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Companies covered: ACG, CGS, IVX, PBT

	Bioshares Portfolio
Year 1 (May '01 - May '02)	21.2%
Year 2 (May '02 - May '03)	-9.4%
Year 3 (May '03 - May '04)	70.6%
Year 4 (May '04 - May '05)	-16.3%
Year 5 (May '05 - May '06)	77.8%
Year 6 (May '06 - May '07)	17.4%
Year 7 (May '07 - May '08)	-36%
Year 8 (May '08 - May '09)	-7.4%
Year 9 (May '09 - May '10)	50.2%
Year 10 (May '10 - May'11)	45.4%
Year 11 (May '11 - May '12)	-18.0%
Year 12 (May '12 - May '13)	3.1%
Year 13 (May '13 - Current)	66.6%
Cumulative Gain	**494%**
Av. annual gain (13 yrs)	**20.4%**

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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 - Editor
Ph: (03) 9326 5382
Email: blake@bioshares.com.au
Mark Pachacz - Research Principal
Ph: 0403 850 425
Email: pachacz@bioshares.com.au

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Bioshares

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Prana Biotechnology Achieves Some Positive Signals in Phase II Huntington's Disease Trial

Of the 12 or so trials that have been conducted in Huntington's disease, not one has been able to generate a positive effect on the functional capacity of patients with this disease. According to Dr Ira Shoulson, Prana Biotechnology (PBT: $0.86) is the first company to do so, with a favourable signal from Prana's Phase II trial results reported this week. Dr Shoulson's comments are important as he is the Chair of the Huntington Study Group which represents clinical researchers worldwide working in this disease area. Dr Shoulson said the results were heart warming and that there was a genuine level of optimistic support for a larger trial with PBT2 in Huntington's disease.

Clinical Study

Prana has completed a Phase II study of its drug candidate PBT2 in a trial that enrolled 109 patients with mild-to-moderate Huntington's disease. Patients were treated daily for six months, with either a 250mg dose, a 100mg dose or a placebo.

Huntington's Disease

Huntington's disease is caused by a mutation of the Huntingtin gene, which was discovered in 1993. If affects around 30,000 people in the US and over 80,000 people worldwide, with disease symptoms occurring from around 30 years of age. It affects men and women alike causing involuntary movements, behavioural changes and cognitive decline. There is only one treatment available to help control muscle movement and no treatments approved to help cognitive performance.

Phase II Results

The results from Prana's Phase II trial were somewhat mixed but with some encouraging outcomes. The primary endpoint from this trial was safety and tolerability. The drug was well tolerated and the safety profile appeared reasonable. There were 10 serious adverse events, with nine of these being in patients taking PBT2, but only one of these events (not disclosed) was linked to the drug candidate. Overall a positive outcome was that the drug has now been tested for twice the length of time to that previously, which was in a three month Phase II trial in patients with Alzheimer's disease.

Looking at the eight tests for cognition, there was a statistically significant improvement in one of these measure, that being the Trail Making Test Part B. In this test, patients are required to effectively join the dots (in the following order: 1, A, 2, B, 3, C, 4, etc…). Those taking the highest dose of PBT2 achieved a 4 second improvement, compared to a 12 second decline in the 100mg PBT dose and a 14 second decline in the placebo group at 26 weeks. This relates to around a 10-15% clinical improvement according to Dr Ray Dorsey, the Principal Investigator on the trial. The p-value was less than 0.001 at 12 weeks and 0.042 at 26 weeks, both statistically significant.

Cont'd over

There was no improvement in Trail Making Part A test, however this is a much more straightforward test where patients join dots in numerical order (1,2,3,4,5…etc).

On the executive function composite score, there was a 'trend toward improvement', which means that statistical significance was not achieved. The p-value for the group was 0.069, which was above 0.05, the cut off for statistical significance. However, in those with only mild Huntington's disease, statistical significance was achieved, with a p-value of 0.038. In fairness to the company, it did not power the study to achieve statistical significance. So when that is achieved in such studies, it is a very encouraging result.

In a small subset of six patients, there were also signs of less brain atrophy in those taking PBT2.

That a statistically significant improvement was achieved in cognition (as measured by the Trial Making B Test) in those patients taking the highest dose of PBT in such a small trial is very encouraging for the company. Also of interest is that in Prana's earlier Phase II trial with PBT2, there was also a positive outcome in the same measure using Trail Making B test. It was also encouraging that there were signs of improvement in executive function, which has never been seen in any other Huntington's disease clinical trial. However, the trial showed that PBT2 had no impact on motor function or behaviour. However Dr Shoulson said that patients with uncontrolled motor function were excluded from this trial.

Discussion

The results from this Phase II Huntington's disease trial will place the company in a good position to raise additional funds, to conduct a partnering deal, and to progress the program into larger clinical studies. Prana will meet with the FDA to discuss the next trials for PBT2 in this indication, and whether that trial might be a Phase III study that will allow the drug candidate to gain approval. CEO Geoffrey Kempler said the company is leaving open the options as to whether the next trial will be funding by Prana or by others (a partner).

According to the company, more than 200 people tuned in to Prana's conference call this week, indicating substantial interest in Prana and in the field of Huntington's disease.

In coming weeks, Prana is expected to announce results from its Phase II trial with PBT2 in patients with early stage Alzheimer's disease. That trial treated 42 patients with either a placebo or a 250mg dose of PBT2. The trial was completed at the end of last year.

If results are positive from Prana's Phase II trial in Alzheimer's disease, then not only will the company be in a position to look at progressing a treatment for two indications, but the results may also support the benefit of this drug in Huntington's disease if more positive data on cognition is achieved as measured by the Trail Making Part B test.

For Prana, its lead application for PBT2 would appear to be the orphan drug treatment for Huntington's disease. Developing PBT2 for Alzheimer's will be a much longer and larger program, with Phase III trials taking at least three years.

Prana is capitalised at $363 million. The company had $19.3 million in cash at the end of last year.

Recommendation

Prana's share price has had a spectacular run in the lead up to the announcement of the Phase II Huntington disease trial results, with profit taking occurring even prior to the announcement. However, the stock has been fuelled by investor exuberance. We recommended investors to **Take Profits** when the stock was at at $0.685 (refer to *Bioshares* 533) and we now place a **Sell** on the stock.

Bioshares recommendation: **Sell**

Bioshares

Cogstate's Canadian Experiment

Cogstate (CGS: $0.35) posted a half year loss of $2.68 million from revenues of $5.4 million. The bulk of the company's revenues are derived from clinical trials contracts, which accounted for $4.8 million in sales in the half year ending December 31, 2013.

However, a resurgence of clinical trial activity by pharmaceutical companies developing drugs for neuro-degenerative diseases (e.g. Alzheimer's disease) means that Cogstate has US$18 million in contract revenues on its books (as at January 31) compared to US$11 million in December 2012.

A number of large contracts were awarded in December 2013 and January 2014. Of the $7 million contracted in December, $3 million will be recognised in the current second half of FY2014, $2.7 million in FY2015, and the balance in periods thereafter.

Update on the Cognigram 'Experiment' in Canada

Cognigram is Cogstate's specially branded cognitive function test as directed to an elderly demographic, with an emphasis on baseline reporting and monitoring. It evaluates psychomotor function, visual attention, visual learning and working memory.

Cogstate's venture with Merck Canada to market Cognigram (Cogstate's branding of its cognitive function test as directed to an elderly demographic) in Canada was described at the start as a pilot program. The intent was to learn as much as possible about patient and doctor usage from a smaller healthcare market before tackling a larger market such as the USA.

Cognigram was launched in Canada in March, 2013. More than 500 Canadian family doctors have registered to use the test and 20 testing centres now support the test (from a total of Bayshore's 150 nationwide centres). However, Merck and Cogstate have been perplexed by low takeup rates from doctors who have registered to use the product. Investigations by Merck (the marketing partner) revealed that doctors perceived that Cognigram was difficult to use.

Cont'd on page 4

Invion Lays the Foundations for Inhaled Drug Programs

Invion (IVX: $0.089) has addressed its low cash position by raising $5 million through a placement to institutional investors in Melbourne, Sydney and Singapore. Until this time there have been no institutional investors on the Invion register. As a company, Invion came into existence through the merger of ASX listed CBio and the privately held US company Inverseon, in August 2012.

The company will also conduct a 1 for 20 rights issue, which could result in a further $2 million being raised. The rights issue is at 7.5 cents per share, equal to the price offered under the placement.

Potential Non-dilutive Funding

The licensing or sale of Invion's biologic drug candidate IVN103 (CPN-10) and related data assets could yield income later in 2014 or in 2015. CPN-10 failed in development as a treatment for rheumatoid arthritis. However, it may offer benefits in treating the autoimmune condition systemic lupus erythematosus (SLE).

Invion's business development activities through January, which were aligned with the JP Morgan meeting in San Francisco, have led to interest from pharmaceutical companies. What sets CPN-10 apart from other programs in the specific area of cellular stress response proteins is that it is the only molecular entity that has entered the clinic, albeit for rheumatoid arthritis, and has data from 250 patients to re-evaluate for its therapeutic potential with SLE. The safety and toxicology data from those 250 patients is also of some value to potential partners as they assess the asset.

Invion is conducting a randomized, controlled Phase II trial of INV103 in 32 patients with SLE, with results expected mid-year. The trial is investigating the ability of INV103 (CPN-10) to reduce blood levels of the cytokine IL-6, a marker associated with SLE. Presumably, results from this trial would feed into licensing and partnering discussions for INV103.

Respiratory Drug Programs

Aside from its CPN-10 asset, Invion's drug development program is focused on two molecules that have been approved by the FDA. Invion is repurposing nadalol from its original use as a beta blocker (a drug to treat hypertension) and is resurrecting an inhaled version of zafirlukast, which was developed but then shelved by AstraZeneca for portfolio reasons. AstraZeneca completed seven trials of an inhaled version of zafirlukast, which are obsolescent because of the propellant used in the device.

Invion in-licensed zafirlukast from AstraZeneca in October 2013. Zafirlukast was developed by Invion's Chief Medical Officer, Dr Mitchell Glass while he was employed by AstraZeneca. Zafirlukast is an oral leukotriene receptor antagonist approved for the treatment of chronic asthma in adults and children over five.

Invion has been positioning itself as a chronic respiratory diseases drug developer, with its INV104 (zafirlukast) being positioned for the treatment of exercise induced asthma and mild to moderate asthma, and INV102 (nadalol) being positioned to treat mucous metaplasia conditions such as chronic bronchitis, COPD and cystic fibrosis. However, to achieve the goal of building a strong respiratory diseases franchise, both compounds must be transitioned from oral delivery formulations to inhaled formulations, which is why the company announced a key collaboration with 3M, which among many business activities, is a manufacturer of drug delivery products.

The development of an inhaled version of INV104 (zafirlukast) is especially important because delivery direct to the lungs could (or should) overcome a range of side effects that stem from oral delivery. The existing drug label for zafirlukast includes warnings against liver damage, neuropsychiatric events (e.g. suicide) and it advises that decreased bioavailability occurs following food intake.

An inhaled formulation should mean that less drug needs to be delivered and first pass effects through organs such as the liver eliminated, with zero to negligible levels of circulating drug.

Collaboration with 3M to Develop Inhaled Products

Invion will work with 3M to develop inhaled versions of INV102 and INV104 using 3M's pressurized metered dose (pMDI) technology.

Key points for these two programs include the filing of Investigational New Drug applications with the FDA. In the lead up to those filings, the reformulated drugs will be put through dosing and toxicology studies, the results of which may be useful indicators of progress, positive or otherwise. Invion is not yet able to reveal a detailed timetable for the inhaled drugs development programs, but has targeted Phase II trials to commence in Q2 2015.

INV102 (Oral) Smoking Cessation Study Recommences

In December 2013, the FDA placed a clinical hold on Invion's Phase II trial of INV102 in smoking cessation of patients with pre-existing COPD. The hold was put in place following the FDA's shifting of its internal oversite of the program from one division to another, the Division of Anasthesia, Analgesia and Addiction in November. DAAA then requested changes to the trial design. The hold was released in late January 2014 following Invion's response those to requests. These changes have caused Invion to re-launch the study.

The rationale for the trial is to demonstrate nadalol's beneficial effect on mucous build up in the lungs of patients trying to give up smoking prior to surgery. These subjects typically experience chronic coughing while they are trying to stop smoking.

Interim data from this trial was originally expected to become available towards the end of 2013. Data from the now re-started trial is expected towards the end of 2014.

Summary

Invion's collaboration with 3M is a big step forward for the company because the development of inhaled versions of INV102 and INV104 should result in better drugs being made which should ultimately be far more attractive to larger pharmaceutical companies on the hunt for new products.

– Cont'd over

Bioshares Model Portfolio (21 February 2013)

Company	Price (current)	Price added to portfolio	Date added
Invion	$0.089	$0.089	February 14
QRxPharma	$0.890	$0.620	December 13
Impedimed	$0.220	$0.245	December 13
Analytica	$0.025	$0.025	December 13
Imugene	$0.017	$0.022	November 13
Oncosil Medical	$0.135	$0.155	September 13
IDT Australia	$0.350	$0.260	August 13
Viralytics	$0.305	$0.300	August 13
Tissue Therapies	$0.370	$0.255	March 2013
Somnomed	$1.69	$0.94	January 2011
Cogstate	$0.350	$0.13	November 2007
Universal Biosensors	$0.39	$1.23	June 2007

Portfolio Changes – 21 February 2014

IN:

Invion has been returned to the Model Portfolio, following its recent capital raising.

Recommendations: IVX - **Spec. Buy Class A**

OUT:

No changes

Recommendations:

For purposes of consistency, Bioshares stock recommendations and Model Portfolio decisions are now managed together by the Editor.

– Invion cont'd

While Invion is not without risk, as shown by FDA actions which delayed the smoking cessation trial, it is worth remembering that nadalol and zafirlukast are well characterised chemical entities which have been approved by the FDA. This lessens the overall development risks for these re-purposed and/or re-formulated drugs.

Invion is capitalised at $47 million.

Bioshares recommendation: **Speculative Buy Class Class A**

Bioshares

– Cogstate cont'd

'It came across as complicated,' said Cogstate CEO Brad O'Connor, with doctors primarily wanting to be satisfied that it worked and that it was easy to use.

Its status as a non-reimbursable test was found to be less of an issue, coming last as a concern. Merck and Cogstate are now changing their marketing to doctors in favour of messaging that spells out the ease of use of Cognigram, as well as its effectiveness.

Summary

Based on contracts signed in recent months, Cogstate's base clinical trials business looks to have been restored to a relatively healthy state.

However, the company's current major challenge in Canada is to prove Cognigram is both a clinically relevant tool in a specific healthcare segment and is also a commercially meaningful product. If adoption and testing rates grow in Canada, even without reimbursement being widely available, confidence in Cogstate's plans to introduce Cognigram into other markets will improve.

Cogstate is capitalised at $35 million.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Atcor Medical Update

Similar to Cogstate, Atcor Medical (ACG: $0.135) saw a slowing in sales to pharmaceutical companies conducting drug trials the FY2014 H1.

However, Atcor's sales drop was more dramatic, falling by 51% to $2.7 million. Atcor provides its instruments to pharmaceutical companies to measure central blood pressure and arterial stiffness. For the half year, the company generated a loss of $1.0 million

The poor first half by both companies appears likely due to timing issues in completing contracts, with Cogstate having seen a sharp increase in December and January. The fall in sales follows six consecutive quarters of positive cash flow by Actor. However, the current steep drop in sales reflects a business characterised by what remains volatile earnings for Atcor. About 60%-70% of the company's income is generated from sales to pharmaceutical companies for drug trials. The remainder of the income comes from use by doctors in the clinic and from researchers.

For Cogstate, which provides services and products to measure changes in cognition in drug trials, its sales fell by only 11.5% to $5.4 million in the December half. Cogstate has future revenue booked in of $18 million from signed contracts, where Atcor has a pipeline of potential new business of $16 million for which the company is bidding. Cogstate has also expanded its product offering which has helped the company to generate income.

Actor is capitalised at $21 million with $4.1 million in cash at the end of last year.

Bioshares recommendation: **Speculative Hold Class B**

Bioshares

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: Starpharma Holdings, Cogstate, Bionomics, Impedimed, QRxPharma, LBT Innovations, Tissue Therapies, Viralytics, Phylogica, pSivida, Antisense Therapeutics, Benitec BioPharma, Admedus, Calzada, Invion, Circadian Technologies, Imugene, Analytica

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