ISSN 1443-850X

In this edition...
Alchemia will spin-off its cancer drug assets into a Nasdaq- and ASX- listed company named Audeo Oncology. A statement filed with the SEC authorises capital raisings of up to $60 million. Alchemia shareholders will receive shares in Audeo Oncology. Audeo will also be responsible for Alchemia's VAST carbohydrate platform, with Alchemia retaining income from its share of sales of fondaparinux. Sirtex Medical's sales grew at 23% for the FY2012, maintaining a strong trajectory. CBio shareholders will asked to vote on a merger with the privately-held, US-based Inverseon, a company repurposing a heart failure drug to treat respiratory conditions. We also introduce readers to GKC Corp, which is developing a system to measure movement disorders that characterise Parkinson's disease
Companies Covered: ACL, CBZ, SRX, GKC Corp

	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 - current)	-11.6%
Cumulative Gain	**205%**
Av. annual gain (11 yrs)	**17.8%**

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:(03) 9348 9317
Email: pachacz@bioshares.com.au

Individual Subscriptions (48 issues/year)
$375 (Inc.GST)
Edition Number 463 (13 July 2012)

Bioshares

13 July 2012
Edition 463

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

Alchemia's Audeo Oncology Files Registration Statement in Preparation for US IPO

Alchemia (ACL: $0.50) has reorganised its oncology unit. Alchemia Oncology has now become a wholly-owned subsidiary of the newly formed **Audeo Oncology.** Audeo Oncology has become a wholly-owned subsidiary of Alchemia. The plan is to demerge Audeo Oncology and list it both on the Nasdaq exchange (primary listing) and the ASX (secondary listing through Chess Depository Receipts).

The registration statement indicates that up to $60 million can be raised under that filing, however what the company intends to raise is to be determined by the company, its investment bankers Leerink Swann and Oppenheimer & Co, and will be dependent on market sentiment and market appetite for this product offering.

The demerger was announced in November last year. It is expected that the demerger will be put to a vote in September/October this year with a court hearing on the demerger, which will be effected through a scheme of arrangement, likely by early October.

Once approval is received, Audeo Oncology will seek to raise funds and list on the Nasdaq and ASX. Audeo Oncology received a $7.5 million loan from Alchemia last month, which was converted to equity. (Total loans that have been converted to equity that have been made by Alchemia to Audeo Oncology total $37.6 million.) Alchemia shareholders, not Alchemia, will own the shares in Audeo Oncology once the demerger is complete.

Audeo Oncology will trade on the Nasdaq under the code AURX. Alchemia's CEO Pete Smith and CFO Charles Walker will become Audeo's CEO and CFO, remaining at Alchemia for a short period after the demerger. The directors of Audeo Oncology are Pete Smith, Tracie Ramsdale (a founder of Alchemia) and chairman Stephen Hill.

Audeo Oncology is currently conducting a 390 patient study in colorectal cancer, using a combination of hyaluronic acid (which targets the tumour cells) and irinotecan (now a generic oncology drug), called HA-Irinotecan. Data from 39 patients was released in May showing no unexpected toxicities with the drug. The company has previously indicated it expects this trial to reach its primary endpoint in the second half of 2013.

Cont'd over

– Alchemia cont'd

Audeo Oncology – US Interest

Audeo Oncology is operating in two areas of oncology where there is active interest in US capital markets, those being drugs to specifically target cancer stem cells, and also in re-engineered versions of the oncology drug irinotecan.

Audeo Oncology's HyACT technology is believed to target cancer stem cells, with the HyACT binding to the activated CD44 receptor, which is expressed by cancer stem cells. Cancer stem cell company **Verastem**, has been one of the few biotechs to list in the US this year, raising US$55 million in January. It is capitalised at US$210 million. In March this year, **Merrimack Pharmaceuticals** listed in the US, raising US$100 million. Merrimack is also developing a new formulation of irinotecan for the treatment of pancreatic cancer. It recently started a Phase III trial in pancereatic cancer, and has a Phase II trial ongoing and two Phase I trials underway. Merrimack is currently valued at US$671 million.

Other Competition

According to the S-1 registration statement, other competitors include **Nektar Therapeutics**, which is developing a pegylated version of irinotecan. That drug candidate is in a Phase III trial in breast cancer and in two Phase II trials in metastatic colorectal cancer and in ovarian cancer.

Other Information from S-1 document

The S-1 filing by Audeo Oncology provides a helpful summary of the company's business, including opportunities and key risks. The patent position around the HyAct platform provides patent protection out to between 2020-2026, without taking into account any possible patent extensions.

The company may need to in-license two patents from **Pfizer** to commercialise parts of its technology, including the HA-Irinotecan therapy.

Also the regulatory risk has been raised, with which Australian investors have become very familiar. Audeo Oncology is using progression-free survival (PFS) as its primary endpoint in the current pivotal study underway. Whilst some cancer drugs such as Erbitux and Abraxane have been approved on a PFS endpoint, the FDA's policy is that the final endpoint in cancer drug trials be overall survival. The FDA may ask for a second pivotal study, which we believe will depend on the clarity of the results from the current Phase III study, and it may ask that overall survival be the primary endpoint of any subsequent studies, either pre or post-approval.

In the Phase II study with HA-Irinotecan in 76 patients with metastatic colorectal cancer, the progression-free survival was 5.2 months, almost three months more than patients taking irinotecan alone (2.4 months). This result was statistically significant. The overall survival benefit was 1.9 months, and this result was not statistically significant.

Phase II Lung Cancer Trial Underway

In September last year, an investigator-sponsored Phase II study in small cell lung cancer was initiated. About 40 first line patients are expected to be recruited. This is a very useful trial because it may prove the company's belief that HyACT targets cancer stem cells. In preclinical studies, it has been shown that HA-Irinotecan can target and kill the small cell lung cancer stem cells. The primary endpoint in this trial is the proportion of cancer stem cells remaining after HA-Irinotecan therapy compared to those patients taking irinotecan alone.

VAST Licensing Agreement

Audeo Oncology will exclusively license Alchemia's VAST technology in all but for one family of patents that are currently licensed to another party. Audeo Oncology will pay Alchemia 5% of revenue received by Audeo Oncology. Audeo Oncology will have to employ four full time equivalent researchers to exploit the VAST platform and will need to spend $1.5 million per year on developing the technology.

Market Opportunity

As a branded drug, irinotecan was sold by Pfizer as Camptosar. It generated sales of US$950 million in 2007, before it went generic in 2008.

The HyACT platform has shown to deliver superior results in at least eight different types of cancer therapies. The Phase III trial underway will be very important to validate the technology, which if successful, we believe will result in the technology being trialed with many existing cancer therapies, including use in conjunction with cancer monoclonal antibody drugs.

Summary

The demerger and listing of Alchemia Oncology provides an opportunity to unlock unrecognised value in Alchemia for shareholders. It also provides the company with separation and independence from the fondaparinux revenue and an opportunity to build a dedicated oncology drug business.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Sirtex Medical Sales Show Signs of Strength

Sirtex Medical (SRX: $6.30) sells a liver cancer therapy throughout the world. The technology, called Sir-Spheres, uses short half-life radioactive silicon spheres to kill tumour cells inside the liver. The company has delivered a very strong year of sales growth, with acceptance of the technology by oncologists strengthening.

For the full year, unit sales increased by 23% to just under 6,100 units (or treatments). This was an improvement on the 19% increase in FY2011. Sales in the third quarter of this financial year increased by a very impressive 34%, and in the fourth quarter the increase was 26% in unit sales. It should be noted however the strong un-turn in the fourth quarter of FY2011, which makes results from the quarter just passed even better.

In the first half of FY2012, Sirtex generated revenue of $36.8 million, with just under 2,700 units sold. Unit sales in the second half increased by 26% over the first half, which we estimate should translate into sales for the half of $46 million, and around $83 million for the full year (with the currency against the USD being constant on average in the two halves).

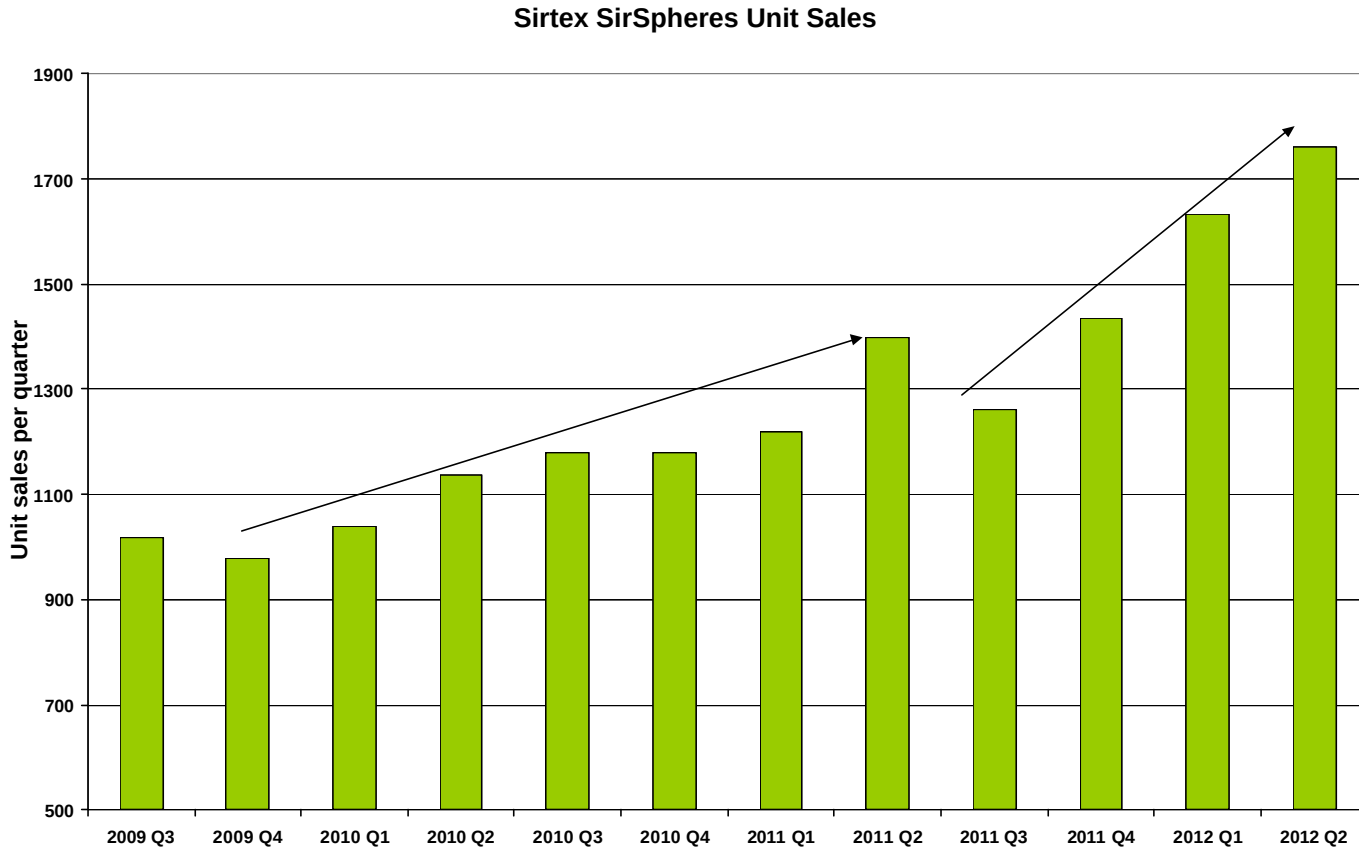
Sirtex is investing $60 million over five years into four major clinical studies involving 1660 patients. It is two years into this investment. Its first major trial is expected to be fully enrolled by the end of this year with results two years away (expected in the second half of 2014). This study is looking at Sir-Spheres with chemotherapy therapy as a first line therapy compared to just chemotherapy alone.

Over the next three years, Sirtex's profitability will be affected because of its investment in these major clinical studies. Its net profit in the first half of FY2012 was $6.1 million.

There are signs the global adoption of the Sir-Sphere's therapy is gaining some momentum. The company has secured just 1% of its addressable market. Sirtex is a stock that has the potential to deliver excellent long term growth prospects, being relatively less effected by global economic instability.

Sirtex is capitalised at $351 million.

Bioshares recommendation: **Buy**



Private Company Profile – GKC Corporation

GKC Corporation is a private company based in Melbourne and founded in 2007. It has been commercialising a system for measuring movement disorder as experienced by people suffering from Parkinson's disease (PD). The system was first developed at the Florey Neurosciences Institutes in Melbourne.

PD is a progressive disease that is caused by the death of dopamine cells in a part of the brain called the substantia nigra. Diagnosis is generally derived through examination and the study of a patient's history. Smell testing has a moderate sensitivity for determining PD, but is not recommended. The symptoms of PD include bradykinesia (i.e. slowness of movement), hypokinesia (poverty of movement), rigidity and tremor at rest.

The leading drug used to treat PD is levadopa, a precursor form of dopamine, which is deficient in PD patients. Levadopa is converted into dopamine by dopa decarboxylase.

However, a problem with levadopa/dopamine is that it can contribute to the development of motor complications, for example, dyskinesias or abnormal involuntary movements and an effect termed 'wearing off' which describes the weakening of the drug's influence and an introduction of a greater unpredictability between what is called the 'on' state and the 'off' state.

The PKG System (Parkinson's KinetiGraph)

GKC's measurement system is made up of a PKG datalogger, which is worn on the wrist by the patient for capturing movement data. This is worn for ten days then returned to clinician. The next part of the system is a charge cradle which accepts the information from the datalogger, encrypts, it de-identifies it and then sends it to the GKC cloud-based data warehouse. The cradle also recharges the device

The data warehouse is where the data is analysed using a proprietary algorithm which produces reports which are sent by email to the clinician by PDF or to a practice management system or downloaded to the charge cradle.

Although the GKC system is an integrated hardware and software system, the business model is better characterized as the provision of information about individual patient responses to their medication in relation to their symptoms. In general, 90-95% of GKC's income is expected come from the reports with the balance from the devices. In a market such as the UK, where it is currently seeking market access, GKC would most likely roll the cost of the devices for any health trust into the cost of the reports, aiming to write two year contracts from which income is generated on a patient report basis.

The Market Opportunity

GKC stratifies the Parkinsons population into three groups, in contrast to the more accepted 1 to 5 scale. According to GKC, about 50% of patients sit in Stage II of the disease which is defined by the people who are taking more than three doses of levadopa a day. These are patients at the early stage of the disease. They are not infirmed and not at the point where levadopa therapy is no longer effective and hospitalisation is required.

The addressable market is based on the 50% of patients who are in Stage II. The market opportunity is between one and four reports per year per patient if looking at the total addressable market. In Australia there are an estimated 65,000 patients with PD of which 32,000 fit GKCs definition of Stage II disease.

Generally, a clinician will use the device to create a baseline measurement and then take another test after a patient has changed medication to see if an anticipated effect has taken place.

Business Model

GKCs business model is based on developing a system that is point-of-care measurement tool for neurologists and professional carers in its first stage of market development. It will not sell (as yet) into the research tool market or sell directly to patients.

The plan is based on the view that it is clinicians who treat the symptoms of the disease in conjunction with their patients. It is clinicians who see the disease on a regular basis and understand symptoms and prescribe medications for those symptoms.

According to CEO Andrew Maxwell, putting the PKG system into clinicians' hands is the best way to get it adopted in the market place. At a later date, if the system becomes "the vernacular for the management of the disease then the research market and possibly the consumer market may open up to us to at some point in time. Without clinicians using it I don't think it will get widespread adoption and without clinicians using it I don't think you can get reimbursement in any market."

Impact on Clinical Practice?

While it is too early to say that the PKG system has changed clinical practice, early clinical use is showing clinicians whether a patient is over or under treated with levadopa or dopamine replacement therapy. They now can tell if patients are taking their medicine or not. Perhaps most significantly, clinicians have a different type of communication with their patients, and clinicians and patients can now both interact over a visual report and both grasp what each other are talking about. "From the feedback we a getting, that makes a huge difference" said Maxwell

"That's one of the key things coming out of this. One of the big issues, is that patients have not been good at describing what tremor is versus what dyskinesia is and when dyskinesia is happening, at what time of the day and when in relation to medication. And having a visual manifestation of that, in the form of the report has been very important in many cases in helping patients to better manage symptoms."

Bioshares

The Inverseon-CBio Merger: Repurposing a Well Known Heart Drug to Treat Asthma and COPD

Shareholders in Brisbane-based CBio (CBZ:$0.063) will vote to approve, before the end of August, the merger of the company with privately held Inverseon, currently based in San Francisco and founded in 2004. Inverseon is developing a drug currently approved for the treatment of congestive heart failure, nadalol (company codename INV102), for the treatment of respiratory conditions such as asthma and COPD.

When used to treat heart failure, nadalol and the more widely prescribed carvedilol, block hormones called catecholamines which are elevated in case of heart failure. Nadalol itself has been used to treat eight million people.

The merger if successful would result in Inverseon shareholders holding a stake of 37.5% of the merged entity, with CBio shareholders holding 62.5%. The merged entity would be renamed Invion.

The merged entity would primarily focus on the development of INV102 and secondarily continue to explore the feasibility of developing Xtoll as a treatment for Lupus (SLE).

CBio History

CBio has been so far unsuccessful with its attempt to commercialise the immunomodulator Xtoll (also know as Cpn10), having seen the drug fail in a Phase II trial in rheumatoid arthritis patients in August 2011, with dosing issues cited as a factor.

CBIO held cash assets of $5.7 million at March 31, 2012.

The Scientific Basis for INV102 - Inverse Agonism

Receptors that exist on cell walls can be targeted by drugs to generate a signaling effect. Receptor theory accepts that drugs (e.g. a small chemical entity) could bind to a receptor to activate a cell signaling pathway by binding to that receptor. Molecules that activate signaling are also described as agonists.

Another class of receptor binding molecules are ones which sit in the receptor to simply neutralise cell signaling activity. Molecules that act in this way can be described as antagonists or blockers (hence the term 'beta blockers'.)

Yet another class of drug receptor binding molecules are those that bind to the receptor which suppress signaling, especially signaling that has or is taking place without a drug sitting in the pocket to turn on the signaling in the first place. A molecule which binds to a receptor to suppress signaling or to turn off mutation- based signaling is called an inverse agonist.

Inverseon's INV102 is an inverse agonist of the beta-2 adrenoreceptor.

One historical confounding issue with the use of beta-blockers to treat heart failure is that historically they had been contraindicated for use with asthmatic (or similar) patients i.e. not recommended for use. What stimulated the interest of the scientific founder of Inverseon, Dr Richard Bond, was the observation the rates of respiratory illness have been lower in patients taking beta-blockers. Various investigations led the scientific founders of Inverseon to consider that chronic dosing of beta-blockers, if titrated carefully from a very small starting dose, could be effective in treating respiratory conditions. The Inverseon hypothesis was supported with additional insights when it was found that certain beta-blockers acted as inverse agonists.

Phase IIa Trials of INV102

Inverseon has completed two Phase IIa studies of INV102. One study, now published, enrolled 10 patients with mild asthma and showed an 80% dose related response rate in both cohorts of five patients who were treated for 9 weeks following a two week run in. Eight patients experienced a reduction in airway hyper-responsiveness.

Patents

Inverseon brings one key patent (US PTO 7,288,175) to the CBio-Inverseon merger, which is a method-of-use patent describing the use of nadalol in respiratory diseases. The patent expires in 2026.

The patent describes a method to treat respiratory conditions such as asthma with a specific beta-2 adrenergic inverse agonist, nadalol, starting with a low dose followed by monitoring of the patient followed by dose escalation based on pre-determined criteria (e.g. a 20% decline in FEV1) until a maximum tolerated dose is reached and can be sustained.

The inherent weakness of a use patent is that a potential competitor could invent a compound to achieve the same ends and apply the methods in a similar way. It should come as no surprise that Inverseon intends to discover a new, specific beta-2 inverse agonist and will commence a drug discovery program in 2013.

Development Plans

Inverseon's business plan, as inherited through the merger and assuming funding is secured, for 2012 includes completion of CMC (Chemistry, Manufacture and Control) related tasks along with the manufacture of drug material for clinical trials.

It also intends to complete formulation and development of an inhalation device for INV102 and submit an IND for INV102 for the application of smoking cessation in patients with chronic bronchitis.

Inverseon is in receipt of an Investigational New Drug certification with the FDA for the development of INV102.

Inverseon has a Phase II trial in planning supported with US$4.4 million in funding from the National Institutes of Health in the US. The proposed trial will enrol approximately 100 subjects with asthma at three sites (Baylor College, Washington University - St Louis and Duke University) and will be completed in 2015. Inverseon also intends to initiate a 'smoking cessation' study that will take up to 18 months to complete. Smoking cessation represents a niche segment of the broader COPD market.

Cont'd over

Bioshares Model Portfolio (13 July 2012)

Company	Price (current)	Price added to portfolio	Date added
Nanosonics	$0.510	$0.495	June 2011
Osprey Medical	$0.40	$0.40	April 2012
QRxPharma	$0.77	$1.66	October 2011
Mayne Pharma Group	$0.385	$0.435	September 2011
Somnomed	$0.85	$0.94	January 2011
Phylogica	$0.040	$0.053	September 2010
Biota Holdings	$0.70	$1.09	May 2010
Tissue Therapies	$0.47	$0.21	January 2010
Atcor Medical	$0.06	$0.10	October 2008
Bionomics	$0.29	$0.42	December 2007
Cogstate	$0.250	$0.13	November 2007
Sirtex Medical	$6.30	$3.90	October 2007
Clinuvel Pharmaceuticals	$1.85	$6.60	September 2007
Pharmaxis	$1.00	$3.15	August 2007
Universal Biosensors	$0.54	$1.23	June 2007
Alchemia	$0.500	$0.67	May 2004

Portfolio Changes – 13 July 2012

IN:
No changes

OUT:
No changes

– CBio/Inverseon cont'd

Investment Points

The proposed merger of CBio with Inverseon is appealing for several reasons. Firstly, the risk profile of INV102 is much less than the risk profile of Xtoll (a novel biological). INV102's risk profile is also significantly reduced compared to new chemical entities given its established use for the treatment of heart failure.

The clinical development program for INV102 (oral and inhaled) should be relatively less expensive overall and it should less expensive to see the company progress to the pivotal proof of concept stage. Inverseon's current development budget for the four years ending 2015 is US$16 million, which takes the company to the commencement of a Phase III trial in smoking cessation.

Inverseon's IND status for INV102 as well as NIH trial funding are indicative of the professional capabilities of Inverseon's management and represent important de-risking steps taken so far in the commercialisation career for INV102. The NIH funding also validates the medical hypothesis as presented by Inverseon as one which is worth testing in a larger clinical trial.

Finally, the markets targeted by Inverseon of asthma and COPD are large, global and in need of new and superior medicines.

CBio's legacy drug candidate may be found to have benefit in treating lupus (SLE), an area that is poorly served by current drugs.

A possible outcome for investors in a merged CBio-Inverseon entity is that the company is acquired by a large pharmaceutical firm once the firm has achieved a number of goals. These include: demonstration that INV102 is an effective treatment for asthma and has potential for treating COPD (from preliminary studies); filing of an IND for an inhaled version of INV102; invented a new chemical entity that acts in a similar way to INV102; and is ahead in any development race with emerging rivals.

Investors should also note that a $5 million capital raising has been proposed to follow the completion of the merger.

Bioshares recommendation: **Vote for the Merger**

Bioshares

Correction
In Bioshares 463 (page 3) we stated that Tissues Therapies had been subject to a regulatory setback. This was not the case, with the company supplying information to a notified body as part of a normal process of review.

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: Pharmaxis, Starpharma Holdings, Cogstate, Bionomics, Circadian Technologies, Biota Holdings, Impedimed, QRxPharma, LBT Innovations, Mesoblast, Tissue Therapies, Viralytics, Phosphagenics, Immuron, Phylogica, Bluechiip, pSivida, Antisense Therapeutics, Benitec BioPharma, Allied Healthcare Group, Genetic Technologies, Calzada, Bioniche

Subscription Rates (inc. GST)

48 issues per year (electronic distribution): **$375**

For multiple email distributions within the same business cost centre, our pricing structure is as follows:

$590	2-3 email addresses
$800	4-5 email addresses
$1020	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 _____

_____

_____