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In this edition...
Biotech is running hot in the US, galvanised by a string of acquisitions late in 2011 and early this year. With a bevy of ASX-listed companies either initiating a US listing or thinking about it, their timing may be spot on. One of these companies is Biota, which with a US government contract may achieve recognition in the US that it is struggling to gain locally. Improvements made to Phosphagenics' pain drug patch look promising. Genetic Technologies has modified its positioning for its breast cancer risk assessment tool and Clinuvel is considering its funding options.
The Editors
Companies Covered: BTA, CUV, GTG, POH

	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 - May'11)	45.4%
Year 11 now commenced	-25.9%
Cumulative Gain	**212%**
Av. annual gain (10 yrs)	**21.2%**

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Bioshares

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Edition 443

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

Cross-Border Listings Ramp Up With Surging US Biotech Sector Interest

Interest in the US biotech sector is on the way up. The Nasdaq Biotech Index has surged 39% since August last year, opening up a biotech IPO window in the US.

What is driving the interest in US biotechs? Well for starters in November last year **Gilead Sciences** made a bid for **Pharmasset** worth US$11 billion. Why this deal is so stunning is that Pharmasset has just moved into Phase III trials with its lead program in the area of Hepatitis C (HCV). That transaction was completed in January.

Also in November, **Regeneron Pharmaceuticals** gained approval from the FDA for its drug, Eylea, for the treatment of wet age-related macular degeneration. Regeneron's stock price has tripled in the last 12 months and is now valued at US$9.5 billion. The company has just increased its sales forecast for this year to US$250-US$300 million for Eylea.

In January, **Roche** made a hostile bid for diagnostic group **Illumina** for US$5.7 billion, which Illumina is trying to fend off. And then Amgen announced it would buy Micromet for US$1.16 billion. This deal was also announced in January this year.

Also in January, **Bristol-Myers Squibb** did not want to be left behind and announced a bid for **Inhibitex**, which has a mid stage clinical drug candidate in a similar space to the Pharmasset program. BMS paid US$2.5 billion in a deal that was finalised this month.

HCV is a hot area of biotech at the moment. In October last year **Roche** made a successful bid for **Anadys Pharmaceuticals** for US$230 million, which is also in the HCV space.

To throw a spanner in the works, on Friday Gilead announced a setback with its just acquired Pharmasset HCV drug candidate. In a subset of patients on the therapy with GS-7977, six of eight patients had a viral relapse within four weeks after stopping therapy. It is not going to be as clear cut as Gilead had been hoping for. An analyst covering the stock for Deutsche Bank said that whilst it was disappointing it was unlikely to be a disaster scenario, according to *BusinessWeek*. Gilead's market value fell US$5.9 billion on Friday.

Not surprisingly, there has been a ramp up in listing activity within the Australian biotech sector. Australian biotechs are headed for the US as the US funding window now looks to be opening.

Sunshine Heart

Accessing US capital markets appears to be the reason for three local biotech companies seeking to list on US exchanges. This week Sunshine Heart announced its shares had been successfully listed on the Nasdaq as well as trading on the ASX.

Sunshine Heart has been increasing its focus on US investors in the last 12 months. A

Cont'd over

– from Page 1

Nasdaq listing was a requirement linked to an earlier US capital raising. The company will need access to larger pools of capital, with up to $40 million required to complete its pivotal study with its C-Pulse heart assist device.

On the ASX the shares trade as Chess depository interests (CDIs), with Sunshine Heart being a US company. Each Nasdaq listed share corresponds to 200 CDIs on the ASX. The stock is trading on the Nasdaq under the code SSH. Trading on the first day was very thin, with only 1,674 shares traded.

Prima Biomed

Prima Biomed this week announced it filed a registration statement with the US SEC as part of the process to make a Level II ADR Nasdaq compliance listing.

There is considerable interest in the US in the cancer immunotherapy space following Dendreon's success in getting Provenge to market. That cancer vaccine is heading towards generating US$300 million in sales a year, having made sales of US$82 million in the December quarter.

Another cancer immunotherapy company, Argos Therapeutics, filed its registration statement in mid 2011 and this week announced the pricing of its IPO. It plans to raise US$74 million to fund its Phase III study in kidney cancer. Lazard Capital Markets and Canaccord Genuity are the lead underwriters.

Although US funds can buy Prima shares on the ASX, US brokers can not advise their retail clients on ASX listed companies, but they can if the company has an ADR listing. Prima CEO, Martin Rogers, is seeking to increase interest/liquidity in the US from both retail and institutional investors.

Each Nasdaq share will correspond to 30 ASX listed shares. Prima will trade under the code PBMD.

Biota Holdings

Biota Holdings is seeking to gain better access to US capital markets. Local investors are showing no patience or diminished interest in the stock, and being closer to its most important customer, the US Government, or more specifically, BARDA, is also an important factor.

Biota is looking at how access to the US can be best facilitated. This could be either through a merger or by moving its listing from the ASX to the US. By mid year the company expects to be in a position to know whether or not it wants to pursue this option.

New Listings on the ASX

Since December 2010, three North American companies have listed on the ASX - Reva Medical, Bioniche and GI Dynamics. A fourth company is expected to lodge its prospectus next week. This company has some research links with Australian biotech. Bioshares will provide details once available.

US and Australian companies are matching their needs with the exchange and the capital markets that are most suited to their current needs.

Bioshares

Phosphagenics Oxy Patch Starts to Look Competitive

Phosphagenics (POH: $0.205) has revealed several performance outcomes from improvements made to its TPM/Oxycodone transdermal patch, developed in conjunction with the global adhesives company **3M**. TPM/Oxycodone is being developed as a treatment for chronic pain and it would be the first patch delivering oxycodone, if successfully commercialised.

Phosphagenics technology combines alpha-tocopheryl (phosphorylated Vitamin E) with drug substances, for example, oxycodone, insulin, diclofenac or retinoic acid, to improve the delivery of active drug substances across the skin.

This third generation version of the patch is half the size of, and contains one quarter of the drug material originally incorporated in the first generation patch. The new patch delivers 4.5 times more oxycodone than its first generation patch. The quantity of active drug contained in the patch is now approximately 50mg for a three day application period. The onset of the drug is twice as fast and the rate of delivery is seven times as fast. On a normalised basis (i.e. per square centimetre), the rate of delivery is 15 times as fast.

Its previous version of the patch was achieving CMax at the end of the 72 hours of application, whereas the latest version is achieving CMax within 24 hours, with steady blood concentration levels. (CMax is the peak level a drug reaches after it has been administered.)

Phosphagenics must now characterise the bioavailability of the active drug as determined by its third generation patch and assess drug deposition in the patch once it has been used after three days. The last task is important because the FDA pays close attention to residual drug given the potential for drug abuse to take place where drug abusers can access disposed drug patches.

The next component of Phosphagenics' preparatory trials, which are designed to lead into a single pivotal Phase III registration trial, will include a patch with some further modifications, including one that minimises wear issues such as sliding and movement of the patch. This next stage of the trial is a multi-dose study involving 20-25 subjects assessing wear issues and pharmacokinetics.

Implications

The news for investors is that it appears that the Phosphagenics patch delivers a steady state from the first patch applied. This is very positive achievement, and can be compared to the fentanyl patch (Duragesic) which reached steady state drug levels on the fourth patch.

A rapid time to steady state should in theory provide superior pain management. It would appear that one of the goals of the second stage of the trial to explore steady state levels based on the number of patches applied has now been achieved.

Cont'd on page 7

Biota Holdings – A Stock for the Patient Investor

Biota Holdings (BTA:$0.78) has reported a low revenue first half. Total revenue was $7.8 million. The company generated a net loss of $11.0 million for the half, and retained a cash balance of $56 million at the end of December.

Low & Slow start to Northern Hemisphere Flu Season

The low revenue was directly related to the very mild flu season. In the USA, the number of people visiting their doctor with influenza-like symptoms was only 1.4%, below the baseline level of 2.4%. The level of reported influenza-like symptoms was low or minimal in all states.

In Europe, it has been a slow start to the flu season however the number of cases of influenza infection has been increasing significantly in recent weeks in Western Europe. All 34 circulating strains are sensitive to the neuraminidase drugs Tamiflu and Relenza.

In Japan, there has been a persistent increase in influenza infections in recent weeks.

The relevance for Biota is that it should see increased royalties from Inavir (4% of sales) and Relenza (7% of sales) sales in Japan for this quarter, also from sales of Relenza in Europe, with the US likely to generate continued low sales of Relenza in this quarter. In the US, seven out of eight viruses were covered by the existing vaccine, and all circulating viruses were sensitive to Tamiflu and Relenza.

For a longer-term perspective, a low season this year in the US may result in a high flu season in the next year or two, particularly if there is an antigenic shift in the strain and depending on weather conditions.

Biota receives global royalties from sales of Relenza, with US royalties ending in 2014, in Europe in May 2015 and in Japan in 2019.

Over the next two years, there should be a significant lift in replenishing outdated stockpiles of Relenza by governments around the world, particularly in the US, which should see more of a 50/50 balance between Relenza and Tamiflu, rather than the current 20/80 split in favour of Tamiflu.

HRV Phase IIb trial

Biota's Phase IIb human rhinovirus (HRV) trial has now completed recruitment. HRV is the family of viruses responsible for the common cold. Biota is focusing on a subset of the population in whom HRV infection has more serious consequences. This trial is in people with asthma, where a HRV infection is often more serious, causing up to a two week infection rather than just an infection lasting just a few days. A HRV infection can make the patient's asthma less stable, as well as potentially cause lung damage.

This trial recruited patents over two winter seasons. It initially targeted around 400 patients. The patients were required to self diagnose prior to enrolment, with the viral infection confirmed during treatment with Biota's drug candidate, now called 'vapendivir'. After the first season, Biota looked at how accurately patients were self diagnosed. This diagnosis turned out better than 50% which meant that Biota could then reduce its study numbers to around 300.

Other applications for this potential therapy are for patients who have received a lung transplant, where HRV infection can be terminal, in patients with COPD (chronic obstructive pulmonary disorder) and people on immune suppression treatment.

Results from the trial are due to be released next quarter. If the results are positive, Biota has the option to progress clinical development of the program on its own. This is contingent on accessing further funding. Or it may license the program, if it receives an attractive offer. Both options will be considered and will obviously be dependent on the trial results.

BARDA Contract

Biota's US$231 million contract with BARDA in the US to develop a laninamivir (called Inavir in Japan) for the US market remains the most important program for Biota. In the first half Biota generated $4.3 million in revenue from this contract to develop laninamivir.

Biota is still looking at how it can better access US capital markets and also gain better recognition of its assets, including its BARDA contract with the US Government. This could involve merging with a US company or listing on a US exchange.

A move to the US would give better access to larger amounts of capital which the company may need as it moves up the value chain with completing commercial development of programs without partners.

It may also be in the company's interests to be closer to the US if its man customer is the US government and it will seek to generate hundreds of millions of dollars in future laninamivir sales to BARDA for stockpiling of this long acting (it only needs to be taken once as opposed to twice daily for five days for Tamiflu and Relenza) neuramindase inhibitor flu drug. Details of the options open to the company with respect to accessing US capital markets should be released by mid year.

Summary

For investors the BARDA contract offers a long term gain, with the drug not expected to complete development until around 2016. Closer term drivers will be results from the Phase IIb HRV trial next quarter and a move to the US markets for the company, although it's unclear how that will be structured and how quickly a valuation re-rating will occur.

Clearer drivers for the stock will be government Relenza stockpile replenishment orders, which should occur over the next two years.

Biota is a company with a number of valuable assets. It's a stock that has a high probability of rewarding investors, however some patience is required. Biota is capitalised at $142 million.

Bioshares recommendation: **Speculative Buy Class A**

Genetic Technologies Modifies Brevagen Positioning

Genetic Technologies (GTG: $0.13) markets the Brevagen breast cancer test in the US. The test is a risk assessment tool which enables physicians to assess the likelihood of Caucasian women over the age of 35 who do not have a family history of breast cancer of developing breast cancer. The test combines genetic with clinical information, such as age at which the subject first gave birth and age at menarche. On ascertaining a patient's risk profile, a physician can then make informed decisions regarding the management of the patient, for example, commencing more frequent monitoring or intervening with a drug therapy.

The product was launched in the US in June 2011. Since launch, the company has encountered doctors who have been unsure of what patients to use the test on, given that the test is designed for women with an intermediate risk of breast cancer.

The company has now determined that the messaging for Brevagen is that it is most relevant for women who have had a clinical history and life-time exposure to estrogen. According to Genetic Technologies, more than 75% of breast cancers are estrogen-positive. The Brevagen test contains clinical questions (e.g. regarding obesity) and genetic components related to estrogen exposure.

Despite the uncertainty of physicians towards the most appropriate utilisation of the test, the company says reimbursement levels achieved to date have been positive.

CLIA Certification for Key US States

This week the company received CLIA certification of its Fitzroy, Melbourne laboratories from the US Centers for Medicare and Medicaid. Its initial CLIA certification in April 2011 permitted the company to offer its test in 42 US states. This most recent certification covers the states of California, Florida, Maryland, Nevada, New York, Pennsylvania, Rhode Island and Tennessee. However, Genetic Technologies must still make a submission to New York's State Department of Health, within its Clinical Laboratory Evaluation Program. Such an approval may be achieved in 2013.

Access to Florida and California is important for Genetic Technologies given the large populations of these states. The addressable market in the US for the Brevagen test (Caucasian women over the age of 35) totals 60 million, based on 2009 US Census estimates, with 4.7 million in California, 3.6 million in Florida and 3.6 million in New York State.

There were an estimated 230,000 new cases of invasive breast cancer diagnosed in the US in 2011. Familial breast cancer accounts for 5% of breast cancers; non-familial accounts for the remaining 95%. As mentioned earlier 75% of breast cancers are estrogen-related.

The company will conduct further validation studies to expand the applicability of the test into non-white populations in the US and into women aged 35 years.

Future Sales?

We expect sales of Brevagen to grow slowly as the product continues through a roll-out phase over 2012. Initial selling phases for medical products in US markets are not only complicated by product messaging and sales force reach issues, but also by payment and reimbursement factors.

Brevagen is a test that has the potential to generate attractive margins if it becomes widely accepted in the breast cancer management setting. The availability of an assessment tool that can offer both psychological benefits (to the patient) and economic benefits (to payors) in personalised health management plans is the thesis of the Brevagen investment argument, more so given the fear status breast cancer is awarded by women. However, it is too early to judge whether the test will be widely adopted, one the one hand selling (hypothetically) 100,000 units per annum or, on the other hand, settling as a niche product, selling (hypothetically) 10,000 units a year.

Genetic Technologies recorded net operating cash flows of -$3.5 million and receipts of $3.8 million for the six months ending December 31, 2011. Cash at the end of the half year was $12.6 million. Genetic Technologies is capitalised at $60 million.

Summary

Until unit sales of Brevagen become available and a clear trend is observed, potentially in the second half of this year, we place a Speculative Hold recommendation on the stock and have removed the stock from our Model Portfolio.

Bioshares recommendation: **Speculative Hold Class A**

Bioshares

Contributed Discussion

The Aussie Invasion or Time to go to the US?

In my first article of this series (see *Bioshares* 422), I dealt with structures for US entities seeking to raise cash in Australia. In this article I look at the flipside, Australian companies seeking to raise capital in the US. Often seen to open up new markets, there are many good Australian biotech companies which target the US in the hunt for cash to continue the development of quality Australian technology. It is clearly a two way street in terms of the US / Australian relationship.

For Australian companies used to the regulatory requirements for making an offer of their shares locally, to the extent you are seeking to raise capital in the US, the Australian disclosure / prospectus regime under the Corporations Act do NOT apply. You will still need to comply with the ASX Listing Rules but in terms of the formalities of an offer, you need to comply with relevant US laws.

Exempt US Offerings

The US Securities Act of 1933 (US Securities Act) regulates the offer and sale of any securities to persons situated in the United States. This includes an Australian company making the offer of its securities to persons in the United States.

The US Securities Act is similar to the Australian Corporations Act in that it provides, unless exempted, any offer of securities (including by a foreign issuer) must be made pursuant to a current registration statement (prospectus) that is filed with the Securities Exchange Commission (SEC) and prepared in compliance with US law.

There are a number of exemptions (which are complex) for both US domestic and foreign issuers to enable them to offer securities to exempt investors in the US without being subject to registration under the US Securities Act. Some of the more commonly used exemptions to raise capital in the United States are found under Regulation C (for US domestic issuers) and Regulation D or Rule 144A (for foreign issuers), often referred to as a "safe harbour" exemptions.

A word of warning: care should always be taken in offerings in the US to retain US lawyers as often the devil is in the detail in terms of compliance!

Common Considerations in Exempt Offerings

While it is possible to bring an offer of Australian shares to exempt US investors (for example to certain sophisticated US investors) within a safe harbour (and not require SEC registration of an offer document or prospectus), it is important to understand some considerations in such safe harbour offerings -

(a) An Australian issuer is not permitted to undertake any "general advertising" or "solicitation" in respect of the US exempt or safe harbour offer and you need to be careful that any press release which is published or made in the US complies with the exemption requirements.

(b) Rule 144A offerings are only available in respect of those securities which are not tradeable on any US securities exchange and only to those institutions which the issuer reasonably believes to be "qualified institutional buyers" (QIBs). This term QIB is defined wider than just institutions, but care must be taken that the subscribers do qualify - it does not extend to high net worth individuals.

(c) The Australian shares issued under such safe harbours are not freely tradeable in the US. For example in order to qualify under a Regulation D exemption, the issuer must take steps to ensure the relevant securities are not being acquired in the US with the view they are to be on sold to the US public. Often this is dealt with in seeking warranties or representations from the US subscriber.

(d) Whilst an offer can be exempted and there is no prescribed form of documentation for the offer or subscription, it is important to have some form of subscription agreement where the Australian issuer can secure representations by the US investor as to their status and intentions (for example as to no intention to on sell the securities to the US public).

(e) It is possible to conduct an exempt offer without any information memorandum (or like disclosure document) being made available for the potential exempt investors; the downside to such undocumented offerings is there may be an increased exposure to liability for a US purchaser alleging misleading conduct in respect of any statements made for example by the salesperson making the offer on behalf of the Australian company (see section 3 below).

(f) For Regulation D offerings there are some notification requirements and on sales of the securities may be more restricted than under a Rule 144A exemption offering.

(g) For Rule 144A exempted offerings, where requested by a potential investor, the Australian company is required to provide certain information to the holder of the security or a prospective investor.

The choice of exemption pathway in the US for an Australian company involves a more detailed consideration of the requirements for each exemption which is outside this general discussion. I have also not dealt with all of the exemptions which may be available. The caveat is seek legal advice before rushing off to raise capital in the US.

US Retail offering by Australian companies - ADR program

In the alternative, an Australian company could sponsor an American Depositary Receipt (ADR) program. An ADR is similar to the Australian Chess Depositary Instrument (CDI). Effectively the ADR program allows US investors to trade the securities of a foreign issuer on US markets and facilitates settlement in the US in US dollars.

Under an ADR, a US commercial bank (the depositary) holds the

Cont'd over

underlying shares in the Australian listed company (which have been deposited with the depositary) and then issues negotiable certificates in registrable form - which are exchangeable for the underlying shares. Those negotiable certificates (the ADRs) are then capable of trading in the US.

While there are different "levels" of ADR registration, an Australian company would require a level 3 ADR registration to enable it to register a current registration statement with the SEC for an offer to the US public (including retail investors) of the ADRs.

This is an expensive and time consuming process as the Australian company would effectively need to have its financial accounts reformatted to comply with US GAP (general accounting principles) and the offer document would have to contain much of the material Australian companies are used to in a "long form prospectus", with a complete due diligence. Further your ongoing disclosure obligations do not necessarily match the listed company's disclosure obligations under the ASX Listing Rules.

Also the level of interest in ADRs for US investors will in part turn on the liquidity of the ADRs which does not reflect the liquidity of the primary market (for example the Australian Stock Exchange) of the underlying shares in the Australian company. This requires on going support and coverage by US brokers.

Liability

While there are certainly less specific regulatory disclosures for an exempt or safe harbour offering in the United States as compared to registering a current registration statement with the SEC (no doubt due to the recognition that sophisticated investors are expected to need less regulatory protection than the retail public), there is still exposure for the Australian company in respect of an exempt offer to the general "anti-fraud" provisions of the US federal and state securities laws. This is not conceptually materially different than an Australian listed company would face in respect of an offer of its securities to sophisticated investors in Australia. However it is worth noting that by undertaking a US raising, the Australian company and those involved in the offer also bring themselves within this US liability regime. There have been cases where the US courts have found sufficient connection to the US by a foreign issuer to allow a US investor to bring an action in the US for misleading representations or omissions.

US Legal Opinions

Often US brokers involved in exempt issues / offers may request what is commonly referred to as a 10b-5 negative assurance opinion which states that the US counsel has conducted the due diligence review in respect of the exempt offer and is not aware of any material misstatement or omission in the "offering document/s" - but the appropriateness of such opinions depends on the level of due diligence undertaken in respect of the offer.

For example with an undocumented Rule 144A private placement by an listed Australian company to US QIBs, sometimes the listed company will take the approach that limited or no due diligence is required (given the listed company's compliance with continuous disclosure obligations under the ASX Listing Rules).

Some Practical Considerations

A successful US capital raising does not happen overnight, and from what I have seen in previous transactions, it is usually the result of a long period of establishing a profile in the US together with relationships with brokers and fund managers in the US.

The US investors also tend to be very concerned with suspensions in trading - as it is far less common for US companies to seek a suspension of trading in its securities (as compared to the approach in Australia). This can cause some backlash from US investors.

From a practical viewpoint, it is also prudent for the Australian listed company to check its insurance cover (for example under D&O Insurance) to ensure there is no exclusions for liability arising out of US claims.

Andrew Gaffney is a partner in Middletons Corporate Advisory Group, is head of their Melbourne equity capital markets team and specialises in assisting biotechnology companies. Middletons is a national corporate law firm with offices in Melbourne, Sydney, Perth and Brisbane. The above comments are of a general nature, not exhaustive and should not be relied upon as providing legal advice.

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Bioshares Model Portfolio (17 February 2011)

Company	Price (current)	Price added to portfolio	Date added
QRxPharma	$1.58	$1.66	October 2011
Mayne Pharma Group	$0.300	$0.435	September 2011
Acrux	$3.33	$3.37	June 2011
Bioniche	$0.60	$1.35	March 2011
Somnomed	$0.97	$0.94	January 2011
Phylogica	$0.036	$0.053	September 2010
Biota Holdings	$0.78	$1.09	May 2010
Tissue Therapies	$0.37	$0.21	January 2010
Atcor Medical	$0.10	$0.10	October 2008
Impedimed	$0.53	$0.70	August 2008
Bionomics	$0.47	$0.42	December 2007
Cogstate	$0.25	$0.13	November 2007
Sirtex Medical	$4.90	$3.90	October 2007
Clinuvel Pharmaceuticals	$1.82	$6.60	September 2007
Pharmaxis	$0.99	$3.15	August 2007
Universal Biosensors	$0.72	$1.23	June 2007
Alchemia	$0.405	$0.67	May 2004

Portfolio Changes – 17 February 2011

IN:
No changes

OUT:
Genetic Technologies has been removed from the portfolio at 13 cents. See page 4.

Clinuvel Pharmaceuticals Files Scenesse for Approval in Europe

Clinuvel Pharmaceuticals has filed its drug Scenesse for approval with European regulators (EMA). The first indication is for the treatment of a condition called erythropoietic protoporphyria (EPP), which is characterised by a severe intolerance to sunlight.

It's an orphan drug indication, with the product already available in Italy and generated sales of $1.04 million in FY2011.

It will take anywhere from 12-18 months to be reviewed by the EMA. In the meantime, Clinuvel will need to address its funding position. The company had $11.7 million in cash at the end of December. At its current spend rate, it has about 10 months cash only.

There was a strengthening in the company's share price prior to filing for approval, with the stock retracing some of that ground in the last two weeks. There may be more price weakness ahead as the company addresses its funding position.

There are three options open to the company. One is a licensing deal, licensing the drug outright, or for an indication or a region. The second is a bridging loan. And the third and the most likely is raising funds through equity markets.

An outright sale of the business is also a possibility, although this would be more suitable once European approval has been gained.

Clinuvel is capitalised at $56 million.

Bioshares recommendation: **Speculative Hold Class B**

– POH from page 2

Phase III Trial

The next major step in the development of the Oxy patch is the design and initiation of a Phase III trial.

A pain patch that recently gained FDA approval was **Purdue Pharma's** Butrans, a patch that delivers buprenorphine. Butrans was evaluated in one 12 week study that enrolled 1,024 opioid-naive patients and in another 12 week study that enrolled 1,160 patients with chronic lower back pain. In this second study, Butrans was administered at a dose of 20 mcg/hour versus a low dose 5mcg/hour and placebo.

A key question for investors will be what size of trial the FDA will demand of Phosphagenics, with trial costs a clear function of size. Previously Phosphagenics has flagged a Phase III trial with small numbers, however, the Purdue Butrans program was very large to begin with, partly driven by an almost 50% discontinuance rate. That may be less of an issue with TPM/Ocycodone.

Summary

Phosphagenics' concentrated focus on a single product in the pharmaceuticals arena is beginning to yield results. The company is in the process of elevating its internal capabilities on the commercial side of the development of TPM/Oxycodone, which we expect will lead to further product development gains going forward.

Following a $27 million capital raising in the fourth quarter of 2011, the company's new found ability to attract capital is now a strong positive with the stock, with key investors indicating a willingness to support future capital needs so long as execution remains on track. Phosphagenics is capitalised at $209 million.

Bioshares recommendation: **Speculative Hold Class A**

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

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