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In this edition...
Getting into business with the right people might sound like a jaded cliche but it begins to make sense when synergies can be gained by all parties. For Cogstate, Merck Canada and Bayshore Home Health, each party stands to gain benefits above and beyond the notional transactional benefit that stems from the rollout of Cognigram in Canada. Cognigram is the name for Cogstate's test for evaluating cognitive function (decline) in the healthcare setting. Oncolytic virotherapy company Viralytics has made strides in enrollments (now at 33 of 63) for its Phase II trial of CAVATAK. Even better has been discussion of interim results from ten patients by investigator Professor Andtbacka, with half of those melanoma patients achieving objective tumour responses. The progress of this trial will be worth following closely.
Companies Covered: CGS, VLA

	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 - current)	-3.2%
Cumulative Gain	**234%**
Av. annual gain (11 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 - Editor
Ph: (03) 9326 5382
Email: blake@bioshares.com.au
Mark Pachacz - Research Principal
Ph:(03) 9348 9317
Email: pachacz@bioshares.com.au

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Bioshares

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Edition 503

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

Synergistic Partnerships Support Cogstate's Rollout of Cognigram in Canada

In June of 2012, Merck Canada signed with Cogstate (CGS: $0.33) to promote and market Cogstate's cognitive function test exclusively in Canada. The test, rebadged as Cognigram, was launched in March of this year.

Cogstate has since its inception in the late 1990's envisaged that its cognition test could be used to help identify people experiencing the early stages of Alzheimer's disease, or similar neurodegenerative conditions in which cognition declines.

What has changed since the late 1990s and early 2000's is that advances in other technology spheres, especially with the Internet, has allowed Cogstate to shift from offering downloadable software to offering internet or web based access to the test. In earlier days, download speeds were much slower which limited the attractiveness of the test to users.

Another important change that has taken place since the late 1990s and early 2000's is that stakeholders in the healthcare system have emerged who now see clear benefits from applying detection technologies to uncover the signs of the earlier stages of the onset of Alzheimer's disease, or more broadly cognitive decline associated with dementia.

The second reason is that undiagnosed dementia patients can require costly emergency care and also experience a whole range of problems that relate to less care or lack of care. These all add costs to national healthcare budgets which are pressed to find savings every year. In short, dementia screening or dementia awareness is now recognised as a public health issue.

The Relationship with Merck Canada

Cogstate formed its relationship with Merck because that company is developing a strategic interest in Alzheimer's disease. Merck is developing MK-8931 which is inhibitor of the beta-site amyloid precursor protein cleaving enzyme 1 (BACE). This orally available drug is currently in a 1,960 patient Phase II/III trial which is scheduled for completion in 2017.

However, Merck is also interested in what it calls 'adjacent' technologies, being products or services that serve the same patient or clinical group. This underscores their interest in Cogstate's Cognigram, which could give them a potential competitive advantage if and when their drug gets to market by cementing relationships with doctors many years in advance.

The business exercise in Canada is to make available to doctors in general practice a product that has been widely used in the clinical research setting for many years so that they can assess their own patients.

Cont'd over

The gap between the time the deal with Merck was announced and the launch of Cognigram was spent putting the product together. This includes the systems and processes that wrap around the product, to work with a third party, Bayshore Home Health, which manages testing centres, and to conduct market research with doctors and patients. The market research delivered several key learnings that caused Cogstate to adapt their business model for Canada.

The first was that the product should be marketed to doctors, not to patients, because it would be used as a tool to assist decision making by doctors. Cogstate's focus group work revealed that patients will generally do what their doctors tell them to do, which in this case is to receive the Cogstate cognition test.

An implication of a doctor centric marketing model is that the preparation of materials for Continuing Medical Education is elevated in importance, as are presentations at conferences and the publication of medical evidence to support the test.

Cogstate also learnt that doctors did not want to conduct the test in their own clinics but would prefer to have it done off site, similar to how cholesterol or other blood tests are done at pathology labs. Their preference was to follow-up with a patient once a report had been sent back to their clinics.

The Relationship with Bayshore

The search for a business that offered testing services resulted in Cogstate signing up Bayshore Home Health, a comprehensive health care business with 150 facilities located across Canada. These facilities offer pathology style testing services in addition to transfusion and specialised drug delivery services. What also set Bayshore apart ,from Cogstate's point of view, was its focus on the elderly segment of the Canadian population. Bayshore offers hospice care, assisted transport, in-home nursing care and wound care amongst a diverse set of services for elderly people.

Bayshore is positioned as a partner that neatly complements Cogstate and Merck. From Bayshore's perspective Cognigram is a product that can offer synergistic benefits to its own operations. A consequence is that Cogsate's margins for Cognigram (priced at CAD$125 per session) exist at level that could be described as 'comfortable' rather than 'thin'.

The synergies with Bayshore are very important. These include the fact that Bayshore can increase staff and facility utilisation at times of the day when processing is slow. Typically, blood collections are done early in the day. In contrast, Cognigram tests can be scheduled for later in the day, when blood collections slow down.

Bayshore is also staffed by nurses and nurse practitioners. The administration of the Cognigram test by well trained staff was a factor deemed to give greater comfort to prescribing doctors. Bayshore staff are also specifically trained to supervise the Cognigram test.

According to Cogstate CEO Brad O'Connor, Bayshore could also see a marketing benefit from supplying testing services by drawing traffic to its centres from the elderly demographic which drive the overall business. In O'Connor's view, for Bayshore Cognigram 'was more of an investment'. Bayshore was prepared to treat Cognigram as an investment because they could see that other benefits could flow to them.

However, O'Connor recognised that the arrangement with Bayshore could not have been cemented without the initial marketing deal with Merck Canada being in place, to lend the necessary credibility and marketing capability to the business plan.

Investor Expectations?

How should investors consider the first 12 months of the roll-out of Cognigram in Canada?

First, expectations of large revenues occurring should be put to one side. A realistic approach it to monitor rates of adoption of the test (which may or may not be made available by Cogstate.) Rates of adoption (from prescription rates at the doctor level) will help Cogstate distinguish between doctors who have been comfortable with the test and those who have not. Studying the differences between these two groups will allow Cogstate and Merck to refine the marketing program.

The most important point for investors to note about the Cognigram program in Canada is that it is a pilot program. If Cognigram is relatively successful beyond its launch phase, then Cogstate will be able devise plans for other territories where the early detection of neurodegenerative conditions is accepted as an important public health policy. Whether Cogstate aligns with Merck in other territories is an unknown at this stage.

The sustainment of commitment by Merck Canada to sell Cognigram sits as the leading market-based risk for this aspect of Cogstate's business.

Summary

There are five factors that together can potentially make Cognigram a success for Cogstate in Canada. These are a more convenient distribution of the test in a web-based format, public health policy now recognising the need for the early detection of cognitive decline caused by neurodegenerative diseases, a sales partnership with a credible company (Merck) of size and capability, a testing services partnership with a business (Bayshore Home Care) with a vested interest in serving an elderly demographic, to which is added Cogstate's successful track record in supply its cognitive function testing to the clinical trials industry.

The investment lesson at work in Canada is that finding alignment and unlocking synergies may form the basis for a major blue-sky opportunity for Cogstate. However, it must be stressed that this is a longer term prospect and validating the business model in reasonably sized healthcare market such as Canada is a necessary first objective to achieve.

Cogstate is capitalised at $25 million.

Bioshares recommendation: **Speculative Buy Class A**

Viralytics Update

Viralytics (VLA: 28.5 cents) reported some positive interim data from its Phase II trial in patients with late stage melanoma. The company's core technology is an oncolytic virus therapy using a wild-type Coxsackievirus as opposed to an engineered form of the virus. The Coxsackievirus is associated with the common cold.

The use of viruses to treat cancer may initially sound far-fetched. However, in 2011 Amgen acquired another oncolytic virus therapy company, Biovex, paying an upfront US$425 million in what could turn out to be a billion dollar deal (future milestone payments of US$575 million). Amgen/Biovex uses a modified (engineered) herpes virus to treat cancer.

Phase II Trial Underway

Viralytics is conducting a Phase II trial with its CAVATAK oncolytic virus therapy (called CALM or CAVATAK in Late Stage Melanoma), seeking to recruit up to 63 patients with late stage melanoma (Stage IIIC or Stage IV). To date the company has recruited 33 patients. There have been two interim readouts from this trial so far.

The first was because the FDA put a requirement on the trial to have an 'interim efficacy futility clause'. This meant the company needed to get at least three objective responses from the therapy in the first 35 patients, otherwise the trial would not continue past 35 patients. That milestone was reached in December last year from the first 13 patients. An objective response is defined by a 30% or more decrease in the total body tumour burden.

Effectiveness of Intralesional Therapies for Late Stage Melanoma

Therapy	Response rate	
	At injected lesion	At non-injected systemic lesions
IL-2	70-97%	0%
BCG	45-91%	0%
Allovectin-7	19%	21%
T-Vec	26%	18%
PV-10	49%	33%

Table reproduced from Assistant Professor Andtbacka presentation
There are some minor differences noted between data in the text obtained from the presentation and data in the above table

Results from First 10 Patients

In March this year, one of the medical investigators in the trial presented results from the first ten of the patients he has treated so far with CAVATAK in the CALM study. Assistant Professor Andtbacka is a key medical figure in the field of intralesional therapy. He is on the Advisory Board for Amgen's T-Vec program and an investigator on Amgen's Phase III OPTiM trial (see next page). He is also on the Advisory Board for the Allovectin-7 program, a gene-based immunotherapy being developed by Vical Inc, also for late stage melanoma. Andtbacka was also an investigator in the Allovectin-7 Phase III trial.

In the 10 patients treated with CAVATAK in the CALM study, five (50%) have achieved objective tumour responses, which is an excellent result. Three patients have had stable disease and two patients have experienced disease progression.

In this trial the therapy has been injected directly into the tumour. What is important in treating patients with this type of therapy is that the anti-cancer effect is not only seen in the tumour into which the therapy has been injected, but also at metastatic (non-injected) lesions. This has been observed in some of the first 10 patients (no overall details released). In one patient, CAVATAK was injected into a tumour on the forearm and a tumour in the chest disappeared within six months. The lesion on the forearm was still in place, which is not unusual, however, upon excision it was analysed and found to be fibrous tissue only (no longer a melanoma).

In these 10 patients, three have also achieved immune related progression free survival (irPFS). This makes allowances for any initial progression of the disease before the immunotherapy starts to take effect.

Presentation by Professor Andtbacka

Recruitment into this trial was slow although has recently accelerated. Andtbacka has now enrolled 14 patients into the CALM study with a further four patients being screened. He recently made a scientific presentation (a link is available on the Viralytics website) which is of particular interest to investors in Viralytics because it compares a number of these immunotherapy-based approaches to treating late stage melanoma.

Andtbacka stressed that he is looking not just for local treatment of the melanoma but to activate the immune system to attack disease that may already be elsewhere in circulation by using what's called an 'intralesional therapy' for melanoma. What is wanted is a robust immune response as well as local ablation of the tumour said Andtbacka, a high concentration (of therapy) and with limited side effects.

Suitable candidates are patients with in-transit disease (those with Stage IIIB and Stage IIIC disease). These patients can have high lymph node disease which can be surgically treated but not be surgically curative as they may develop distant metastatic disease. Patients with Stage IV disease are also suitable for intralesional therapy although the therapy is more effective when received earlier.

Andtbacka summarised the progress that has been made with these types of therapies for the treatment of late stage melanoma. Only two therapies have been assessed in Phase III randomised trials. These are Amgen's T-Vec and Vical's Allovectin-7. Other intralesional therapies that have been explored in the Phase II setting include BCG, IL-2, PV-10 and Viralytics' CAVATAK.

Cont'd over

BCG & IL-2

BCG is effective locally but not in distant tumours (see table). Interleukin-2 (IL-2) can be very effective locally, with a complete response rate of up to 80% but a 0% response at distant tumours. Andtbacka said you need to see a response at distant tumours as well because this is what kills the patient.

Allovectin-7

The response rate is directly proportional to the survival rate. Allovectin-7 was shown to achieve a complete or partial response rate in 12% of patients with a 13.8 month duration of response in a Phase II 133 patient study (note in the table provided a response rate of 19% is listed overall). The medium time for a response to occur is four months, which is similar to other immune therapies, as it takes time for the therapy to take effect. Allovectin-7 achieved a 21% response rate at distant tumours as well. Results from a 375 patient Phase III study, which has now been completed, are due in Q3 2013.

T-Vec

In a Phase II trial with T-Vec (talimogene laherparepvec), a 26% overall response rate was achieved. The one year survival rate in responders was 93% and only 40% in non-responders. There was also an 18% response rate at non-injected distant tumours.

In March this year Amgen reported some top line results with T-Vec from its 430 Phase III OPTiM study in patients with late stage melanoma (Stage IIIB, Stage IIIC and Stage IV). The result delivered a statistically significant result over the control arm, although the durable response rate at six months or more was only 16%, compared to 2% in the control arm. Later in 2013 the company expects to be in a position to report overall survival data.

PV-10

PV-10 has been assessed in an 80 patient Phase II study in patients with Stage III and IV melanoma. PV-10 is a 10% solution of Rose Bengal disodium. It accumulates in the lysosomes of the cancer cells and promotes exposure of cancer antigens to the immune system. The response rate in the target lesions was 51%, with half being a complete response and half a partial response (more than 30% reduction in overall tumour burden). In the non-target lesions, a response rate of 33% was achieved.

Andtbacka said that if the injected lesion responds, then so should the remote lesions. A Phase III study is planned for PV-10 in 180 patients this year.

Comments

The results from Viralytics Phase II study to date look very encouraging. A response rate of 50% is very impressive in the first 10 patients. This compares to only a 26% response rate in the T-Vec Phase II trial and a 16% durable response in the T-Vec Phase III trial. It is in line with the Phase II study with PV-10 which achieved a response rate of 51% in an 80 patient Phase II trial. What is unknown with the current Phase II CAVATAK trial is the response rate at distant tumours. There have been responses seen locally and at distant tumours according to Andtbacka.

An important comment made by Andtbacka is that these intralesional therapies are all extremely well tolerated, with it very rare to have Grade 3 or 4 toxicities. The therapies do, however, take a while to take effect (8-40 months for T-Vec) and patients can often see new lesions form as the therapy takes effect. An aspect that is now being explored, including in Viralytics' CALM study, is trying to work out early which patients are responding to treatment.

Other CAVATAK Trials

Viralytics is seeking to start a Phase I/II study in the UK this year in patients with a variety of solid tumours using an intravenous formulation of CAVATAK. Success with an IV-delivered product will broaden the indications for this therapy as well as make it easier to deliver. This study will seek to recruit patients with lung, prostate and bladder cancers, as well as patients with melanomas. Up to 30 patients will be recruited. The study will start as a monotherapy and will then move into a combination therapy with the appropriate chemotherapy regiment.

Other Oncolytic Virus Therapies

The other company with a Phase III trial in the oncolytic virus area is Oncolytics Biotech. The company is conducting a Phase III trial in patients with head and neck cancer. The company has a market value of US$233 million. However, the company has had problems with recruitment, it has been unwilling to release initial progression-free survival data as planned, and will now be waiting for overall survival data.

Summary

Bioshares expects the current Phase II CALM trial to complete recruitment this year and we expect results to be available in the second half of 2014. However, being an open label study, more interim results may emerge before then.

Viralytics is capitalised at $26 million. It had $6.3 million in cash at the end of March, which is about one year's cash.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

Bioshares Model Portfolio (17 May 2013)

Company	Price (current)	Price added to portfolio	Date added
Atcor Medical	$0.073	$0.082	May 2013
Circadian Technologies	$0.230	$0.270	March 2013
Tissue Therapies	$0.120	$0.255	March 2013
Allied Healthcare	$0.041	$0.026	February 2013
Psivida	$3.10	$1.550	November 2012
Benitec	$0.014	$0.016	November 2012
Nanosonics	$0.485	$0.495	June 2012
QRxPharma	$1.20	$1.66	October 2011
Somnomed	$0.90	$0.94	January 2011
Cogstate	$0.330	$0.13	November 2007
Clinuvel Pharmaceuticals	$1.90	$6.60	September 2007
Universal Biosensors	$0.70	$1.23	June 2007

Portfolio Changes – 17 May 2013

IN:
No changes

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. 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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