ISSN 1443-850X

Companies covered: MSB, PAA, SUD

	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)	50.5%
Cumulative Gain	**436%**
Av. annual gain (13 yrs)	

Bioshares is published by Blake Industry & Market Analysis Pty Ltd.

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Individual Subscriptions (48 issues/year)
$400 (Inc.GST)
Edition Number 532 (6 December 2013)

Bioshares

6 December 2013
Edition 532

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

Pharmaust's PPL-1 – Will it Set a New Safety Benchmark for Cancer Drugs?

Pharmaust (PAA: $0.011) acquired Sydney-based Pitney Pharmaceuticals in August 2013. The acquisition re-positioned Pharmaust wholly in the pharmaceutical space, combining its longstanding drug chemistry business Epichem with the drug discovery and development operations of Pitney Pharmaceuticals.

Pharmaust is developing albendazole as treatment for ascites, a condition in which fluid builds up in the abdomen and which can then cause organ damage and death if not treated. Two Phase I/II studies have been completed and a Phase II/III is planned.

The program of primary interest to investors is PPL-1, which is being investigated as a treatment for cancers. In a research report based on the analysis of a published patent by Pitney Pharmaceuticals, RM Research concluded that PPL-1 is a compound known as monepantel (also AHC 2102225). Its full chemical name is (N-[(1S)-1-cyano-2-(5-cyano-2-trifluoromethyl-phenoxy)-1-methyl-ethyl]-4-trifluoromethylsulfanylbenzamide).

There is only one monepantel product available commercially, Zolvix, which was developed as a sheep drench by Novartis Animal Health. The chemical has an anti-parasitic function and is used for the treatment of nematodes (worms) in sheep. The product received approval by New Zealand's Environmental Risk Management Authority, and Agriculture and Veterinary Medicines authority in 2009 and from the Australian Pesticides and Veterinary Medicines Authority in 2010.

Pharmaust has signed a research and option (license) agreement with a global animal health company owned by a major pharmaceutical company. An analysis by a reasonable person, based on some of the information outlined above, could deduce this to be Novartis Animal Health.

The Discovery of PPL-1

PPL-1's potential as a treatment for cancer was discovered by Pharmaust director and Chief Scientific and Clinical Officer, Professor David Morris. He is the Head of the Department of Surgery at St Georges Hospital, Sydney and is a Surgical Oncologist. Professor Morris also oversees a research laboratory at St Georges Hospital. He also runs his own sheep property. He hypothesized that the drench (monepantel) could be efficacious in killing cancer cells. This hypothesis stemmed from his earlier work with another anti-parasitic compound albendazole, which the company is evaluating as a treatment for ascites. Morris synthesized the active pharmaceutical ingredient of Zolvix (monepantel) to avoid limitations on research results that could have been imposed by the marketer of Zolvix if their material had been used, and found it effective on more than 30 cancer cell types and on tumours grafted onto animals (mice).

What makes PPL-1 (monepantel) an interesting candidate in the field of cancer drug research is that it has an unusually interesting and arguably very favourable toxicity

Cont'd over

profile as established from its extensive studies for use as a veterinary medicine.

Toxicology Studies

According to the APVMA product review of monepantel, 'Zolvix Monepantel Broad Spectrum Oral Anthelmintic for Sheep, has low acute oral and dermal toxicity in rats (LD50s both > 2000 mg/kg bw). It was a slight skin and eye irritant in rabbits and a skin sensitiser in mice.'

In animal studies, monepantel has been shown to have most effect on the liver but also on the thyroid gland.

In a 52 week study in dogs, the NOAEL (no observed adverse effect level) was calculated to be 2.96 mg/kg body weight per day.)

In a repeat dose study in sheep, of eight administrations repeated every three weeks, and up to 18.75 mg/kg body weight, there were 'no findings considered to be toxicologically significant'. (See table below)

In summary, monepantel has a well characterised long term safety profile in different species of animal, which suggests there is potential to use the compound at high to very high therapeutic doses without incurring the very severe side effects that exist with many current cancer drugs. This would place the compound in that very small set of cancer drugs with a wide therapeutic index, but it is even possible that it could be a sole occupier of that set. PPL-1 has the potential to set new standards for safety and efficacy for small molecule cancer drugs. However, it will take robust clinical studies to prove this.

Rapid Deal Making by Large Pharma

PPL-1 is significant for another reason in that a large pharmaceutical company has moved very quickly (while data is at the level of cell-based studies) to work with Pharmaust to further develop the compound in the veterinary arena but also to position itself in a prime position if positive clinical trials results emerge in 2014.

Novel Mechanism of Action

Pitney researchers believe the PPL-1 (monepantel) has a novel mechanism of action for killing cancer cells, by acting on the mTor pathway, in contrast to its action as a blocker of acetylcholine receptors specific to nematodes (worms). More specifically, it blocks the Hco-MPTL receptor in worms.

At the same time, the company has generated data which shows that normal kidney cells remain largely unaffected by PPL-1 (monepantel). The publication of this data in more detail in addition to similar investigations is something investors should look forward to and monitor closely.

– Cont'd over

Summary of Monepantel Animal Toxicology Studies

Species	Duration	Dosing (ppm*)	Selected Findings	LOAEL	NOAEL
Mice	13 weeks	0,30,120,600,6000	Inc. bilirubin levels, inc inc of fatty liver change	30ppm (=5.27 mg/kg bw per day)	
Rats	4 weeks	0,1000,4000,12000	Inc. cholesterol, tryglycerides and phospholipid levels at all doses; inc in abs and rel liver weights	1000ppm (=86 mg/kg bw per day)	
Rats	13 weeks	0,50,200,1000,12000	Inc. in abs and rel liver weights; heptocellular hypertrophy at higher doses		200ppm (=15.2 mg/kg bw per day)
Rats	52 weeks	0,50,200,1000,12000	Inc. in abs and rel liver and kidney weights		1000ppm (=54.4 mg/kg bw per day)
Dogs	4 weeks	0,5000,15000,40000	Non dose dependent increase in alkaline phosphatase levels; abs. & rel. thymus weights reduced at all levels		
Dogs	13 weeks	0,300,3000,30000	Inc. in alkaline phosphatase levels at all doses; inc in abs and rel liver weights		300ppm (=9.9 mg/kg bw per day)
Dogs	52 weeks	0,100,300,3000	Inc. in alkaline phosphatase levels; inc ALT; inc in abs and rel liver weights; inc in thyroid weights		100ppm (=2.96 mg/kg bw per day)
Sheep	Single dose	10 x rec dose 3.75 mg/kg bw	No findings considered to be toxicologically significant		
Sheep	Repeated dose	3.75 mg/kg bw, 11.25 mg/kg bw, 18.75 mg/kg bw - 8 x 3 weeks	No findings considered to be toxicologically significant		

* parts per million
LOAEL low est-observed-adverse-effect level
NOAEL no-observed-adverse-effect level
NOEL no-observed-effect level

Source:
Toxicological evaluation of certain veterinary drug residues in food / prepared by the seventy-fifth meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA).
(WHO food additives series ; 66)

– Pharmaust cont'd

One cancer cell line that PPL-1 (monepantel) has been shown to kill is that of temozolimide-resistant Giloma U251 cells.

Another feature of PPL-1 (monepantel) is that it appears to work synergistically with other chemotherapeutics, such that the effective doses of these other drugs could be reduced, and therefore reducing their toxic effects.

Discussions with the Originator of the IP Covering Monepantel

Pharmaust is conducting discussions with an international firm that is the head licensor of the IP covering monepantel for veterinary applications. The purpose is to strengthen Pharmaust's access to the IP originator's library of analogues of monepantel.

While Pharmaust is in a leading position with its patent applications covering the cancer applications of monepantel, the logic to work cooperatively with the company in possession of a library of similar compounds is a sensible tactic.

Clinical Studies

Pharmaust's next steps with PPL-1 will be to initiate a Phase I study in patients with advanced cancers. The efficacy of the drug can be measured in part by its effect on a biomarker, p76sk. The company is working with a CRO to finalise the protocol for the trial.

Pharmaust will also commence a study of PPL-1 in dogs with a range of cancer types.

Summary

Pharmaust is developing a cancer drug for which the progress in the next 12 months should be viewed by investors and pharmaceutical companies with a great deal of interest. The favourable toxicology profile of PPL-1 (monepantel) as a veterinary medicine marks it out as a drug candidate of interest. The serendipitous discovery of the compound's potential as a cancer drug by a very experienced surgical oncologist also marks it out as a drug candidate of interest.

Furthermore, investors can note that a repetition of the strategy adopted by the company's executive chairman, Dr Roger Aston, to discover and develop drugs which have a history of previous development in other therapeutic or industrial settings, thereby greatly reducing development costs and timeframes.

This stock has the potential to be re-rated in the next few months, with opportunities to acquire the stock at current prices having a stong likelihood of disappearing.

Pharmaust is capitalised at $16 million.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

Mesoblast Diabetes Trial Results

Mesoblast (MSB: $5.84) announced the results in one of two Type 2 diabetes trials it is conducting with its adult mesenchymal precursor stem cells.

The Phase II trial evaluated three different doses of MPCs, of 0.3, 1.0 and 2 million MPCs per kg over 12 weeks in 61 subjects. The average duration of diabetes in these people was 10 years. The subjects received a single IV infusion.

Mesoblast reported that the MPCs were safe and well tolerated with no treatment related adverse events observed. Glycemic control, as measured by a reduction in HbA1c levels, improved. The highest dose of 2.0 million cells per kg stimulated a peak decrease in HbA1c levels of 0.4% at 8 weeks but a 0.3% reduction at 12 weeks.

The MPCs had different effects on subsets of patients; patients with less well controlled diabetes in the high dose cohort experienced a 0.6% decrease at 8 weeks. In subjects with a history of better management of diabetes, five out of eight subjects in the high dose group saw their HbA1c levels drop to below 7%, which is the upper limit for normal HbA1c levels. In contrast, none of the seven subjects in the control cohort saw a reduction in HbA1c levels. All of the trial subjects were on metformin medication, with 50% also receiving one oral agent.

Overall, Mesoblast believes the results support the further development of MPCs for the treatment Type 2 diabetes.

Comments

The trial delivers several positive outcomes for Mesoblast, the first being the confirmation of a dose related response to MPCs. What should also be clearly noted is that the impact of the MPCs was achieved from one single infusion. This raises the need to explore the potential benefits of repeat dosing of MPCs (and exclusively in the area of diabetes) as well as higher doses. CEO Silviu Itescu said that 'as we move forward we will consider even higher and multiple doses.'

The trial in reality forms the basis for the more focused development in patients suffering complications of diabetes, such as diabetic nepthropathy (kidney complications), in which the immunemodulatory actions of MPCs could also potentially repair diseased organs and tissues.

Mesoblast is currently conducting in Melbourne a study in 30 patients with diabetic nepthropathy, but which is not scheduled to deliver results until late in 2014. Two doses, of 150 million and 300 million cells respectively are being evaluated.

From a strategic point of view, it makes stronger commercial sense for Mesoblast to target difficult to treat patients, or patients with end stage complications, because if the treatment benefits were significant, then payments for an MPC based therapy could be substantial.

Bioshares recommendation: **Speculative Class A [Look To Buy Under $5]**

Bioshares

Suda Looks to Transact Oral Spray Drug Assets in 2014

Suda (SUD: $0.065) was formerly Eastland Medical Systems. Eastland had two core assets. One was a safety syringe technology and the other was a sub-lingual drug treatment for malaria.

The company's core focus is now on the latter, and earlier this year acquired a suite of oral spray drug assets. For 2014, the focus for the company is to transact licensing deals for its drug assets in development. Suda also has a surgical products business that last year generated $4 million in revenue and is expecting high growth this year.

The acquisition price included an upfront payment of $400,000, and the issuance of 50 million Suda shares (around $3 million at the current share price) and 10 million options over Suda shares exercisable at 5 cents.

The acquisition came with 19 drug programs, of which Suda is currently focusing on five (see table for summary of top three programs).

Suda's Drug Development Pipeline

Drug candidate	Indication	Status	Estimated Market (US$)
ArtiMist	Malaria treatment	Registration	>$0.5 B
SUD-001	Migraine, oral spray version of sumatriptan	Pivotal study to be completed. Ready for licensing	$200 M in the US
SUD-002	Nausea and vomiting from chemotherapy. Oral spray version of Zofran	Pivotal studies competed. Ready for licensing	$2.5 B
SUD-003	Oral spray version of Viagra	Pivotal study to be completed. Ready for licensing	$4.1 B

ArTiMist – A Sub-lingual Spray for Treatment of Malaria

The original ArTiMist technology was licensed in 2006 from ProtoPharma. In 2010, Suda commenced a Phase III clinical trial in 150 children in Africa. That trial was completed last year and in July this year, the company released the final report from that trial.

It was a very good trial result, comparing the ArTiMist spray delivered under the tongue against intravenous delivery of the gold standard drug quinine in children with malaria. The trial showed that ArTiMist achieved a more than 90% reduction in parasite count in 95.6% of children in 24 hours, compared to success in 40.6% of children given quinine. The clearance time for ArTiMist was 30 hours compared to 68 hours with quinine.

ArTiMist is the first sub-lingual spray for the treatment of malaria. The active ingredient of ArTiMist is artemether, which is given as an infusion and in a tablet form.

Earlier this year, Suda revised the contractual arrangement with its licensor ProtoPharma. Rather than receiving a direct royalty from product sales, the ArTiMist assets have been placed into a new Australian company called Malaria Research Company, of which Suda owns 80% and ProtoPharma owns 20%.

Together with ProtoPharma, the two companies will prepare full documentation for this product that will be used in regulatory submissions, with the first approval application to be submitted in mid 2014 in Ghana according to the company. Torreya Insights will assist with transacting a licensing deal for the product in 2014 or a potential trade sale.

Suda also plans to install a Scientific Advisory Board sourced from the malaria treatment field to support this product. The size of the malaria treatments market is estimated at over US$500 million a year by the company.

Other Oral Spray Drug Delivery Programs

In April this year Suda acquired oral spray drug delivery assets from NovaDel. NovaDel had spent around $100 million in developing a suite of drug assets that can be delivered as a spray into the mouth.

Sumatriptan – US$200 Million sales

The first of those, SUD-001, is a reformulation of the drug sumatriptan for the treatment of migraine. Sumatriptan, brand name Imitrex, is sold by GlaxoSmithKline in a tablet and nasal spray form. Sumatriptan generates sales of US$200 million in the US.

Two trials in 45 subjects have been completed with SUD-001 showing improved performance over Imitrex with respect to faster onset of action and more effective pain relief. The company believes that one pivotal study may be all that is required to get this drug to market. The company has assigned Torreya Partners to effect a partnering deal in 2014 for this program. A small marketing study will be undertaken in coming months to look at market potential, pricing and reimbursement.

The faster onset of action, by delivery into the oral mucosa, of a migraine drug would have clear market appeal.

Nausea Treatment – US$2.5 Billion Market

The second drug candidate, SUD-002, is an oral spray drug candidate of GSK's Zofran tablets for the treatment of chemotherapy induced nausea. A fast working drug that does not need to be swallowed has obvious advantages in the nausea treatment market. This drug candidate has been tested in over 300 patients against Zofran showing bioequivalence and faster absorption. The company believes this drug candidate may be ready for registration with regulators.

Viagra Market – Over US$4 billion Existing Market

The third program for Suda in its oral drug spray assets is a metered oral spray of the drug, sildenafil, which is sold as Viagra by Pfizer. Generics have been launched for Viagra but there are no oral spray formulations. A trial in 24 men has been completed with this drug candidate showing bioequivalence to Viagra. A pivotal study would be required to get this drug on to market.

Cont'd over

Bioshares Model Portfolio (1 November 2013)

Company	Price (current)	Price added to portfolio	Date added
Imugene	$0.017	$0.022	November 13
Oncosil Medical	$0.125	$0.155	September 13
Calzada	$0.070	$0.073	September 13
Invion	$0.097	$0.060	August 13
IDT Australia	$0.420	$0.260	August 13
Viralytics	$0.350	$0.300	August 13
Circadian Technologies	$0.210	$0.270	March 2013
Tissue Therapies	$0.230	$0.255	March 2013
Benitec Biopharma	$0.480	$0.40	November 2012
Somnomed	$1.20	$0.94	January 2011
Cogstate	$0.390	$0.13	November 2007
Universal Biosensors	$0.50	$1.23	June 2007

Portfolio Changes – 6 December 2013

IN:
No changes.

OUT:
No changes.

– *SUDA cont'd*

Intellectual Property

Suda has 70 patents over its technologies. In its annual report, the company listed seven granted US patents, which are likely to expire between 2016-2023. Some of these granted patents are outside of the company's lead programs such as antifungal treatments and the treatment of dermatitis. More recently files patents will give the company coverage out to 2031 if granted.

Migraine Treatment

The company has a granted US patent out to at 2023 for the treatment of pain, including migraine. The company has a filed patent in Japan around the oral spray delivery formulations of migraine treatments. The company has a granted patent in Europe which should cover the delivery of the migraine drug sumatriptan (buccal delivery of analgesics or alkaloids).

Ondansetron (nausea)

One granted US patent includes delivery of anti-emetic agents via the oral mucosa, which would potentially give protection of the chemotherapy induced nausea program out to 2022. The company has filed patents around the delivery of ondansetron via the oral mucosa (for treatment of chemotherapy induced nausea) in Europe, Hong Kong and Israel. It also has broad patents filed in Europe and Japan for the treatment of nausea.

Sidenafil

The company has filed patents for delivery of sildenafil (branded drug Viagra) via the oral mucosa in the US, Europe, Canada, Australia and Brazil.

Surgical Products Business

Suda owns a surgical products business called Westcoast Surgical and Medical Supplies. This business generated $4 million in FY2013. In the September quarter, the company secured a large government contract, which contributed to a 200% growth in sales over the previous corresponding period, of $3.3 million and a net profit of $720,000.

Management

Suda's chairman and CEO is Steve Carter, who was formerly CEO of Solbec Pharmaceuticals. The company has recently appointed the experienced Nick Woolf (formerly at Phylogica) as its chief business officer.

Capital

In November Suda raised $5.6 million at 3.3 cents a share. In December last year Suda secured a $7.6 million convertible note with Bergen Global Opportunity Fund. The remaining balance of that funding facility is $3.6 million and the company has now postponed access to that funding mechanism following its recent capital raising. In September the company raised $1.9 million via a convertible note, with $420,000 of that amount raised provided by directors of the company. The notes convert at 3 cents a share any time after six months from issue.

Summary

Suda is capitalised at $60 million. It has a number of programs it is seeking to transact in 2014. The company is in an improved funding position following its recent capital raising and has recently strengthened its management team. Its patent position appears to offer good protection although patents around sildenafil (branded drug Viagra) have yet to be granted.

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

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