ISSN 1443-850X

Bioshares

10 March 2017
Edition 687

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

Companies covered: IMC, FTT

	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 - May '14)	26.6%
Year 14 (May '14 - May '15)	23.0%
Year 15 (May '15 - May '16)	33.0%
Year 16 (May '16 - current)	16.1%
Cumulative Gain	**756%**
Av. Annual gain (14 yrs)	**18.6%**

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

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Individual Subscriptions (48 issues/year)
$440 (Inc.GST)
Edition Number 687 (10 March 2017)

Immuron Files Prospectus for US Capital Raise

Immuron (IMC: $0.30) has filed a Form F-1 to list on the Nasdaq as it plans to raise up to US$17.25 million in the US with its securities to trade as American Depository Shares. The company is seeking to capitalise on continued, heightened activity in the NASH (non-alcoholic steatohepatitis) space. The process is being coordinated by US investment group Joseph Gunnar & Co which is acting as sole bookrunner.

Immuron has completed recruitment of 120 patients into its Phase II NASH trial. This is the company's lead program, with results from that trial expected in Q4 this calendar year.

However, the company expects to have readouts from four Phase II trials by the end of next year, all based on the company's polyclonal antibody approach to treat diseases mediated by inflammation and infection in the digestive tract.

The F-1 document filed by Immuron provides an extensive background on the company including its core technology, mechanism of action and preclinical and clinical results from its lead program, IMM-124E.

Phase II NASH study with IMM-124E

Immuron started its Phase II NASH study two years ago in February 2015. It took 15 months to recruit half of the patients in the study with a slow recruitment due to overly stringent entry criteria.

The company had set very high ALT liver enzyme levels as an entry criteria. However, this measure can fluctuate considerably and lowering this entry level has accelerated and helped achieve the recruitment target.

Earlier this month the company announced it had achieved its 120 patient recruitment target with its entry criteria including a NASH activity score of 4 or more.

The study is being conducted at 25 sites that are predominantly located in the US with six sites in Australia and two in Israel.

There are two active arms which involved treatment with 1800mg and 3600mg per day of IMM-124E for six months with a placebo comparator group.

The two key endpoints in the study are reduction in liver fat levels and reduction in liver ALT levels.

Comparisons with Phase I/II study

In 2010 Immuron reported results from a single arm study of IMM-124E that treated 10 patients over 30 days. The patients received a daily dose of IMM-124E of 1800mg per day. That study was conducted in Israel at the one hospital site. These patients had biopsy-

Cont'd over

confirmed NASH as well as well as Type II diabetes and/or insulin resistance.

Results from that study offered some encouraging results which are listed in the prospectus. HbA1c levels were reduced by 14% (or 0.5% in absolute terms). With respect to changes in liver enzymes, seven of the 10 patients experienced a 10% of more drop in AST or ALT levels. Serum cholesterol levels were also reduced, by 11% over the 30 day treatment period.

Immuron has also shown supportive preclinical results from two mouse model studies (CCl4 and ob/ob mice) which is indicative of the therapy having an anti-fibrotic and anti-inflammatory effect as well as a positive metabolic effect.

However these are not NASH mouse models. In recent years new mouse models for NASH have been developed and Immuron intends to confirm the mechanism of action of IMM-124E in these models this year to elucidate the action of the drug at a cellular level.

Mechanism of Action - Why IMM-124E May Impact NASH

IMM-124E is thought to have an application in NASH because of the anti-inflammatory effects of this drug candidate. IMM-124E is produced by vaccinating cows and extracting the polyclonal antibodies from the colostrum produced. The product's composition is 40% immunoglobulins.

IMM-124E has been designed to bind to LPS (lipopolysaccharides) present on E.coli bacteria. The product was originally developed as an over-the-counter product to treat travellers' diarrhea and that product is currently on the market, sold as Travelan (sales 1H FY2017 of $0.7 million).

LPS is common on other gram-negative bacteria in the gut such as salmonella, shigella, helicobacter and pseudomonas. The toxins produced from the bacteria are believed to ramp up inflammation in the gut and in organs throughout the body.

The liver has a very high exposure to antigens and endotoxins from the gut microbiota. Increased LPS in the blood stream has been linked to several liver diseases including NASH, ASH (alcoholic steatohepatitis) and cirrhosis. LPS is engaged by different cell types in the liver and fatty liver has shown to have increased sensitivity to LPS. Increased permeability of the gut is also believed to increase dietary lipid absorption and then higher fatty acid synthesis in the liver.

Binding to LPS is believed to neutralise the activity of the pro-inflammatory LPS on the bacteria, prevent formation of toxins which also increase inflammation, and maintain the integrity of the gut lining which restricts movement of LPS from the gut into circulation in the body and the liver.

The immunoglobulins in IMM-124E also effect a cell mediated anti-inflammatory response in the bloodstream, thereby reducing the inflammatory load in the body.

Immuron also believes that the broad anti-inflammatory properties of IMM-124E has an effect on other organs in the body, such as the pancreas, which would reduce insulin resistance in the body and therefore reduce fat build up in the liver. In the Phase I/II study discussed above, glucose levels and cholesterol levels were reduced in patients receiving IMM-124E.

Pediatric NAFLD Phase II trial

Earlier this month, Immuron announced that Emory University in Atlanta had initiated a 40 patient study investigating the treatment impact IMM-124E has on treating children with NAFLD (non-alcoholic Fatty Liver Disease) which is a precursor to NASH.

The university was awarded an NIH grant in August last year to fund the study.

The trial will be placebo controlled and the primary endpoint will be a reduction in liver enzyme ALT levels. The trial is expected to take around one year to recruit. With 12 weeks of treatment, results may be available around mid 2018.

Researchers at Emory University had previously shown that children with NAFLD had increased inflammation activity in the body, increased gut permeability, a destabilisation of the microbiome in the gut and the presence of endotoxins in the blood.

Immuron believes that by addressing bacterial infections in the gut, helping restore the microbiome in the gut, and dampening any inflammatory processes in the body, IMM-124E will have a positive impact on NAFLD. A large US study based on autopsies of 742 children that had an accidental death found that 17% of those aged 15 - 19 years had NAFLD, for which there are no current treatments.

Emory University's work in this field explain its interest in trialling Immuron's drug candidate to interrupt the cascading liver disease process with polyclonal antibodies against LPS through anti-infective and anti-inflammatory processes.

Phase II ASH study

In January 2015, Dr Arun Sanyal, the Principal Investigator of the company's Phase II NASH trial underway, started a Phase II trial in ASH (alcoholic steatohepatitis) at the Virginia Commonwealth University. Dr Sunyal is a leading authority in NASH and is currently Chair of the Liver Study Section at the NIH.

This trial is seeking to enrol 66 patients who will be treated with IMM-124E for 28 days. The trial has completed around 50% of recruitment with results expected towards the end of 2018. This trial is also funded by an NIH grant.

Phase II Trial to Treat C. difficile Infections

In April/May this year, Immuron intends to start a trial with a second drug candidate, IMM-529, to treat a bacterial infection, C. difficile (CDI), which has become a serious issue in hospitals and in long-term care residences.

This trial will be conducted at Hadassah University in Israel and will seek to recruit 60 patients, with two thirds in the treatment arm

with IMM-529 and one third receiving placebo. It's expected to take one year to recruit patients, and if that occurs, results should be available around mid-2018.

Similar to the targeted antibodies against LPS in NASH, in CDI, IMM-529 is expected to work in a three-pronged attack, inhibiting the bacteria itself, the toxins it produces and the spores that attach to the gut lining. The therapy is also expected to promote healthy microbiome in the gut to prevent CDI occlusion to the gut wall.

For Immuron, the IMM-529 program for CDI could have as much potential relevance as the NASH program with IMM-124E. While a smaller addressable market, with recurrent CDI affecting around 100,000 people each year in the US, the endpoint for CDI is more easily measured, and the mechanism of action is more straightforward, that being to bind to a bacterial infection in the gut and to a promote health gut microbiome to prevent infection recurrence.

Recurrence rates of CDI are high following treatment with antibiotics. There is a 25% chance of recurrence of infection in patients treated with the antibiotic vancomycin, which increases to a 50% chance of recurrence following secondary infection, with increasing resistance rates for each course of treatment. The last line of treatment, which is not pleasant, a faecal transplant, is 90% effective.

Immuron has conducted preclinical testing with this program which has yielded some exquisite science, according to Immuron CEO Thomas Liquard.

In preclinical tests conducted in mice and reported in January this year, treatment with IMM-529 in combination with vancomycin reduced mortality to 22% compared to 89% mortality with vancomycin treatment alone.

The work was conducted by researchers at Monash University in Melbourne. The same researchers, led by Assoc. Prof. Dena Lyras, also showed that IMM-529 is 80% effective in treating and preventing CDI in a mouse model.

IMM-529 contains antibodies to the toxin B, the infectious spores and the vegetative cells that bind to the gut. Lyras is a world renowned expert in CDI, according to the company, and was the first to report the significance of toxin B in C.difficile infection.

Summary

Immuron is capitalised at $32 million. The company had $3.1 million in cash at the end of last year and is planning to raise additional funds in coming weeks through a Nasdaq listing.

Data from a 120 patient NASH trial, which is expected towards the end of this year will be a major driver of this stock over this period.

With consistent preclinical evidence of efficacy, a solid rationale for the mechanism of action, and encouraging early clinical data, there is a strong potential for a positive outcome from this study.

Follow-on results from three other Phase II trials underway or due to begin, particularly in the treatment of C. difficile infection, will be stock drivers for Immuron in 2018.

Expected Milestones

– Nasdaq listing (Q2 2017)
– Start Phase II C.difficile infection trial (Q2 2017)
– Phase II NASH trial results (Q4 2017)
– Phase II pediatric NAFLD results (mid 2018)
– Phase II ASH study (Q4 2018)

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

Competition in NASH Space

Company	Stage of development	Compound name	Mechanism of action
Intercept	Phase III (2065 pp)	Ocaliva	Modified bile acid
Genfit	Phase III (1000 pp)	GFT505	Anti-inflammatory, improves glucose sensitivity through PPAR pathways, decreases LDL-C lipids
Allergan (from Tobira acquisition)	Phase III to start (1000 pp)	Cenicriviroc	Inhibits CCR2 and CCR5 inflammation pathways
Novo Nordisk	Phase II (372 pp)	Semaglutide	GLP-1 agonist analogue
Novartis (Conatus licensed drug)	Phase II (330 pp)	emricasan	Pan-caspase inhibitor
Shire	Phase II (266 pp)	volixibat	Inhibits bile acids to liver
Novartis	Phase II (250 pp)	LJN452	Anti-inflammatory
Galmed Pharmaceuticals	Phase II/III (240 pp)	aramchol	Fatty acid / bile acid conjugate to reduce liver fat
Gilead Sciences	Phase II (125)	GS-9674	FXR agonist
Gilead Sciences	Phase II (125 pp)	GS-0976	ACC inhibitor
Immuron	Phase II (120 pp)	IMM-124E	Anti LPS and anti-inflammatory
Novartis	Phase II (100 pp)	LMB763	Anti-inflammatory
Gilead Sciences	Phase II (50 pp)	selonsertib (in combination with GS-9674 & GS-0976)	ASK1 inhibitor
Boehringer Ingelheim (Pharmaxis asset acquired)	To start Phase II	-	Inhibits SSAO to reduce inflammation

Factor Therapeutics Phase II Recruitment Update Ahead

The next milestone for Factor Therapeutics (FTT: $0.068) will be an for update investors on the progress of its Phase II venous leg ulcer (VLU) trial of its wound care drug, VF-001, at the end of 2017 Q1.

VF-001 is a biologic drug product that combines the growth factor IGF-1 with the adhesive glyco-protein vitronectin. This novel drug compound works to aid wound healing by promoting the migration and re-population of skin cells and by providing an anchor point for new cells in the wound bed.

What will be of most interest for investors in the short term will be information the company will be able to provide about recruitment progress into the trial.

Up to 26 sites in the US will be used for the trial, with the clinical trials.gov record [NCT02973893] for the trial listing 24 sites, and of those, 17 are indicated to have initiated recruitment.

The company has also qualified an additional 32 sites if it needs to boost recruitment.

The first of the 168 patients entered the trial in December 2016.

The estimated completion date for the trial is November 2017. To achieve this target, the last treatment for the last patient would have to occur towards the end of August.

Trial Design

The trial will compare two doses of VF-001 against a placebo, alongside standard care, in a randomised, double blind trial in patients with chronic VLUs.

The low dose formulation will contain 14 micrograms of active drug, and the high dose 140 micrograms of active drug.

Each patient will be treated for 12 weeks (the treatment phase), and then followed up for 12 weeks.

Standard care therapy will include venous moisture retentive ulcer dressing and multi-layer compression therapy, with Mepitel and Coban2 having been selected for this trial.

This trial of VF-001 differs significantly from the earlier VitroCard trial of the drug product by being a multi-dose, placebo-controlled, randomised trial.

More importantly, the patients screened for inclusion in the trial will have wounds that are, after debridement, between 2.5cm^2 – 5 cm^2 in size and not less than 6 months in duration; or between 5 cm^2 – 15cm^2 and not more than 6 months in duration.

Patients that show a 30% change, either increase or decrease, in wound area in response to debridement and standard care therapy in the two week screening period will be excluded from the study.

These two categories match the Margolis Severity Score 1, which is also defined as having a 65% probability of healing with limb compression within 24 weeks.

Patients with a Margolis Severity Score 1 wounds were shown in the earlier VitroCard study of having a statistically significant wound area reduction from baseline and three times faster healing. The insight from the VitroCard study was that VF-001 converts non-healing wounds to healing wounds (except for the most severe Margolis Severity Score 2 wounds, which constitute 6% of wounds.) The design of the current Phase II trial reflects an improved understanding of the potential benefits and market opportunity for VF-001.

Endpoints

The primary endpoint of the trial will be the percentage reduction in the area of each ulcer within the 12 week treatment phase.

Secondary endpoints will include the proportion of patients with complete study closure within the 12 week treatment phase and the time to complete study ulcer closure within the 12 week treatment phase.

MiMedx VLU Epifix Trial to Complete Mid-Year

Factor Therapeutics is positioning VF-001 to be used in the community care setting as opposed to the special care setting in which a number of advanced wound care products such as Apligraft and Epifix are used.

Of interest is a Phase II trial of Mimedx's Epifx for the treatment of VLUs that is expected to be completed in July 2017 [NCT02011503]. Epifix is a dehydrated human amnion/chorion membrane (dHCM), which has shown to be effective in treating diabetic foot ulcers (which are generally much smaller than VLUs and have a very different disease etiology).

This 123 patient Phase II trial is evaluating Epifix over 12 weeks of treatment with standard-of-care versus standard-of-care alone (multi-layer compression therapy). Endpoints for this trial include time to complete wound closure and proportion of patients with complete wound healing at 12 weeks. Inclusion criteria include wounds of an area between 1 cm^2 – 25cm^2 after debridement, and wounds showing a 25% or less area reduction in a two week run in period after the initial debridement. It appears that the trial has allowed for the inclusion of severe VLU's, so precise comparability between this Epifix trial and the VF-001 Phase II trial will not be straightforward.

However, data from this trial will be of interest to investors in Factor Therapeutics because of the potential for Epifix to become more widely used for treating VLUs. Which type of VLUs remains an unknown but what could occur is that the Epifix product may be better suited to treating large and difficult to treat VLUs, and for those wounds that must be treated in speciality clinics, as opposed to in the community care setting.

What needs to be learnt from the Epifix trial is how many applications of a dHCM allograft (and by area) will be needed to achieve wound closure. More grafts over larger areas will increase the cost of treatment. Mimedx quotes an average of 2.5grafts to achieve

Bioshares Model Portfolio (10 March 2017)

Company	Price (current)	Price added to portfolio	Recommend-ation	Cap'n ($M)	Date added
Dorsavi	$0.390	$0.480	Spec Buy B	$65	December 2016
Pharmaxis	$0.280	$0.260	Spec Buy B	$89	December 2016
Factor Therapeutics	$0.068	$0.054	Spec Buy B	$50	September 2016
GI Dynamics	$0.036	$0.024	Spec Buy C	$19	May 2016
Adherium	$0.205	$0.495	Spec Buy A	$35	March 2016
Bionomics	$0.375	$0.295	Spec Buy A	$181	March 2016
Rhinomed	$0.017	$0.032	Spec Hold B	$14	December 2015
AirXpanders	$0.910	$0.745	Spec Buy A	$259	September 2015
Osprey Medical	$0.432	$0.695	Spec Buy B	$111	September 2015
Clinuvel Pharmaceuticals	$7.00	$4.15	Spec Hold A	$334	December 2014
Innate Immunotherapeutics	$0.710	$0.190	Spec Hold A	$158	November 2014
Opthea	$0.930	$0.160	Spec Buy A	$141	November 2014
Impedimed	$0.755	$0.245	Spec Buy A	$283	December 2013
IDT Australia	$0.125	$0.260	Spec Buy B	$31	August 2013
Viralytics	$1.030	$0.300	Spec Buy B	$247	August 2013
Somnomed	$3.66	$0.94	Buy	$208	January 2011
Cogstate	$1.100	$0.13	Spec Hold A	$124	November 2007

Portfolio Changes – 10 March 2017

IN:
No changes

OUT:
No changes

– Factor Therapuetics cont'd

full closure of generally smaller DFUs. Reimbursement values (from 2014) for Epifix's allografts range from US$331 (1.54cm^2), to US$1,322 (2cm x 3cm), to US$3,529(4cm^2) and to US$6,615 (6 cm^2). The largest Epifix product is 49 cm^2.

Factor's VF-001 is being positioned price-wise to cost between US$1,000-US$1,200 per course of treatment, which may confer a cost benefit over other products in the market place, in addition to benefits resulting from location of use (the community care setting) and skill level required to administer VF-001.

At a minimum, data from the Epifix VLU trial may increase investor interest in companies working in a space which has few novel products in development.

Summary

Factor Therapeutic's forthcoming trial update will provide information on recruitment rates into its Phase II study, which will be an important metric to show that the turnaround in this company continues to be in progress.

The company has designed a trial that should clearly show whether VF-001 works to accelerate the healing of VLUs, especially converting non-healing wounds into wounds that do heal, and sensibly allowing for a dose-dependent effect to be evaluated at the same time.

Factor Therapeutics is capitalised at $50 million and retained cash of $12.6 million at December 31, 2016.

Bioshares recommendation: **Speculative Buy Class B**

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: Cogstate, Bionomics, Impedimed, LBT Innovations, Viralytics, pSivida, Opthea, Reproductive Health Science, Innate Immunotherapeutics, Anatara Life Sciences, ResApp, Pharmaxis, Starpharma, Antisense Therapeutics, Atcor Medical, Dimerix, Cyclopharm, Adalta