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In this edition...
Peplin has again presented more clinical data to support the commercialisation of PEP005, this time suggesting a suitable dose for application of PEP005 to sections of skin on the face and scalp. Peplin continues to impress with its single-mindedness in driving PEP005 to the market.

Although the bigger biotech companies have tended to dominate investor interest in this sector, there is value to be found in amongst the micro-cap biotechs. We suggest three stocks that represent good value at current prices. We also update readers on progress and developments at Cytopia, QRxPharma and Patrys.

The editors
Companies covered: CGS, CYT, HTX, NDL, PAB, PEP, QRX

	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 (from 4 May '07)	-14.0%
Cumulative Gain	**181%**
Av Annual Gain (6 yrs)	**26.8%**

Bioshares is published by Blake Industry & Market Analysis Pty Ltd. The company also provides market and company analysis of the Australian pharmaceutical and biotech industries for local and international funds management institutions, venture capital funds and other related industry groups. For further details contact David Blake (see details below).

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Bioshares

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

More Positive Results Boost Peplin's PEP005

Peplin (PLI: 78 cents) has completed another trial with its drug candidate, PEP005. The Phase IIa trial in 88 patients, generated positive results, once again, this time in the treatment of pre-cancerous skin lesions (actinic keratosis) on the face and scalp. The trial was termed a field therapy, whereby an area on the face or scalp with several AKs was treated with the topical drug candidate.

Results from the trial showed that a complete response was achieved in 38% - 100% in all groups except for the lowest concentration group. The trial was not structured to achieve statistical significance, but to establish the maximum tolerable dose for treating the face and scalp to remove pre-cancerous skin lesions.

This is another consistently good result for the company with its drug candidate PEP005. The trial was important also because the results can be compared against a competing drug on the market, Aldara, which was tested in the treatment of AKs on the face and scalp. Aldara is approved for the treatment of non-cancerous skin lesions only on the face and scalp. The efficacy against Aldara is comparable however Aldara requires a 16 week treatment course, compared to two to three days for PEP005.

The subjective patient assessments in the latest Peplin trial also showed that the overall level of satisfaction - as measured by healing time, cosmetic outcome, ease of use and comparison with prior treatment - was very high, achieving a score of between 6.4 - 6.9 (from a possible score of 7.0) in the different dosage groups.

Peplin is currently in a quiet period having filed to IPO on the Nasdaq market in the US. The listing will coincide with a capital raising in the US where up to US$75 million will be raised.

The company plans to begin is first Phase III study in the first quarter of 2008. Our estimate is that the company should be in a position, if it achieves positive results, to file an NDA (new drug application) in the US in 2009 with marketing approval we expect in late 1010.

It will be a record year in 2009, when at least four other companies we anticipate will file drugs for regulatory approval, assuming positive results, including Pharmaxis, Clinuvel Pharmaceuticals, QrxPharma and Acrux (Testosterone MD-Lotion).

Peplin is capitalized at $161 million with $30 million in cash at September. Its core patent expires in 2018 and may achieve a patent extension out to 2023 for its drug candidate. The company has 100% intellectual property ownership over its asset. The business plan is to develop its own sales and marketing teams for the US, Australia and New Zealand and use third parties to sell the drug in other regions.

Bioshares recommendation: **Speculative Buy Class A**

Three Best Stocks Under $20 million

Of the 131 life science companies listed on the ASX, approximately 50 companies are capitalised at less than $20 million. Often called micro-caps, companies in this category are often termed penny dreadfuls, with the sub- $20 million cap category being perceived as a graveyard for companies that may once have been worth much more (by capitalisation) but have fallen out favour as business plans and strategies have gone awry.

However, not all biotech companies in the sub- $20 million cap class rate as investment discards. Some companies are small from a capital perspective because their business scope (revenues and markets) is modest, yet the chances of profitably can be achievable in the short-to-medium term.

While companies with a capitalisation less than $20 million cap (or even $50 million!) lack the liquidity profile that many investors prefer, for some investors, quality small cap stocks can be exceedingly attractive if the opportunity exists for significant investment stakes to be obtained for relatively small outlays. To follow, we feature three of the best value stocks in the sector valued under $20 million.

Healthlinx (HTX: 11 cents)

What it does

Healthlinx's goal has been to develop a blood-based ovarian cancer diagnostic, Ovplex, that is superior to the industry standard CA125 test. The CA125 test is unsuitable as a screening test for ovarian cancer. Development of an efficient screening test for ovarian cancer would be a major advance as ovarian cancer is associated with ambiguous symptoms. The issue is that if diagnosed at the localised stage (early stage) then the 5-year survival rate is 95%. However, the problem is that roughly only 20% of cases are diagnosed at that stage.

Latest developments

Healthlinx recently released results of a clinical study for its first generation Ovplex diagnostic, which the company said was 15% more efficient that the current CA125 test.

The company has in-licensed additional biomarker technology and antibodies from the University of Liverpool. With these resources, Healthlinx intends to develop a second generation Ovplex product with increased potential to detect early stage (stage I and II) ovarian cancer. Such a product may be potentially used as a community based screening test, however several trials will need to be conducted over 2008 and into 2009 to validate the test.

Why it is attractive

Healthlinx is attractive at current prices because it has made significant advances towards the first sales of a diagnostic technology in its first release. It has successfully completed a restructuring of its drug discovery assets into the private vehicle **Proaegis Biosciences**. And it has a clear set of milestones for investors to monitor in 2008. Healthlinx expects Ovplex Mark I to be commercially available through its pathology services partner **ARL Labs** in Q2 2008.

Neurodiscovery (NDL: 16 cents)

What it does

Neurodiscovery owns a fee-for-service business **Neurosolutions**, that specialises in electrophysiological research services, with expertise in neuropathic pain. This business is based at the **University of Warwick**, UK, and it has completed contracts with many small and large drug developers. The company also has interests in several clinical phase compounds.

Latest developments

Neurodiscovery has recently commenced two Phase II trials in Peru of NSL-101, a natural product pain drug. One 50 patient trial will compare the analgesic efficacy of NSL-101 with 5% lidocaine gel, as a pain treatment for dental work involving scaling and root planing. The results of this trial are expected in or around Q2 2008. Another 50 patient trial will evaluate the analgesic benefit of NSL-101 to manage pain following molar extraction, with results expected in Q2 2008. NSL-101 has a history of use as a natural medicine to treat dental pain.

Neurodiscovery is developing on a 50/50 joint venture basis the compound NSL-043 (or SD118) with Sosei of Japan. NSL-43 is a known compound that failed in a Phase III study in another indication, but may be beneficial in treating neuropathic pain. NSL-43 (oral administration) is progressing through a single dose and a multiple dose escalation studies in the UK.

Why it is attractive

Neuropathic pain is a drug development area of great interest to pharmaceutical companies. Neurodiscovery is well placed to progressively offer a number of potential compounds for license or acquisition by pharma companies. The company is capitalised as $9 million. Less cash at hand at September of $3.6 million, a technology value of $5.5 million can be ascribed Neurodiscovery. The company's fee-for-service business brought in revenues of $1.7 million for FY2007, followed by $640,000 in the September quarter. Valuing the service business at a conservative 2 time sales for FY2008 of $2.5 million essentially shows that little if no value is being attributed to Neurodiscovery's clinical stage (Phase II) assets and other pre-clinical programs. The scientific expertise of Neurosolutions brings advanced knowledge of pain drug development to table which reinforces the current attractiveness of the Neurodiscovery proposition.

Company	Code	CMP	Cap'n ($M)	Latest Cash ($M)	Tech. Value ($M)	Comments
NeuroDiscovery	NDL	$0.16	$9.1	$3.6	$5.5	Residual value ascribed to drug development program, inc. 2 Ph II trials
HealthLinx	HTX	$0.11	$8.3	$1.7	$6.7	OvPlex (Mk 1) ovarian cancer test to be available on Aust market Q2 2008
Cogstate	CGS	$0.14	$6.8	$1.5	$5.3	Strong growth in sales in current first half of FY2008

Cont'd over

Cogstate (CGS: 14 cents)

What it does

Cogstate markets computerised cognition tests. The company has established a modest foothold in the clinical trials industry. Drug companies use tests such as those developed by Cogstate to evaluate the effects of drug candidates on cognitive function. The tests can both serve to evaluate cognitive improvements or evaluate negative cognitive side effects.

Latest developments

Up until November 22, Cogstate announced it had signed 10 contracts valued at $2 million, surpassing the FY2007 figure of contracts signed of 17 contracts worth $1.96 million.

Why it is attractive?

At a capitalisation of $6.8 million, Cogstate is an attractive investment opportunity as it verges on the cusp of being cash flow positive for FY2008. While the company has a challenge to manage its cost base, growth in the number of bigger value contracts and the development of a reputation as a preferred supplier may mean a shift to profitability in 2008.

Bioshares recommendations:

NDL – Speculative Buy Class B
HTX – Speculative Buy Class B
CGS – Speculative Buy Class B

Patrys – Commercialising Natural Human Antibodies

Patrys (PAB: 50 cents) listed on the ASX on July 13, 2007, raising $25 million off an IPO price of 40 cents per share.

Patrys is an antibody therapeutics company with a number of points of difference with many other antibody firms. Patrys is a developer of natural human antibodies. Unlike 'humanised' antibodies derived typically from mouse antibodies or 'fully human' antibodies derived from a transgenic mouse expression systems, Patrys' natural human antibodies are far less likely to generate immune responses that might nullify the modulating benefit of the therapeutic antibody. This is because of residual mouse proteins or decorative sugar structures that originated with the mouse antibody or through the transgenic mouse or other non-human expression systems and continue to be marked as foreign matter warranting attention and removal by the human immune system.

An even more attractive feature is that these antibodies are not subject to many of the technology licensing obligations that beset many developers of monoclonal antibodies. Obligations exist for the accessing of proprietary methodologies to discover antibodies, for example phage display, and for accessing methods to humanise (engineer) and optimise antibodies.

The products that Patrys can produce therefore offer the benefits of reduced or negligible immunogenicity and a reduced royalty stack, of which the latter can make or break the investment viability of antibody products.

There is a third aspect to the Patrys technology that underscores its investment relevance. This is the potential therapeutic advantage that stems from the derivation of Patrys' antibodies, which are derived in the human body as natural responses to a molecular target that is implicated in a disease. Human antibodies discovered as the natural response can theoretically be much more (tissue) specific to antibodies generated by alternative approaches that are screened against molecular targets with varying degrees of affinity and specificity. Patrys claims that its two lead antibodies react with more than 90% of tumours sampled from 400 patients covering ten different tumour types. More importantly, the company has screened the antibodies against healthy tissue, with no binding observed

> *Patrys claims that its two lead antibodies react with more than 90% of tumours sampled from 400 patients covering ten different tumour types*

Progress since listing

Selected assets and know-how from two firms, **Oncomab GmbH** (Germany) and **Acceptys Inc** (USA), have been transferred to Patrys, which was incorporated as an Australian company on December 8, 2006. Oncomab was founded in 2001, based on human antibodies discovered at the **University of Wurzburg**. Acceptys was founded in 2002 to advance similar technology developed at **Colombia University**. (Acceptys continues to develop an infectious diseases antibody program, with Patrys holding a fully diluted 28% stake in Acceptys.)

The most advanced products Patrys is developing under its own direction and management are PAT-LM1 for the treatment of lung cancer and PAT-SM6 for the treatment of pancreatic cancer. With a funds from the IPO, the company has been able to step up its manufacturing program, which is necessary from a proof-of-capability point of view but also to build supplies for a clinical programs that are expected to commence towards the end of 2008. Historically, human antibodies that have been produced from human hybridomas have struggled to overcome manufacturing performance challenges relating to stability, yield and scale-up. However, the company looks to be on track to overcome these issues.

The company's third product under development is PAT-CM1, for the treatment of colon cancer, which continues in pre-clinical development. PAT-SM6 has recently been evaluated as a potential treatment for melanoma, and has proved promising in early tests with melanoma cells.

Patrys has also developed pharmacokinetic and immunogenicty assays to support animal and human testing of its lead products. This is an important and necessary step towards the company's

Cont'd over

objective of filing INDs in support of its lead candidates.

Partnering

Patrys has several collaborations and partnerships underway with other pharmaceutical firms, including Takeda, AstraZeneca (PAT-SC1 Gastric) and Debiopharm (PAT-PA1 Pancreas). Takeda now has selected five antibodies for evaluation (PAT-NM2, PAT-PM2, PAT-BA1, PAT-BA3, PAT-BA4). While these partnered programs offer the potential for Patrys to earn success fees and royalty payments, the company is heavily focussed on advancing the development of its internally managed products to points at which significant value is created.

Milestones to monitor

- Q4 2007 Commence large scale production of PAT-LM1 for clinical program
- Q1 2008 Pre-IND meetings with FDA for PAT-LM1 and PAT-SM6
- Q1 2008 Commence large scale production of PAT-LSM6 for clinical program
- H2 2008 IND filings for PAT-LM1 and PAT-SM6
- Late 2008 - Commence clinical programs

Summary

Patrys is a well-managed, high quality operation that has the foundations now in place to build an internationally recognised and competitive position in the antibody drug space. The company has the capacity to develop a staged pipeline of assets, with which it can mitigate individual product risk, but also exploit its ever-increasing knowledge concerning natural human antibody manufacturing, and clinical and regulatory development. Patrys is capitalised at $78 million.

Bioshares recommendation: **Speculative Buy Class A**

House of Lodge Gets Behind Cytopia & Competitor Rigel Surges on Positive Results

Cytopia (CYT: 50 cents) this week announced it had raised $5.1 million from existing and new institutional investors. The raising was conducted at a slight discount to the market price, at 46 cents a share, and represented the maximum 15% that can be raised without shareholder approval.

The raising itself is not all that significant, in terms of funds raised. However the selection of the broking house, **Lodge & Partners** is (the placement was conducted by Lodge Corporate). Lodge is an institutional broker and has the ability to generate considerable buying support through its network of investors and with research support from its respected biotech analyst. Lodge has helped raise funds for several biotechs that have performed exceptionally well from listing. These include **Cellestis** (listing price 25 cents, share price high $4.60), **Evogenix** (recently sold to Peptech) and **Mesoblast** (listed at 50 cents, share price high $2.60).

Four weeks ago (*Bioshares* 241) we featured Cytopia in Bioshares comparing it to other small-molecule kinase-focused drug developers. Our closest comparator was **Rigel Pharmaceuticals**, which at the time was capitalised at US$153 million. Following the release of some stunning results in arthritis, that company's share price has surged ahead and it is now valued at US$805 million, more than a fivefold increase!

Rigel yesterday reported data from a Phase II study in 189 patients with rheumatoid arthritis. The results were statistically significant with positive effects experienced by patients as soon as one week after treatment was initiated. The drug candidate is a small molecule, taken orally. The excitement around the result is that it may potentially compete against the biologic anti-TNF drugs such as Remicade, which generated sales of US$10.9 billion in 2006. There were side effects in about 10% of patients with the drug, which apparently were manageable and reversible.

This particular drug candidate is a syk kinase inhibitor. Similar to Cytopia, the company also has a JAK3 preclinical program to treat transplant rejection and rheumatoid arthritis, and a Phase I program to treat solid tumours although with an aurora kinase inhibitor.

The result is strong endorsement for Cytopia's core drug development programs and its core expertise in the inhibition of signal transduction pathways in cells (JAK2 and JAK3 pathways). Kinase inhibitors (Gleevec) have been shown to be very successful in oncology and this is another disease application that will help validate this very specific drug development approach.

(It's also very significant for listed biotech Incitive, which is developing small molecule drugs that hit the MAP signalling pathways inside cells to inhibit production of TNF-alpha as a potential treatment for rheumatoid arthritis. Although still at the preclinical stage, it helps articulate the potential value creation path that company is seeking).

Bioshares recommendation: **Speculative Buy Class A**

QrxPharma - Starts Second Phase III Trial

QRxPharma (QRX: $1.225) is developing a combination therapy using two existing opioid drugs, morphine and oxycodone. The company has just started two Phase III trials for the treatment of acute post-surgical pain. Completion of these two trials, if successful, should be sufficient to allow the company to file an NDA in 2009, with a view of getting its drug onto the market in the US in 2010.

There is a valid rationale for reducing the level of morphine for the treatment of pain. The use of morphine is associated with a range of side effects, including severe constipation, psychological dependence and sedation. Companies such as **Sucampo Pharmaceuticals** are developing therapeutics (in Phase III trials) to re-

duce the bowel dysfunction effects from opioid use. In Phase II clinical trials, QRxPharma has shown its combination therapy can reduce the level of morphine use by 34%-40%.

Change of Phase III indication

QRxPharma has changed the Phase III indication from chronic moderate-to-severe lower back pain and osteoarthritis to post-surgical acute pain. The lead indicator considered by the FDA is in the post-surgery removal of bunions. Other studies, such as acute pain following hip and knee replacement surgery, are likely to be conducted to expand the label.

The legal opioid market in the US is worth US$6.6 billion, with about US$2.5 billion of this market being for acute pain. QRxPharma is developing a controlled release version Q8011CR, to target the chronic pain market and the immediate release Q8003IR, to target the acute market. The controlled release version is expected to move into Phase I trials in 2008.

The reason for changing the indication of the immediate release version is to broaden the coverage for acute and chronic pain, but more importantly, it allows the company to keep to its timelines of filing the drug for approval in 2009, with the acute pain indication providing a quicker path to market.

Similar to **Peplin**, QRxPharma is likely to build its own sales force in the US, aiming to gain access to 30% of the market with a sales team of between 120-150 people. The first of the company's core patents expires in 2016 with the potential of up to five years patent extension.

Well-funded

The company has sufficient funds to complete its Phase III studies. Final trial design still needs to be negotiated with the FDA, in particular the trial size. Technical risk remains with this company, as does the regulatory risk. There is also a market risk, where the company intends to charge a premium for the combination of two existing drugs. However the need to reduce opioid use side effects in pain management certainly exists.

QRxPharma listed in May this year at $2.00 a share. It raised $50 million and its technology value on listing was $100 million. It was a high valuation for the Australian market and the declining share price is not surprising. The company now has a technology value of $48 million with $44 million in cash and is now a more appealing value proposition.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares Model Portfolio (14 December 2007)

Company	Price (current)	Price added to portfolio	Date added
NeuroDiscovery	0.16	0.16	December 2007
Bionomics	0.43	0.415	December 2007
Cogstate	0.135	0.13	November 2007
Ventracor	$0.65	$0.625	October 2007
Sirtex Medical	$4.70	$3.90	October 2007
Clinuvel Pharmaceuticals	$0.36	$0.66	September 2007
Progen Pharmaceuticals	$2.54	$3.52	September 2007
Starpharma Holdings	$0.39	$0.37	August 2007
Pharmaxis	$4.11	$3.15	August 2007
Universal Biosensors	$1.40	$1.23	June 2007
Biota Holdings	$1.28	$1.55	March 2007
Tissue Therapies	$0.42	$0.58	February 2007
Probiotec	$1.43	$1.12	February 2007
Phylogica	$0.21	$0.42	January 2007
Peplin Inc	$0.78	$0.83	January 2007
Arana Therapeutics	$1.18	$1.31	October 2006
Sunshine Heart	$0.15	$0.19	September 2006
Chemgenex Pharma.	$1.08	$0.38	June 2006
Cytopia	$0.50	$0.46	June 2005
Optiscan Imaging	$0.28	$0.35	March 2005
Acrux	$1.32	$0.83	November 2004
Alchemia	$0.69	$0.67	May 2004

Portfolio Changes – 14 Dec 2007

IN:

Neurodiscovery has been added at 16 cents.

Refer to commentary on previous page.

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, Cygenics, Cytopia, Biodiem, Arana Therapeutics, Starpharma Holdings, Cogstate, Xceed Biotechnology, Incitive, Optiscan Imaging, Bionomics, ChemGenex Pharmaceuticals, Medical Therapies, Circadian Technologies, Biota Holdings, Stem Cell Sciences, Halcygen Pharmaceuticals, Peplin, BioMD, Impedimed, QRxPharma

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	$950	6-10 email addresses

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