300	Spec Buy B	$133	August 13
Somnomed	$2.74	$0.94	Buy	$139	January 2011
Cogstate	$0.200	$0.13	Spec Buy A	$21	November 2007

Portfolio Changes – 10 July 2015

IN:
No changes

OUT:
No changes

Analytica to Raise $3.7 million

Analytica (ALT: $0.011) has announced a renounceable rights issue to raise $3.7 million. Paterson Securities is the lead manager and the company is finalising arrangements with the manager to partially underwrite the issue. The rights issue is being conducted at 0.8 cents a share, which is well down from the company's 12 month high of 4.2 cents a share.

The funds raised will be used to support the launch of the company's PeriCoach pelvic floor training product in the US, where a promotional campaign commenced last month with the official sales launch on 23 June. The funds will also be used to launch the product into Europe with official marketing in the UK starting also last month.

Analytica recently announced the appointment of a distributor for the US market, Current Technology Inc. The distributor has been selling products into the pelvic rehabilitation market for 24 years and will be marketing the PeriCoach system through its existing sales force. Current Technology will purchase the PeriCoach at wholesale prices from Analytica. It is a non-exclusive arrangement and will supplement Analytica's own direct sales efforts.

The company's securities commence ex-rights trading from Tuesday 14 July. It's an important raise for the company to support the commercial launch of the PeriCoach system. At the end of March, Analytica had $2.0 million in funds, with a cash burn of $3.2 million in the nine months to March.

Bioshares recommendation: **Speculative Buy Class C**

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, Admedus, Invion, Imugene, Analytica, Circadian Technologies, Reproductive Health Science, Regeneus, Innate Immunotherapeutics, Anatara Life Sciences, ResApp, Pharmaxis

Subscription Rates (inc. GST)

48 issues per year (electronic distribution): **$440**

For multiple email distributions within the same business cost centre, our pricing structure is as follows:	$700	2-3 email addresses
	$940	4-5 email addresses
	$1200	6-10 email addresses

To subscribe, post/fax this subscription form to:

Bioshares
PO Box 193 Richmond VIC 3121
Fax: +61 3 9329 3350

I enclose a cheque for **$** made payable to **Blake Industry & Market Analysis Pty Ltd**, or

Please charge my credit card **$** MasterCard ☐ Visa ☐

Card Number ☐☐☐☐ ☐☐☐☐ ☐☐☐☐ ☐☐☐☐

Signature _____ Expiry date _____

Subscriber details

Name _____

Organisation _____

Ph ( ) _____

Emails _____

_____

_____