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In this edition...
We provide coverage of the Pharmaxis Investor Day held in Sydney, where a summary of clinical data recently presented at the US Cystic Fibrosis conference was made available. With Pharmaxis edging to a pivotal registration point in the commercialisation path of Bronchitol in Europe, it's a stock that will be watched very closely by investors.

We also provide coverage of Bionomics' AGM, with that company also approaching a transformational year in 2011. And we provide more coverage from the recent Ausbiotech 2010 conference held earlier this month.

The Editors
Companies Covered: BNO, PXS

	Bioshares Portfolio
Year 1 (May '01 - May '02)	21.2%
Year 2 (May '02 - May '03)	-9.4%
Year 3 (May '03 - May '04)	70.0%
Year 4 (May '04 - May '05)	-16.3%
Year 5 (May '05 - May '06)	77.8%
Year 6 (May '06 - May '07)	17.3%
Year 7 (May '07 - May '08)	-36%
Year 8 (May '08 - May '09)	-7.3%
Year 9 (May '09 - May '10)	49.2%
Year 10 (May '10 - Current)	8.8%
Cumulative Gain	**215%**
Av Annual Gain (9 yrs)	**18.5%**

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Bioshares

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

Pharmaxis Investor Day – Insights on CF302 Phase III Trial Revealed

Pharmaxis (PXS: $2.82) held an Investor/Analyst briefing day in Sydney this week, timed to follow the presentation of the results, of the company's second Phase III trial of Bronchitol and 52 week data from the first Phase III trial, at the 24th North American Cystic Fibrosis Conference, held in Baltimore.

CEO Dr Alan Robertson provided an update of the company's pipeline, COO Gary Phillips along with CMO Dr Howard Fox discussed cystic fibrosis and the Bronchitol Phase III program, with Phillips providing additional commentary on the commercial plans for Bronchitol. The company also invited Dr Peter Cooper from Westmead Hospital to give a clinician's perspective on cystic fibrosis.

Bronchitol Update

Pharmaxis is developing a highly engineered formulation of Bronchitol for the treatment of cystic fibrosis (CF), bronchiectasis and COPD. The company has now completed two pivotal Phase III CF studies, with the first of these, CF301, providing data in support of the company's marketing application with the EMA. CF301, together with CF302, will form the basis of Pharmaxis' New Drug Application with the US FDA.

In CF patients the liquid that sits on the airways of the lungs is depleted, which means that tiny nodules called cilia struggle to beat together to clear away the mucus that forms normally in the lungs. Bronchitol is an inhaled drug, which acts as a mucolytic. It promotes productive cough and assists in clearing the mucous that builds up in the lungs of CF patients.

Rationale of Treating CF Patients

Following the introduction of antibiotics and other medications such as Genentech's Pulmozyne (dnase-alpha) and improvements to diet and lifestyle management, the mean life expectancy of cystic fibrosis sufferers has improved over the last few decades.

However, the lung function of Cystic Fibrosis patients decreases by two to three percent each year. An objective of managing lung function is to arrest this rate of decline and even ideally impact much more significantly in childhood years, before a compliance-based decline occurs in the teenage years.

From the age of six, where lung function is at 95% (of normal), by the time a typical person living with cystic fibrosis is 30 years of age, lung function is at a little over 50% of normal. Lung function declines significantly in the adolescent years when a high level of parent imposed compliance gives way to weaker patient managed compliance.

Hence, the introduction of medicines that can improve lung function even on a single percentage points basis is meaningful in the condition of cystic fibrosis.

– Cont'd over

Bronchitol Phase III Trials

Pharmaxis CMO Dr Howard Fox provided a more in-depth analysis of the CF302 trial, with comparisons made with the CF301 trial.

CF301

The CF301 trial recruited 295 patients who received 400 mg (10 capsules) Bronchitol or placebo twice a day for 26 weeks. An extension open label phase continued for another 26 weeks with 198 patients (including 86 from the control arm).

At 26 weeks, the CF301 trial showed a statistically significant 120 ml improvement in FEV1 from baseline for patients that received Bronchitol. A **6.5%** mean change in FEV1 from baseline to week 6 through to week 26 was also statistically significant.

CF302

The CF302 trial enrolled 305 patients who received 400 mg (10 capsules) Bronchitol or placebo twice a day for 26 weeks.

One difference between the two trials was that CF301 enrolled patients with an FEV1 of greater than or equal to 30%, whereas CF302 enrolled patients with an FEV1 of at least 40%.

At 26 weeks, the CF302 trial reported a 106.5 ml improvement in FEV1 from baseline for patients that received Bronchitol. However this was not statistically significant (p=0.059).

An **8.2%** mean change in FEV1 from baseline to week 6 through to week 26 was observed, which was statistically significant. A point to note about the CF302 trial was that a greater proportion were also using Pulmozyme (75%) versus 55% in the CF301 trial.

Pooled Data

Pooled data from CF302 and CF301 showed a **7.3%** mean change in FEV1 from baseline from week 6 to week 26.

Three earlier studies CF201, CF202 and CF203 recorded 7%, 8.75% and 6.4% mean change in FEV1 at week 2, week 2 and week 12 respectively.

18- month data

In the CF301 trial, 50 patients continued treatment for an additional six months. The mean change in FEV1 from baseline out to week 80 was **7.9%**, a statistically significant result.

Conundrum

The conundrum thrown up by the CF302 study was that statistical significance was not achieved on the primary endpoint for the absolute change in FEV1, which was something of a surprise given that both trials were both very similar in design and in the number of patients recruited into the trials.

Fox said that by adjusting the baseline to the screening date two weeks prior to the date the trial 'commenced', when lung function measurements were also made, a clearer picture emerges, where the CF302 results were more consistent with the CF301 results.

On an adjusted basis, the CF302 trial recorded a difference of 71 ml improvement over the control arm in FEV1 from the screening baseline (significant at p=0.0075). This was more in line with the 93 ml difference between the treatment arm and the control arm in the CF301 study.

Fox's conjecture was that what might have occurred between the screening date and baseline date for the study was that even only a few patients in the control arm may have experienced a major unplugging of mucous in their lungs which could have then contributed a to a very large increase in lung function, which then skewed the control arm average.

Fox said that Pharmaxis "will take to the FDA a proposal to use both the baseline and screening values because when you do that you see a very similar result." [The company will be holding a pre-NDA meeting with the FDA shortly.]

Fox said a precedence exists for using the screening date, with Pulmozyme and other CF antibiotic drug submission data also using screening dates to take into account variability in lung function.

Drop out rates

In the CF302 trial there was a 7.1% dropout rate in the treatment arm due to adverse events. In contrast, in the earlier CF301 trial there was a 15.8% drop out rate due to adverse events. The drop-out rate in the CF302 trial was better because more attention was paid to educating patients to set expectations that more coughing would occur with the use of Bronchitol.

Exacerbations

One other measure to emerge from the CF301 and CF302 studies was the number of exacerbations experienced by patients. (An exacerbation is a severe event usually requiring hospitalisation.)

Combined data from CF301 and CF302 showed a 29% drop in the number of patients having exacerbations and 25% decrease in the rate of exacerbations. However, both figures were not statistically significant.

Commercialisation Comments

Gary Phillips compared Bronchitol with its main rivals, contrasting it with dornase-alpha (Pulmozyme - **Roche**), **Inspire Pharmaceuticals** denufosal and hypertonic saline (see table on next page).

According to this comparative analysis, Bronchitol arguably offers the greatest improvement in lung function, as measured by FEV1 over a 26 week period, of 6-8%. This is quite an achievement considering that the Bronchitol Phase III trial recruited patients with the lowest FEV1 score, and an average FEV1 that was just slightly above the average for the Pulmozyme trial.

The data indicates that Bronchitol is competitive against both denufosal and hypertonic saline, with these two therapies delivering a 5% and 3% improvement in FEV1 over 12 months.

Bronchitol is differentiated as the only drug delivered by a dry inhaler and as offering a significant improvement in administration time per dose. It is also portable, does not require electricity

– Cont'd over

and does not require sterilisation after use, which is required for nebulisers.

The point of the comparison is that Bronchitol appears to have generated a significant 12 month improvement even as many patients continued to use Pulmozyme and antibiotics. In other words, the Bronchitol benefit was additive to the benefit provided by those medicines. Also worth noting was that the Bronchitol Phase III study was completed about 15 years after the Pulmozyme study, a time period in which significant changes in the treatment of CF have occurred.

Recent Market Research

Pharmaxis also presented findings from recent syndicated market research conducted in five European countries (about 20 physicians per country, that represented about 1,000 patients) to find out how CF patients progress over time and what factors play the greatest roles in a patient's prognosis, ascertain how doctors are using 'lung clearance' products and gauge awareness of Bronchitol.

Phillips said that the research was important because Bronchitol would not be used by every cystic fibrosis patient; instead it had to be positioned as a drug for those that could obtain a benefit and as quickly as possible.

The survey revealed that 60% of CF patients were hospitalised in the preceding twelve months. However some are hospitalised 2-3 times a year with each hospitalisation lasting up to 15 days. Expectations are that around 60% of patients would have improved or stable pulmonary status over the next 2 years, suggesting a pool of 40% of patients in greater need for improved therapies.

People with cystic fibrosis take on average 5.5 classes of medicine but 7.1 classes of medicine in cases of chronic *p. aureginosa* infection (which is highly correlated with the severity of the disease).

In terms of lung clearance, just under half of patients use Pulmozyme, with 56% have having trialed it at some point. Pulmozyme treatment is associated with a decrease in the rate of lung function decline.

Pulmozyme use also increases if patients become colonised with *p.aureginosa*. But hypertonic saline is used instead as only as an adjunct to physiotherapy and not if patients become colonised with *p.aureginosa*.

In terms of Bronchitol awareness, the survey found that more than 80% of physicians were aware of Bronchitol and that they would use the product with about 40% of their patients, typically aged greater than 10 years and with poorer lung function.

Registration and First Sales

Pharmaxis is expecting a response from European regulators regarding its application for the marketing of Bronchitol by Q4 2010. Assuming approval, the company will launch immediately in the UK and Germany, where national pricing approval is not required.

	Dornase-alpha	Bronchitol	Denufosal	Hypertonic Saline
Company	Roche	Pharmaxis	Inspire	n/a
Status	Market	Phase III	Phase III	unregistered
Administration	Nebulizer	Dry inhaler	Nebulizer	Nebulizer
Dosing	1-2x daily	2x daily	3x daily	2-4x daily
Admministration Time (per Dose)	15 mins	2-5 mins	15 minutes	15 minutes
Year of Study	1994	2009	2008	2004
Patient entry FEV1	>40%	>30%	>75%	>40%
Average FEV1	61%	65%	93%	73%
Pulmozyme Usage	n/a	55%-75%	77%	39%
Inhaled antibiotics	35%	61%	37%	18%
Azithromycin	?	44-53%	40%	0%
Change FEV1 - 6 months*	6%	6-8%	2%	n/a
Change FEV1 - 12 months	n/a	8%(OL)	5%(OL)	3%

* - from base line
OL - Open label

Source: Pharmaxis

It will aim to have launched in the top 5 countries (representing 30,000 CF patients out 48,000 patients across Europe) by the end of 2011. In Europe that drug will qualify for up to 12 years of Orphan Drug exclusivity. [Note: US - 30,000 CF patients; 7 years OD exclusivity - FDA response on NDA expected mid-2012]

Manufacturing Capacity

Pharmaxis operates two manufacturing plants. Its No. 1 facility manufactures Bronchitol for clinical trials and compassionate use. Its No. 2 facility is currently being validated. This second facility will have an initial capacity for supplying drug material to treat 40,000 patients per annum, which can be expanded to 80,000 patients if a second spray drier is installed

Summary

Key points from the investor day were: Bronchitol delivers up to an 8% 12-month improvement in lung function, which is significant given that CF patients' lung function declines on average by 2-3% per year; Pharmaxis will seek to discuss an adjusted baseline measure from the CF302 trial with the FDA as part of its NDA submission; Bronchitol can address a heightened need for improved therapies for about 40% of CF patients in Europe; and product awareness is reasonably high amongst CF physicians in the five major EU countries that represent 30,000 CF sufferers.

Pharmaxis is capitalised at $637 million.

Bioshares recommendation: **Speculative Hold Class A**

Bionomics AGM Coverage

Confidence was riding high at this year's Bionomics AGM, held on 15 October. The chairman, Chris Fullerton, suggested that the year ahead as the most critical year in the company's history. CEO Deborah Rathjen described 2011 as being a transformational year for Bionomics. This is because the company will have crucial data emerging from three clinical programs.

BNC105 Update

The first flagged data release will be from the company's cancer drug candidate, BNC105, in the treatment of patients with kidney cancer in a Phase II study. The first stage of the trial, for which interim results should become available in the first quarter of 2011, will be from use of BNC105 used in combination with the **Novartis** drug Afinitor, in patients who are no longer responding to Afinitor.

This first part of the trial will initially look at whether combing the two drugs in patients is safe. After the first patient is treated for 21 days, more patients will be treated with the combination therapy. There will be no efficacy comparison between BNC105 and Afinitor. That will occur in the second stage of the trial, once safety of the combination of the two drugs is established. In preclinical studies, Bionomics has shown that there is a synergistic effect from combining the two drugs.

Efficacy data should also be available in this interim analysis from images of changes to the solid tumours, and the company will also be able to monitor the blood levels of tubulin which will act as a market of tumour destruction.

The Phase II Mesothelioma Trial

The Phase II mesothelioma trial is recruiting well. This is a very difficult disease to treat and in *Bioshare*s view, the expectations that BNC105 will be effective should be lower that in kidney cancer. However there is a high unmet clinical need for treating mesothelioma. It is a solid tumour and one patient in the Phase I trial with mesothelioma (and one with kidney cancer) showed signs of stabilized disease following treatment with BNC105.

There is no staggered start to the mesothelioma trial, with the safety of BNC105 delivered on its own already established. The interim results, which should be available in the first half of 2011, should give sufficient detail on efficacy of the drug to either (a) stop the trial if there is no evidence of efficacy or (b) continue the trial if the drug is showing to be effective and seek a licensing arrangement.

Data from the interim results from the kidney cancer study should also be sufficient to enter into licensing discussions if the drug is showing to be effective.

BNC105 is a variation of the drug candidate Combrestatin A4 (CA4) which was discovered at the NCI in the US in the 1980s as a natural compound. Scientist Bernard Flynn, founder of **Iliad Chemicals**, synthesised BNC105 using his Multicore chemistry platform. Iliad was acquired by Bionomics in 2005 and its Mutlicore chemistry is behind Bionomics' three lead programs.

BNC105, a tubulin polymerisation inhibitor, has a dual effect, stopping the blood flow to tumours and thereby rapid tumour destruction from the inside out. The drug candidate also inhibits cell mitosis (cell division) similar to the alkaloid drugs such as Taxol which target tubulin, and starts apoptosis (cell death). This is believed to be because the compound interrupts with the microtubulin assembly. However, unlike the alkaloid cancer drugs, BNC105 is believed to be not subject to resistance mechanisms.

The issue with CA4, according to Flynn, was that its half-life in the body is too short, being around 40 minutes, which is too short a time to elicit tumour growth inhibition. BNC105 has a half-life of three hours in the body.

BNC105 is also 10 times as potent as CA4 (as measured by IC50 - inhibition concentration, being the concentration of drug required to inhibit disease by 50%), and has 10 times the amount of free drug concentration in the body, because it binds to albumin much less than CA4 (10% free drug function for BNC105 versus 1% for CA4). Presumably that would give BNC105 a 100-fold increased potency over CA4 and a much greater therapeutic window in which to operate.

Antisoma Development - ASA404 On Hold

During the year, a VDA drug program (ASA404) that had been development by **Antisoma** and licensed to **Novartis** was halted due to poor trial progress. The chairman commented at the AGM that with ASA404 now on hold, BNC105 has become the global front runner in the VDA space and that the interest in the VDA space remained strong according to Rathjen. BNC105 is far superior to ASA404, believes Rathjen, with BNC105 having a dual mechanism of action (compared to a single action with ASA404) and the mechanism of action was known for BNC105 unlike for ASA404.

One of the appeals of BNC105 is that it has shown to be a very safe drug. The drug is removed from organs very quickly with no drug in the blood stream the day after delivery. The company has also built a new model that shows that BNC105 also has an effect on renal metastases to the lung. It also has the potential to treat all solid tumour types according to Rathjen. (In 2008 the company indicated that BNC105 had caused almost complete destruction of tumour blood vessels in all six tumour types investigated to date.)

Prospective Licensing Deals

At this year's AGM, there was a commercial focus on comparator companies and comparable licensing deals that Bionomics could potentially achieve. The licensing deal between Antisoma and Novartis for ASA404 generated a $75 million upfront fee in 2007. In 2009 and 2010, the chairman pointed to four relevant licensing deals, presumably setting the scene for what is achievable for Bionomics in the year ahead.

Oncogenix signed a Phase II deal on a prostate cancer compound which included a $20 million upfront payment plus a $10 million equity investment. **Array Biopharma** signed a Phase I deal with Novartis with a $45 million up front payment. **Exelixis** and **Sanofi-Aventis** signed a Phase I/II cancer drug deal with a US$140 million upfront payment and $21 million in research payments. And **TopoTarget** signed a Phase II/III cancer drug development deal

with **Spectrum Pharma** which included a $30 million upfront payment.

Bionomics' Phase II kidney cancer trial was started in January this year and the mesothelioma trial was started in March. Both trials are running according to schedule with the recruitment rate into the mesothelioma trial particularly pleasing. Rathjen believes either program could be fast tracked to Phase III if the Phase II data looks good.

BNC210 Update

Bionomics' third trial is with BNC210 for the treatment of anxiety and now depression. In fact these will be two Phase Ib trials in the same indication. The first trial will look at the effects of BNC210 on 22 volunteers who are induced to develop short-term anxiety and panic-like symptoms (using a peptide CCK-4). Part of the group will be given a placebo and the second group BNC210.

The second trial will compare BNC210 with a valium-like drug (Lorazepam) in 24 health volunteers. The aim will be to compare the side effects of the two drugs such as memory impairment and sedation.

Results from both trials are expected in the first quarter of 2011. If the results are positive, Bionomics intends to partner the program.

Whilst licensing discussions are pending completion of the above trials, relationships have already been formed with the key groups potentially interested in Bionomics' two lead drug candidates and those groups are believed to be watching the progress of these trials.

BNC210 also utilises the company's Multicore platform and was initiated after the Iliad acquisition. The concept came from work published in scientific literature to which the Multicore technology was put to work. The preclinical models for anxiety are well established and transfer well into the clinic. The same pre-clinical models Bionomics has used have all generated consistent data with 10 anti-anxiety drugs currently on the market. In a variety of preclinical models, Bionomics has shown that BNC210 reduces anxiety and depression without the effects to memory or sedation.

There is a strong sense of confidence at Bionomics that BNC210 will also deliver positive clinical trial results that will position the program for a major partnering deal.

KV1.3 – MS program with Merck Serono

The preclinical partnership in multiple sclerosis with Merck Serono was recently extended for another year, presumably so that the first milestone of selecting a lead drug candidate could be achieved.

Non-executive director and scientific advisor, Dr Errol De Souza, commented that the level of interest from key opinion leaders on the BNC105 anf BNC210 was extremely high. Commenting also on the relationship with Merck Serono, De Souza said that the pharmaceutical company viewed its collaboration with Bionomics as one of its best.

Summary

In its two lead programs, Bionomics is seeking to treat diseases or disorders where the current disease is not effectively management with existing treatment (kidney cancer and mesothelioma) and a disorder where there has been very little progress over the last 10 years to improve existing therapies (anxiety and depression). There is significant unmet need for both cancer indications. In kidney cancer, the five-year survival rate for advanced disease is only 2%. For patients with mesothelioma, the life expectancy after first line chemotherapy is only one year.

Bionomics' lead programs are both tackling very large markets. Avastin, an anti-angiogenic antibody drug now generates sales of over $5 billion a year. The anxiety and depression market is worth $26 billion a year with one prescription issued each second for the popular anxiety drug Xanax.

Bionomics is very confident that it will be successful in the transformational year of 2011. Deborah Rathjen commented that a decade of work at Bionomics has produced two very exciting drug candidates. The quality of data that emerges from the current trials will dictate the interest from potential partners.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Ausbiotech 2010 Continued

Investors Unplugged: Everything You Wanted to Ask a Fund Manager but Were Afraid to Ask

In this session five international and one local biotech fund managers were quizzed in a panel session chaired by Hershel Berry from Blueprint Life Sciences. Below is a summary of some of the points made during this sessions that are of interest.

Raj Shah, from RA Capital Management in the US, said he had seen plenty of value destroyed when companies partnered assets. Raj stressed that it is not right to call partnering non-dilutive financing as the technology value drops immediately. The propensity to partner early is misguided according to Raj and he noted that big pharma is desperate right now! This does not mean that companies should not consider partnering, just that they should look at the 'cards' they are holding and consider the options carefully.

Oleg Nodelman, from **Biotechnology Value Fund**, followed up with the comment that just because you go through the partnering process doesn't mean you have to partner. But not to go through the process is criminal believes Oleg. Oleg said there is always a deal to be done if you have a valuable asset, just the price will vary depending on your progress.

Australian fund manager Lawrence Gozlan said management in Australia has improved a lot in recent years however companies still need to make the hard decisions to kill a drug candidate when required. Karl Handelsman from **CMEA Capital** added that this is one of the problems consistent with biotech companies throughout the world that needs to be addressed.

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Bioshares Model Portfolio (29 Oct 2010)

Company	Price (current)	Price added to portfolio	Date added
Phylogica	$0.050	$0.053	September 2010
Sunshine Heart	$0.028	$0.036	June 2010
Biota Holdings	$0.97	$1.09	May 2010
Tissue Therapies	$0.45	$0.21	January 2010
QRxPharma	$0.93	$0.25	December 2008
Hexima	$0.40	$0.60	October 2008
Atcor Medical	$0.08	$0.10	October 2008
Impedimed	$0.85	$0.70	August 2008
Mesoblast	$2.54	$1.25	August 2008
Circadian Technologies	$0.61	$1.03	February 2008
Patrys	$0.10	$0.50	December 2007
Bionomics	$0.28	$0.42	December 2007
Cogstate	$0.27	$0.13	November 2007
Sirtex Medical	$6.05	$3.90	October 2007
Clinuvel Pharmaceuticals	$0.18	$0.66	September 2007
Starpharma Holdings	$0.70	$0.37	August 2007
Pharmaxis	$2.87	$3.15	August 2007
Universal Biosensors	$1.60	$1.23	June 2007
Acrux	$3.00	$0.83	November 2004
Alchemia	$0.53	$0.67	May 2004

Portfolio Changes – 29 October 2010

IN:
No changes.

OUT:
No changes.

– Ausbiotech coverage (from previous page)

An interesting approach quoted by the panel from one of the investors who attended Ausbiotech in 2009 is that the fund in the last year has changed its processes and now insists on a board position with every investment. That group has around $4 billion of funds under management.

There have been almost no IPOs in the last three years and those that have listed have generally had advanced businesses with products on the market. But there have been cases of successes, including Belgium biotech **Movetis** which listed in December at a price of EUR160 million (pre-money) and was acquired in August this year by **Shire Pharmaceuticals** for a technology value of EUR328 million (plus EUR100 million cash).

One fund manager stressed that going public should really just be viewed as an alternative financing and it should really be just business as usual post IPO.

Axel Polack from **TVM Capital** in Germany commented on a new phenomenon in the European biotech sector, that of 'Super Angels', who are investing $70 million chunks into start-ups. "We have never seen this before," said Axel.

One of the risks for biotech companies is to partner and take a compound into Phase III trials that has only a 10% chance of getting across the line. Pharmaceutical companies will take this risk but biotechs shouldn't, because if it falls over, it's the end of the biotech company. The average should be 50% probability that a Phase III trial delivers positive result. Biotechs should conduct further Phase IIb trials to get that chance of success up to 50% before commencing a Phase III program.

Nodelman stressed that biotech companies globally needed to be more transparent in the way they operate. And perhaps the most important comment made was that growth in the pharmaceutical industry will be almost zero in the years ahead, presumably due to major patent expiries. This means pharma will not pay high process any more. Polack says exit prices will be lower, so biotechs need to spend less, there needs to be more capital efficiency and biotech companies need to adopt virtuality!

Bioshares

Dates and location for the 2011

Bioshares Biotech Summit

22 – 23 July, 2011
QUEENSTOWN, New Zealand

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, ChemGenex Pharmaceuticals, Circadian Technologies, Biota Holdings, Halcygen Pharmaceuticals, Impedimed, QRxPharma, Patrys, LBT Innovations, Hexima, Mesoblast, Atcor Medical, BioMD, Tissue Therapies, Viralytics, Phosphagenics

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