ISSN 1443-850X

Companies covered: **15th Bioshares Biotech Summit Reports**

	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 - May '17)	16.8%
Year 17 (May '17 - May '18)	-7.1%
Year 18 (May '18 - May '19)	-2.3%
Year 19 (May '19 - Current)	18.1%
Cumulative Gain	822%
Av. Annual gain (18 yrs)	16.0%

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

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[at}bioshares.com.au

David Blake - Editor/Analyst
Ph: (03) 9326 5382
Email: david[at]bioshares.com.au
Mark Pachacz - Editor/Analyst
Ph: 0403 850 425
Email: mark[at]bioshares.com.au

Individual Subscriptions (48 issues/year)
$500 (Inc.GST)
Edition Number 802 (30 July 2019)

Bioshares

30 July 2019
Edition 802

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

Changing Business Models and Product Offerings

by Emma Armitage, BBiomedSci (Hons) MBioEnt (Hons)

At the **2019 Bioshares Biotech Summit,** the CEOs of four companies with operating businesses in the US – Volpara Health Technologies, Somnomed, Cogstate, and Aroa Biosurgery – each presented their response to the topic, 'Changing Business Models and Product Offerings'.

As the first of two sessions on competition, this ASX-sponsored session explored the evolution of each company's business plan and products, in the context of competing in a changing healthcare marketplace

Volpara's Acquisition of MRS Inc. Moves the Company to Predictive Healthcare

Three years ago, New Zealand-based Volpara shifted from selling breast cancer diagnostic products to providing artificial intelligence software as a service (SaaS) for breast cancer detection.

CEO Ralph Highnam said the shift necessitated a change not only in product development but in business model and culture. In SaaS businesses, strong relationships between the sales team and customers become a necessity for creating recurring value through repeat license renewals.

One of the company's three products, *VolparaDensity*, is an FDA 510(k) cleared clinical decision support tool that analyses breast density. Dense glandular tissue can mask the signal of breast cancer during imaging and is a factor that increases breast cancer risk in comparison to breasts with a higher proportion of fat.

Highnam referred to the Tyrer-Cuzick (TC8) breast cancer risk prediction model, a model that Volpara's density measurements are now included in. *VolparaDensity* is the only commercial product included in this model, with a lead on the competition stemming from independent academic validation. US law will soon mandate that all women are told their breast density score following a mammogram.

Volpara generated annual recurring revenue of NZ$6.6 million for FY19, up 86% over the year. Highnam stated that the company's competitive position draws from its intellectual property, clinical validation, regulatory approvals and marquee clinic partners.

Highnam said that the company's long-term strategy to build on this income and create additional barriers to entry has been boosted by a recent acquisition. Assisted by a $55 million raise in June 2019, Volpara acquired US patient tracking company MRS Systems Inc and its employees.

MRS provides software for breast and lung cancer imaging clinics to provide business intelligence, patient reporting, automation of clinical staff's work, assistance in reimbursement and audit compliance for clinics.

Cont'd over

The clinical data that MRS owns will allow Volpara to pair its diagnostic breast images to long-term patient outcomes within the Mammography Information System sector. With this acquisition, Highnam argued that Volpara now has the capacity to move to predictive healthcare and ultimately prevention, given the level of long term clinical outcome data that the company can now access. This was a major reason for the acquisition.

Volpara anticipates gaining various short-term benefits from the acquisition of MRS, including access to clinical data, experienced US-based staff, and recurring revenues across a greater number of US clinics. In the long term, the company could assist others in identifying candidates for clinical trials, and it may enter the lung imaging market.

In short, Highnam believes that Volpara has the "competition playing catch-up." With MRS now supporting Volpara's long term strategy, the company is ambitious about its growth. Volpara has increased its presence in the US from 7% to 25% of women screened, and its annual recurring revenue now stands at NZ$14.6 million. Volpara was selling its products and services into 407 clinics and MRS has a presence in approximately 1700 clinics across the US.

Somnomed Targets Market Acceptance of an Alternative Therapy to CPAP

Somnomed's CEO Neil Verdal-Austin calls the company's business model "from woah to go" in the treatment of Obstructive Sleep Apnoea (OSA) with oral appliances. The company develops, tests, manufactures, sells and distributes products, with over 500,000 OSA patients now treated to date across 28 countries.

The severity of a patient's OSA is classified as mild, moderate, or severe, depending on the number of apnoea and/or hypopnea events a patient experiences per hour of sleep.

OSA can be treated in a myriad of ways, including positional therapy, weight loss, surgery, use of Continuous Positive Airway Pressure (CPAP) machines, or oral appliance therapy.

CPAP is considered the gold standard for OSA, but despite improvements in machine and mask design, the current non-adherence rate of 34.1% represents very little improvement in compliance over the past 20 years.

Verdal-Austin describes this compliance issue as “the reason SomnoMed exists”. SomnoMed's SomnoDent products are custom-made oral appliances that are fitted to the teeth and move the lower jaw slightly forward to treat OSA. SomnoMed refers to these solutions as Continuous Open Airway Therapy (COAT).

SomnoMed is working to improve manufacturing and connectivity within the device, the latter allowing for compliance tracking.

In 2019, the company announced FDA clearance pf its new SomnoDent AVANT product. AVANT has a treatment effectiveness rate of 90%, compared to 67% with the SomnoDent Flex device.

The company's sales cycle, which Verdal-Austin referred to as “complex”, spans medical and dental sectors. Verdal-Austin said that there is a growing acceptance and preference for COAT amongst medical referrers, particularly in mild and moderate OSA.

Verdal-Austin noted that the company's growth strategy is linked to increasing awareness, adoption, and acceptance across both patients and medical specialists.

Reimbursement of oral appliances varies across geographical markets, so SomnoMed also works to educate insurers.

While the market size for oral appliances is hard to determine due to irregular reimbursement, SomnoMed believes it is a global leader in the COAT market with between 25% - 30% market share.

The presentation ended with a video of patients describing their lives with OSA. Notably, many of these patients were young adults whose quality of life had been severely impacted by OSA. It showed that this ‘public health crisis’ is often underdiagnosed and improperly treated.

Verdal-Austin explained that SomnoMed aims to address this large global market, with its competitive advantage built around clinical research, proprietary materials and design, and its position as the most prescribed oral device for OSA by medical and dental practitioners.

Cogstate Outlines Market Opportunities in and Beyond Alzheimer's Disease

Cogstate was founded to develop brain health assessments for any purpose, for use across different cultures, languages, and sites. Twenty years on from its founding, CEO Brad O'Connor, shared with the Bioshares Biotech Summit audience the realisation of that vision. A long way from its starting goal of “building a better test”, Cogstate provides an expanded product offering that includes proprietary computerized cognition tests, digitised pen and paper tests, and clinical trial rater training and monitoring.

Through more than 400 peer-reviewed publications and use within drug trials for over 70 indications, O'Connor explained that Cogstate has strong validation for its brief, repeatable, and highly reliable tests.

O'Connor noted that Cogstate started out testing traumatic brain injury, and still offers this for markets that include sports. Observing pharma companies' move to Alzheimer's disease treatments, Cogstate has also moved into the primary care market with its Cognigram digital cognitive assessment system.

Cognigram applies Cogstate's validated Brief Battery test to clinical practice, allowing for at home or in-clinic administration of a 10-15 minute computerised cognitive test. O’Connor stated that this HIPAA compliant, FDA 510(k) cleared, CE-marked technology allows for simple assessment and monitoring of cognitive changes. With impairment under-reported and under-diagnosed, improved identification therefore creates significant healthcare benefits.

Cont'd over

Clinical trials that have cognitive measurement as an efficacy or safety endpoint have been Cogstate's largest market, said O'Connor. Despite clinical trial failures in Alzheimer's disease from the likes of Eli Lilly, Janssen, Astra Zeneca and Merck, Cogstate has gained experience with these companies across a range of clinical trial phases, disease stages, and within public-private partnership studies. As an aside to local companies, he noted a lot of opportunity for biotech companies in this space, with big pharma looking to partner to obtain promising treatments.

Within the Alzheimer's disease market for its products, Cogstate expects to see income growth from early stage disease assessment and at-home monitoring of trial outcomes. In addition, Cogstate is applying its programs to trials in paediatric and rare disease, Parkinson's disease, and evaluation of anti-depressant and NMDA modulators. In the last 18 months, work in the Alzheimer's disease space made up only 15% of revenue, compared to around 50% of revenue in the previous 18 months. Work in rare diseases now accounts for 22% of contracts.

In the next 12 months, Cogstate hopes to announce a license agreement for Cognigram, continue to expand its clinical trial assessments, and invest in self-administered tests and expansion to modalities such as smartphones.

O'Connor compared Cogstate favourably to its competition, few of which offer the comprehensive services that Cogstate does. He described Cogstate's strengths as a proven ability to commercialise digitised solutions, a wealth of data from longitudinal studies in healthy and disease states, expertise in global programs, and a regulatory cleared solution.

O'Connor listed a number of outcomes from the AAIC Alzheimer's conference held in Los Angeles this month. Big pharma's focus on beta amyloid has not worked. However, one company, Eisai, remains undeterred, with a five-year, 2,500 patient study planned in subjects with preclinical disease with its beta-amyloid inhibitor. And inflammation has become a new hypothesis and an opportunity for biotechs.

For Cogstate, the opportunities will be more in Phase II studies rather than the larger Phase III trials.

The opportunity for Cogstate is that with the move to preclinical patients, the need for a more sensitive test than ADOS-Cog, such as Cogstate's test, provides an opportunity for the company.

Another opportunity for Cogstate is from the trend to conduct remote assessments of patients, at home, for which the Cogstate test has utility.

Most importantly, Cogstate has a proven ability to establish deep, strategic relationships and a 'trusted partner' position with the likes of Eli Lilly, that lead to the establishment of these solutions that meet their needs. The processes and approaches may be easy to replicate, but the relationships are not.

Aroa Biosurgery Aims to Provide the 'Right Product at the Right Time'

The only private company in this session, Aroa Biosurgery, is a soft tissue regeneration company based in New Zealand. CEO Brian Ward presented an overview of the company's growth from its 2008 founding to sales of $24.2 million ($2.9 million EBIT) in FY19.

Aroa's proprietary Endoform biomaterial comprises an intact extracellular matrix scaffold with vascular channels. This decellularised tissue forms the basis of a wide range of Aroa's products to repair serious injury and wounds, allowing a patient's own tissue to grow into and replace the scaffold.

Ward described Aroa's simple go-to-market strategy, which began with a wound care partnership with US healthcare company Hollister. When Hollister decided to divest its wound care range in 2018, Aroa retrieved the Endoform product that Hollister had commercialised in the US plus sales staff.

Aroa's existing products target diabetic foot ulcers, venous leg ulcers, limb salvage and soft tissue reconstruction through a 50:50 joint venture with Hydrofera (Appulse), and abdominal wall and breast reconstruction through a partnership with Tela Bio. Tela and Aroa's Ovitex product for enterocutaneous fistula has been used in over 4,000 implantations. Across its full range, Aroa's products have been used in an impressive five million procedures in the last 10 years.

Ward gave an overview of current pipeline products, including Symphony (a skin substitute) and Leaf (active post-operative management of dead space with significant cost savings through reduction in surgical site infections and dehiscence).

Ward said that Aroa's approach is to provide the "right product at the right time". This covers a spectrum across wound stabilisation, inflammation correction, providing a scaffold for fibroblast adhesion and infiltration into the product, and remodelling leading to wound closure. Target markets for Aroa products include outpatient wound centres and in-patient acute settings such as operating rooms.

While Aroa's competitors do include big players such as 3M and Smith & Nephew, Ward believes Aroa is quicker to innovate than these large companies and has the scientific and clinical experience to compete against smaller companies. Its sales success comes from high product quality and clinical outcomes, at a reasonable product cost. He outlined how partnerships with Hollister, Hydrofera and Tela Bio underlie this sales success, as does Aroa's comprehensive supply chain and access to markets.

Over the next 12 months, Aroa will be expanding its North American sales capability and ex-US distribution, advancing its current pipeline, expanding manufacturing, and looking for partial liquidity for early investors (which could include an IPO).

Continued on page 5

Gut Health & the Microbiome Session Report

by Max Liddle

Background

The microbiome is the community of bacteria, viruses, fungi, worms and other varieties of microbe that exists in the body of a higher organism. The mutualistic relationship of the body of the higher organism and the microbiome of that organism creates what is sometimes referred to as a Super-organism.

In a 'healthy' state the balance of these microbes supports and even enhances the host body, which in turn provides a stable environment supportive of the microbiome. In an unhealthy or dysbiotic state, the microbiome can damage the body, triggering inflammatory processes designed to protect the host body which negatively impact the microbiome.

The microbiome has become a hot area for research and each study published tells a similar story, that the health of the human body and the condition of its microbiome are inseparable.

The condition of the microbiome has been linked to an ever growing list of health conditions. It has been linked to multiple neurological conditions including anxiety, depression, autism, dementia and others, via the Gut-Brain Axis, metabolic disorders such as diabetes (Type I & II) and weight gain, multiple inflammatory disorders, including IBS/IBD, allergies, cancer, and autoimmune conditions.

Intriguingly, it has also been shown that particular species interfere with the action of pharmaceutical drugs, impacting (for better or worse) on the ability to treat these conditions with conventional medical methods. It may appear that these feedback loops are self-perpetuating.

However, it has been shown that certain interventions can work to adjust the content of the microbiome and shift the type of impact it has on the host body.

It is obvious from the above that being able to target interventions at the microbiome is a valuable capability. At present there are a number of interventions that exist for targeting the microbiome. These fall into two general categories: therapies focused on altering a single part of the microbiome; and those that act broadly on the whole microbiome.

Examples of specific therapies include use of probiotics, bacteriophage therapy, and helminth therapy. Broad therapies include antibiotics, dietary intervention, and faecal microbial transplants. All these therapies have documented impacts on the microbiome and are being developed or are in use as a commercial proposition.

However, the mechanisms of action are poorly understood. This lack of understanding stems from an inherent difficulty in understanding the full context of the microbiome.

Given the growing knowledge of how the microbiome impacts health, there is clearly substantial opportunity to provide services and products targeted at untangling the complexity of the microbiome.

The companies which presented in the Gut Health and Microbiome session at the **2019 Bioshares Biotech Summit** are approaching the problem of untangling the complexity of the microbiome from different directions.

Anatara Lifesciences – Seeking Clinical Validation for GaRP

Steve Lydeamore, CEO of Anatara Lifesciences, outlined their strategy of utilising a specific dietary element to target the interface of the microbiome and the body.

This product, named GaRP (Gastrointestinal Reprogramming Product), acts to "remove bacteria with pro-inflammatory properties" and "stimulate mucosal healing". At present no human trials have been initiated.

The function of this product seems to be similar to that of a prebiotic, an emerging but competitive niche in the gastro-intestinal health market.

Anatara Lifesciences' strategy of seeking clinical validation for this product will do well to set it apart from other prebiotics which usually trade as nutritional supplements, although clinical data showing efficacy in humans is much needed.

Atmo Biosciences – Gas Sensing Capsule

Malcolm Hebblewhite, CEO of Atmo Biosciences, discussed studying of the composition of the microbiome buy using a consumable and disposable capsule that measures the gaseous metabolic products of intestinal bacteria. Analysis of these products is used in ecological surveys and agriculture to determine the diversity of species in coral reefs and the stage of growth of cereal crops.

The application to gut health is an interesting innovation. This technology is particularly interesting as it could help determine the precise location of disturbances to the microbiome within the gut, something that traditional faecal analysis is not able to achieve.

A question remains as to how finely the technology will be able to differentiate different syndromes in the gut, and whether it can be used to drive better clinical outcomes as a result.

The initial results for the Phase I trials of the technology indicate it is able to differentiate between a person consuming a high fibre or low fibre diet, though this is also easily achievable by many available stool tests. Hydrogen and oxygen levels were accurately detected, with the capsule detecting gas concentration measures more than 5000 times higher that using a breath test.

Cont'd over

Bioshares Model Portfolio (30 July 2019)

Company	Code	Price (current)	Price added to portfolio	Recommend-ation	Cap'n ($M)	Date added
Telix Pharmaceuticals	TLX	$1.500	$0.910	Spec Hold A	$373	May 2019
Volpara Health Technologies	VHT	$1.640	$0.375	Spec Hold A	$356	June 2017
Opthea	OPT	$0.790	$0.160	Spec Buy A	$197	November 2014
Alcidion	ALC	$0.170	$0.053	Hold	$138	April 2019
Somnomed	SOM	$2.310	$0.94	Spec Buy A	$145	January 2011
Pharmaxis	PXS	$0.225	$0.260	Spec Buy A	$89	December 2016
Immutep	IMM	$0.021	$0.032	Spec Buy A	$81	March 2019
Bluechiip	BCT	$0.100	$0.053	Spec Hold B	$53	December 2018
Rhinomed	RNO	$0.340	$0.24	Spec Buy B	$54	Jun-19
Micro-X	MX1	$0.330	$0.38	Spec Buy A	$50	May 2017
Adalta	1AD	$0.180	$0.23	Spec Buy A	$29	July 2017
Acrux	ACR	$0.180	$0.31	Spec Buy A	$30	July 2017
Cogstate	CGS	$0.185	$0.24	Accumulate	$22	April 2019
Dimerix	DXB	$0.105	$0.09	Spec Buy B	$17	December 2018

Portfolio Changes – 30 July 2019

IN:
No changes

OUT:
No changes

Stocks Removed from Bioshares Portfolio in TTM

Date removed	Stock
June 2019	CUV
March 2019	CYP
March 2019	CGS, MGZ
February 2019	RNO
November 2018	FTT
October 2018	BNO
September 2018	DVL, MEB, OSP

– Microbiome and Gut Health cont'd

Microba – Gut Bacteria Profiling

Blake Wills, CEO of Microba presented an advancement of the more traditional technique of faecal analysis. The Microba technology categorises bacteria by their metabolic outputs and compares the profiles to a clinical database. This database can then be used to create connections between the status of the microbiome, a patient's health and the efficacy of the microbiome targeting treatments they might receive.

This fills a major gap in the current market as it provides a method for proving the efficacy of therapies as well as improving the understanding of microbiome compositions and their associated pathologies. This information is critical to developing future microbiome focused therapies.

Commentary

The companies discussed above are all substantially focused on the bacterial aspects of the microbiome, and while each is attempting to unravel the complexity of the microbiome, it is difficult to do so while focusing only on a subset of the full context.

The difficulty is that the other components are less well understood at a biological level, and therefore exist as an additional capability that needs to be developed. The next most accessible component of the microbiome is the viral content.

Bacteriophages (viruses that infect bacteria exclusively) are necessarily closely associated to their bacterial hosts, and their presence is a key modulator of bacterial populations in all environments across the world, including in the human microbiome.

Bacteriophages are experiencing a revival in use as a therapeutic agent targeting bacteria, and the microbiome is an excellent candidate for their use. If any of the companies described above were to seek to develop their technologies to also be explanatory of the bacteriophage content of the microbiome, they would be well situated to provide treatments and analysis with far greater power. This would also place them at the forefront of microbiome science and understanding.

Bioshares

– Changing Business Models and Product Offerings cont'd

Summary

Each of the presenters for this session delivered a convincing picture of their company's differentiation to current players and technologies in the sector. In the Summit's final session, BioPacific Partners' Executive Director Andrew Kelly gave honourable mention to several of these presenters and judged Aroa's Brian Ward the winner of 'Best Presentation.' Despite this, the presenters and their companies still have to guard against complacency. Each will need to ensure they keep a close eye on their competition, particularly from emerging technologies.

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 Some 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, LBT Innovations, Opthea, ResApp Health, Pharmaxis, Dimerix, Adalta, Actinogen Medical, Patrys, Cyclopharm, Emvision, Antisense Therapeutics, Heramed, Imugene

Subscription Rates (inc. GST)

48 issues per year (electronic distribution): **$500**

For multiple email distributions within the same business cost centre, our pricing structure is as follows:	$800	2-3 email addresses
	$1100	4-5 email addresses
	$1370	6-10 email addresses

To subscribe, post/fax this subscription form to:

Bioshares
PO Box 193 Richmond VIC 3121
Fax: +61 3 9329 3350

I enclose a cheque for **$** made payable to **Blake Industry & Market Analysis Pty Ltd**, or

Please charge my credit card **$** MasterCard ☐ Visa ☐

Card Number ☐☐☐☐ ☐☐☐☐ ☐☐☐☐ ☐☐☐☐

Signature _____ Expiry date _____

Subscriber details

Name _____

Organisation _____

Ph ( ) _____

Emails _____

_____

_____