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In this edition...
The meltdown in equity markets has seen numerous biotech stocks fall to very low levels. The prices in some cases appear absurb when real and substantial progress in developing their assets has been made. But investors would want to know: What are the choice stocks worth? How big is the discount on the high quality biotechs? In the first of series of valuation exercises we run the ruler over Peplin and the results are surprising.
We also update readers on Cytopia's inaugural R&D Day, results from Mesoblast's bone repair trial and provide further comment on the Biota-GSK settlement.

Companies covered: BTA, CYT, MSB, PLI

	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 - current)	-10.0%
Cumulative Gain	**88%**
Av Annual Gain (7 yrs)	**17.8%**

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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
Ph: (03) 9326 5382
Email: blake@bioshares.com.au
Mark Pachacz
Ph: (03) 9671 3222
Email: pachacz@bioshares.com.au

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Bioshares

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

Peplin Valuation Highlights Market Pricing Disparity

With the biotech sector having fallen by around 50% over the last 18 months and yet strong progress in many of the companies continuing, *Bioshares* will conduct a series of company valuations to examine the disconnect between market prices and strong progress in asset development We will aim to confirm whether it exists or not, and what effect tougher capital markets and lower share prices are having on the estimated net present value of a selected number of later stage biotech stocks that can be valued with a good degree of confidence. The first company to be assessed is **Peplin Inc** (PLI: 32 cents), which is conducting Phase III trials with its lead compound for the treatment of non-melanoma skin cancers.

Peplin is in an attractive position for a biotech company. We judge the technical risk for Peplin as low, with the effectiveness of its topical skin cancer treatment delivering consistent and high quality results. What is also appealing with this company is that it owns the technology outright (no licensing fees payable) and its patents extend out to 2018 in the US with the possibility for a five year extension to 2023.

Peplin has recently experienced a 12 month delay to its timeline, when it was discovered that the therapeutic dose for the treatment required for face and scalp actinic keratosis (AK) to be lower than that required for treatment of AKs on the 'rest of the body'. The company is currently conducting a Phase III AK study on the rest of the body in 250 patients. The results from this study are expected in the first half of 2009.

It is also completing a Phase II dose finding study for the head and scalp treatment which will also look at whether a two or three day treatment will be the preferred option. We expect the AK Phase III head and scalp trial to start in early 2009, from which the results we would expect to see by the end of 2009. The company expects to be in a position to file its drug for approval in the US in mid-2010. We anticipate the drug to reach the market in mid 2011.

There is an existing market for topical treatments of actinic keratosis with 5.5 million visits each year to dermatologists in the US. From these visits 90% receive some type of treatment, split between 70% using cryotherapy and 30% using topical treatments. The shortfalls of cryotherapy are that it can be used on discrete lesions only, not for field therapy, and often does not treat the full condition beneath the skin, resulting in a high recurrence rate. In the US each year about 2000 people die from AKs that have progressed to basal cell carcinomas.

All of the existing topical treatments have shortfalls, specifically the long length of treatment required. Peplin's drug has the advantage of requiring only three applications compared to several weeks for each of its competitors.

Cont'd over

Peplin is conducting its US regulatory trials under a Special Protocol Assessment negotiated with the FDA. This gives the company an added degree of certainty, that if it hits the pre-agreed endpoints, its drug should get the green light from the FDA.

Valuation

Using the assumptions listed at the right, which includes a higher discount factor (15%) due to the tighter credit markets, we value Peplin at **$1.90** a share, with the current share price (32 cents) equating to an 83% discount to this fair value. This includes the additional shares that would need to be issued to fund the completion of the development of PEP005 for AK therapy, resulting in fully diluted shares on issue of 315 million.

Funding

Perhaps the most important factor to be considered in the current climate is the need to raise further capital by the company. Peplin currently has about $25 million in funds, enough to support the next 12 months of operations. Our valuation assumes that $25 million would be raised at current prices (no doubt the company is exploring other options), a further $40 million would be raised at 70 cents a share, and an additional $40 million would be raised from out-licensing rights to PEP005 outside of the USA. This totals $105 million, with $50 million to fund working capital for two years (2009-2011), $15 million to build a second manufacturing plant, and $40 million in funds to launch PEP005 onto the market in 2011.

Summary

Using the assumptions listed at the right, we value Peplin at $1.90 a share. The company is significantly undervalued but risks remain. We believe there is a 75% probability that PEP005 will successfully reach the market, which also means there is in our view a 25% chance this product will fail to get to market. If timelines are stretched out further, the funding need will increase which will negatively impact on this valuation as will the delay in building sales.

The main risk for the company is funding, or rather, the cost of that funding. It is unlikely that Peplin will not be able to access the funds to complete the development of its product in our view, however the price at which those funds will be raised in the future will become a central issue.

The second key risk for the company hinges on it ability to successfully execute is strategy of building a specialty pharmaceutical company and managing that growth in the business. The company has a strong management team and having a supportive US venture capital investor (MPM Capital) will help mitigate these risks.

Bioshares recommendation: **Speculative Buy Class A**

Assumptions

1. There are 5.5 million annual visits to dermatologists each year for the treatment of AKs with 1.5 million of these visits resulting in a topical treatment. Conservatively, we have not factored in growth in these visits.

2. PEP005 will be released in the US in mid 2011.
In the first year the product will get 5% of topical treatment market share, increased to 15%, 25% and 30% in subsequent years.

3. PEP005 will sell for US$500 per treatment dose.
This equates to sales in year one of US$150 million, increasing to US$450 million peak sales in year four.

4. Patents will gain extension to 2023.

5. Drug has a 75% probability of reaching the market.
Discount rate: 15%

6. Future capital to be raised: $25 million at 35 cents a share, $40 million at 70 cents a share, and $40 million licensing of ex-US rights.

7. Peplin will manufacture and sell the drug directly into the USA.

8. A second manufacturing facility will be built in the USA.

Valuation does not include:

1. Possibility that more than one treatment dose will be required per visit.

2. That the proportion of patients treated with a topical treatment (currently 30% topical, 70% cryotherapy) will likely increase with a more effective topical treatment option over cryotherapy.

3. Income from sales outside of the USA.

4. Synergy values from selling other in-licensed dermatology drugs.

5. Use of PEP005 for the treatment of basal cell carcinomas or warts and use of PEP005 as a systemic therapy for treatment of other cancers (leukemia and bladder).

Cytopia R&D Day

On occasion, drug development companies hold R&D Days, the purpose of which is make coordinated presentations on drug development programs in depth to specialised investment and business audiences. While R&D Days are not where 'new' or market sensitive information is typically presented, it is a day where current information can be discussed at greater depth and often qualified with up to date market or clinical information.

The R&D Day style of briefing has been relatively rare in Australia owing to the lack of companies that have extensive product and research development programs that are warrant the analysis and coverage. **CSL** is noted for its annual R&D day. **Biota** has held R&D days and Peter Smith, when he was the CEO of **Amrad** also conducted an R&D day. And just recently Cytopia (28 cents) held its inaugural R&D day.

The Cytopia R&D Day commenced with an introduction by Cytopia CEO, Andrew MacDonald. Gregg Smith, Cytopia's Director of Drug Development and Operations discussed the company's lead program CYT997. Chris Burns, Director of Research described the CYT387 program. Jim Palmer, the company's Head of Chemistry, discussed the company's Novartis partnership program.

CYT997

The CYT997 program is Cytopia's most advanced drug development project. CYT997 is designed to interfere with tumour cell vasculature by targeting a component of cell architecture.

One Phase I dose escalation study concluded in August 2007. No objective responses were seen in 21 evaluable patients. However, stable disease was seen in 17 patients. Two patients with progressive cancers had stable disease after six cycles on doses up to 202mg/m^2 . The maximum dose administered was 357mg/m^2 . The majority of toxicities occurred at or above 269 mg/m^2. At doses of 202mg/m^2, levels of the von Willbrand factor bio-marker peaked at the end of infusion. This marker is known to be related to endothelial cell shedding and is suggestive of intended drug activity.

There are two Phase II studies underway for CYT997. CYT997 has some unique properties which would appear to extend its application beyond solid tumour cancers. Hence, a first Phase II trial is underway in patients with relapsed or refactory multiple myeloma patients. The company stated that the advent of **Celgene's** Revlimid had caused a slowing in enrolment in Australia. Interim analysis is expected in Q4 2008, with final analysis in Q1 2009.

The second trial is in relapsed glioblastoma multiforme (brain cancer). The company is waiting on receipt of ethics committee approval to commence the trial at the first site.

CYT387

CYT387 is a compound designed to treat myeloproliferative diseases. These are blood disorders that occur when too many red blood cells and platelets are produced. It is an attractive disease target because a single mutation (V617F) on the JAK2 kinase is implicated in almost all of the MPD group of diseases.

CYT387 is a dual JAK1 and JAK 2 inhibitor. JAK kinases are proteins involved in cellular communication. The compound is suitable for once a day dosing in an oral form and is described as a very 'clean' compound. Manufacturing and synthesis is described as straightforward.

A Phase I/II study is being planned, which would most likely be a an open label dose escalation study, enrolling between 28-34 patients.

The potential for CYT347 to be a breakthrough drug may emerge quite rapidly following the start of the Phase II component. The trial is expected to be completed by end-2009.

Novartis Partnership

Cytopia signed a partnership with Novartis in 2006 to jointly discover and design compounds that can block the role of the JAK3 kinase when it does not function properly in auto-immune diseases and in transplant rejection cases.

The program has been fully funded by Novartis. Due to confidentiality reasons, very little information can be made available regarding this program. The company stated that regular dialogue and data sharing occurs. Cytopia also stated that it had broken the back of a number of key challenges. It would also be looking to extend the collaboration for a fourth year when the first three year term expires in 2009.

Competitive Position

A feature of each of the individual program presentations was the inclusion of a section that covered each compound or projects competitors. These tables have been replicated on the next page. In the case of CYT997, only two other compounds are further advanced in the clinic, these being **Antisoma's** ASA404 and **OxiGene's** Zybrestat.

For CYT387, there is a smaller field of competitors, which augurs well for Cytopia.

There are even fewer drugs in development in the JAK3 space, which attests more to the high degree of difficulty of designing compounds against that target. Furthermore the most advanced compound, Pfizer's CP-690,550 is not selective for JAK3, which may mean it has limited therapeutic benefit.

Other Notes

The protein crystalography program conducted at Monash University for Cytopia has been very successful with helping the company solve numerous crystal (ie 3D) structures of JAK proteins, especially with drugs complexed to the proteins.

Cytopia has recently appointed a Drug Development Manager, a Preclinical Project Manager and a Clinical Project Manager. The next major appointment will be a Chief Medical Officer, to oversee later stage clinical trials.

Cont'd on page 5

Competitive Landscape for Cytopia's Drug Development Programs
Source: Cytopia R&D Day

CYT997 (Vascular Disruption Agent) (Anti-cancer compound)

Company	Compound	Discovery	Pre-clinical	Phase I	Phase II	Phase III
Antisoma	ASA404	Completed Phase II trials in lung, prostate and ovarian cancer. Commencing Phase III with Novartis				
Oxigene	Zybrestat	In Phase II/III trials for anaplastic thyroid cancer				
Cytopia	CYT997	Oral and IV, multiple Phase II studies				
Myriad	Azika	Initiated Phase II studies for metastatic brain cancer May '07				
Molmed	Arenegyr	Currently in Phase I Establish high dose, MTD and VDA activity				
Oxigene	Oxi4503	Currently in Phase I dose escalation study				
Nereus	NPI-2358	Currently in Phase I				
MediciNova	MN029	Phase I results due Q4 2008				
Epicept	EPC2407	Phase I results due Q4 2008				
Bionomics	BNC105	Phase I initiated Q1 2008				

CYT387 (Kinase inhibitor, myeloproliferative disorders)

Company	Compound	Discovery	Pre-clinical	Phase I	Phase II	Phase III
Incyte	INC18424	Phase II trials underway in myelofibrosis (MF), multiple myeloma and rheumatoid arthritis				
Exelixis	XL019	Phase I for MF. Has CNS issues				
Targegen	TG101348	Phase I trial for MF initiated in Jan 08				
Cytopia	CYT387	IND planned end 2008				
S*Bio	SB1518	IND planned end 2008 ?				
Supergen	SG1252	Late preclinical				
Rigel		Discovery				
AstraZeneca		Discovery				

Joint Novartis Cytopia Program (Selective JAK3 inhibitor for autoimmune indications)

Company	Compound	Discovery	Pre-clinical	Phase I	Phase II	Phase III
Pfizer	CP-690550	Phase III trials for renal transplant rejection, RA - neutropenia AE				
Rigel	R348	Phase I trial (transplant, RA, psoriasis)				
Vertex	VX-509	IND planned mid 2008 ?				
Pharmacopeia	PS020613	Discovery (psoriasis)				

Cytopia. cont'd

Summary

One conclusion to take away from the R&D Day was that Cytopia is not a 'one shot at goal' drug company and holds considerable in-house drug discovery and design expertise. The company could, with additional resources, expand clinical programs for CYT997 and probably bring forward other compounds into the clinical setting. For example, the JAK2 kinase is implicated in a number of cancers and also in pulmonary hypertension.

Cytopia is capitalised at $24 million, and at June 30 held $11 million in cash which it stated in its preliminary final report for FY2008, as being sufficient to fund operations into mid-2010.

The stock is very attractive at current prices.

Bioshares recommendation: **Speculative Buy Class A**

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Update: Mesoblast

Good results from bone trial

Mesoblast reported the final results from a 10 patient trial conducted at the Royal Melbourne Hospital with its adult stem cell technology. The trial was testing the ability of the company's mesenchymal precursor cells to aid bone healing in non-union long bone fractures.

The 10 patients had fractures that all had not healed for between 5 - 41 months prior to the stem cell implant, with some gaps larger than 5 cm in length. The results from this study were very good. Following 12 months follow-up, eight patients achieved complete bone union, with all being able to weight bear and return to normal activities. These eight patients did not require a subsequent bone graft, with the remaining two patients suffering from bone fractures from major traumas.

The current trial was conducted with autologous stem cells (patient's own). Positive results have been replicated in preclinical studies (in over 400 sheep) using allogeneic stem cells (derived from unrelated source) which gives the company confidence that Phase II trials with allogeneic cells will deliver similarly positive results to this autologous trial.

Mesoblast and its investee company Angioblast expect to be conducting Phase II programs in the near term using the allogeneic adult stem cells. These will be in:

Mesoblast trials
Spinal fusion (underway)
Knee osteoarthritis

Angioblast trials
Congestive heart failure (underway)
Heart attack patients (underway)
Diabetic retinopathy/AMD (to be conducted with partner)

Diabetic retinopathy and Age-related macular degeneration

Last month Mesoblast/Angioblast indicated they had found another application for the technology, potentially as a treatment for eye diseases. In a trial in 42 non-human primates, it was found that when these allogeneic stem cells were combined with an existing anti-VEGF drug, Lucentis, used for treatment of eye diseases involving excessive vascularization of the eye, the treatment effect in combination was better and more sustained with Lucentis used in conjunction the adult stem cells rather that Lucentis alone. Given that Lucentis needs to be injected into the back of the eye every six weeks, there is an obvious appeal to patients in reducing the frequency of this treatment.

Mesoblast/Angioblast will look to partner the trialing of this technology in a Phase II setting. The owner of Lucentis, **Genentech**, might be an obvious potential collaborator.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

Biota Holdings: Further Comments

This week Biota Holdings' chairman, John Grant, wrote a letter to shareholders to explain why Biota prematurely ended its litigation with **GlaxoSmithKline**, settling for a $20 million payment from GSK with both parties to pay for their own litigation costs.

Grant said that part of the board's objective of the litigation was to have GSK restore Relenza to an acceptable position in world markets, after repeatedly claiming for the last four years that GSK had failed to effectively market Relenza. The implication is that this objective had been met; in 2004 Relenza generated royalties of less than $600,000 and last year generated a royalty stream for Biota of $40 million and $20 million this year. However, there are major flaws in this argument.

Firstly, in July last year, Biota increased is damages claim against GSK from $308-$430 million to $564-$704 million, one month before it reported its highest annual royalty payment from GSK of $39.8 million.

The second flaw is that while Biota may be receiving around $20 million of royalties from Relenza sales a year at present, Relenza still only has about 20% of the global market for neuraminidase inhibitor flu drugs, of which the only other such drug on the market is the Gilead/Roche drug Tamiflu. Last year, Tamiflu generated royalties of US$414 million for Gilead, 11 times more than Biota's peak royalty last year. It is worth remembering that, the majority of the research for these neuraminidase inhibitor drugs was conducted in Australia, including by Graeme Laver and Peter Colman, and that Relenza was the first neuraminidase drug to get to market.

A third point to make here is that in 2004, there was not a large market for these flu drugs. Since 2004, 75 countries have now stockpiled these two flu drugs to cover 25%-50% of their populations and these stockpiles will need to be replenished. In 2003, Gilead's royalties from Tamiflu was only $15 million and only $62 million in 2004, escalating to a peak in 2007 of US$414 million. Biota's royalty flow may have been low in 2004 when its litigation action was initiated, but the increased Relenza sales can be largely attributed to global government stockpiling, not forcing the hand of a big pharma marketing partner.

The litigation action initiated by the Biota board was a dismal failure and this board should accept its mistake and review its composition with respect to board members who initiated the action, rather than claiming an obscure victory from this disappointing and mis-judged effort.

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Bioshares Model Portfolio (8 August 2008)

Company	Price (current)	Price added to portfolio	Date added
Impedimed	$0.70	$0.70	Aug-08
Antisense Therapeutics	$0.07	$0.07	Aug-08
Mesoblast	$1.25	$1.25	Aug-08
Avexa	$0.31	$0.32	Jun-08
Cellestis	$2.20	$2.27	April 2008
IDT	$1.75	$1.90	March 2008
Circadian Technologies	$0.80	$1.03	February 2008
Patrys	$0.26	$0.50	December 2007
NeuroDiscovery	$0.10	$0.16	December 2007
Bionomics	$0.33	$0.42	December 2007
Cogstate	$0.11	$0.13	November 2007
Sirtex Medical	$2.50	$3.90	October 2007
Clinuvel Pharmaceuticals	$0.34	$0.66	September 2007
Starpharma Holdings	$0.26	$0.37	August 2007
Pharmaxis	$1.83	$3.15	August 2007
Universal Biosensors	$0.73	$1.23	June 2007
Biota Holdings	$0.75	$1.55	March 2007
Probiotec	$1.35	$1.12	February 2007
Peplin Inc	$0.32	$0.83	January 2007
Arana Therapeutics	$1.12	$1.31	October 2006
Chemgenex Pharma.	$1.10	$0.38	June 2006
Cytopia	$0.28	$0.46	June 2005
Optiscan Imaging	$0.25	$0.35	March 2005
Acrux	$1.25	$0.83	November 2004
Alchemia	$0.29	$0.67	May 2004

Portfolio Changes – 8 August 2008

IN:

We have added three companies this week. Impedimed listed in 2007and is tracking well towards key milestones.

Antisense Therapeutics is focusing resources on its acromegaly project and looks like it will survive the current funding crisis besetting the market.

Mesoblast has released favourable results of its first bone fracture trial (autologous cells), which are possibly indicative of the potential of a set of forthcoming clinical trials using allogeneic cells.

OUT:

No changes.

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.

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: Phylogica, Pharmaxis, NeuroDiscovery, Biotech Capital, Cytopia,Arana Therapeutics, Starpharma Holdings, Cogstate, Xceed Biotechnology, Optiscan Imaging, Bionomics, ChemGenex Pharmaceuticals, Circadian Technologies, Biota Holdings, Stem Cell Sciences, Halcygen Pharmaceuticals, Peplin, BioMD, Impedimed, QRxPharma, Patrys, Labtech Systems, Hexima

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