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Companies covered: **CGS, CUV, IMU, SOM, RNO, SARS-CoV-2 Vaccines**

	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)	-35.8%
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 - May '20)	39.5%
Year 20 (May '20 - Current)	0.0%
Cumulative Gain	989%
Av. Annual gain (19 yrs)	17.3%

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Bioshares

11 May 2020
Edition 842

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

12 SARS-CoV-2 Vaccine Candidates now in Clinical Trials

12 vaccine candidates for SARS-CoV-2 have now entered clinical studies, as listed with Clinicaltrials.gov. The first was Shenzhen Geno-Immune Medical Institute's pathogen-specific artificial antigen presenting cell vaccine (aAPC), which entered a clinical study on February 15, 2020. This was registered on March 9, 2020 on Clinicaltrials.gov. The Institute also initiated a trial of another vaccine candidate, LV-SMENP-DC in combination with antigen-specific CTLs, on March 24, 2020.

These vaccine candidates are based on the application of various genetic technologies to design and manufacture which has expedited their rapid entry into clinical studies. These processes have been able to take advantage of the sequencing of the SARS-CoV-2 genome in January along with the identification of structures of the virus such as the Spike protein and receptor binding domain (RBD) that can serve as antigens which can then stimulate the production of protective antibodies.

Twelve candidates in 11 trials, registered withClinicaltrials.gov, are listed in the table on the next page.

According to Biocentury there are 83 vaccine candidates in pre-clinical development.

Shenzhen Geno-immune Medical Institute

Technology: Artificial antigen presenting cell vaccine (inactivated)
Vaccine Design: Selects conserved and critical structural and protease protein domains to engineer lentiviral minigenes to express SARS-CoV-2 antigens.
Manufacturing: N/A
Trial: A 100 subject Phase I/II study commenced on February 15, 2020
Trial Completion: July 2023

Shenzhen Geno-immune Medical Institute

Technology: Lentiviral Minigene Vaccine (LV-SMENP) and antigen-specific CTLs
Vaccine Design: A lentiviral vector system (NHP/TYF) is used to express viral proteins and immune modulatory genes to modify dendritic cells (DCs) and to activate T cells
Manufacturing: N/A
Trial: A 100 subject Phase I/II study commenced on March 24, 2020
Trial Completion: July 2023

Biontech / Pfizer

Technology: mRNA vaccine (mRNA which codes for selected target/s is taken into cells which results in the expression or synthesis of the desired vaccine antigen)
Vaccine Design: BNT162 (as four sub-versions a1, b1, b2, c2) (targets: Spike protein and RBD)
Manufacturing: cell-free enzymatic reactions, lipid nanoparticle (LNP) encapsulation
Trials: A Phase I dose escalation trial has commenced; a 21 arm, 7,200 patient Phase

Cont'd over

I/II vaccine candidate selection trial of sub-versions of four candidates, exploring safety and efficacy has commenced.
Trial Completion: January 2023

Moderna

Technology: mRNA vaccine
Vaccine Design: Encodes for a prefusion stabilized form of the Spike protein, which is then encapsulated in lipid nanoparticles
Manufacturing: cell-free enzymatic reaction system
Trial: A 105 subject study has commenced.
Trial Completion: The trial commenced on March 16 and is expected to be completed in September 2021.

Novavax

Technology: Recombinant protein nanoparticles and Matrix-M adjuvant
Vaccine Design: NVX-CoV2373 (a stable, prefusion protein) and saponin-based Matrix-M adjuvant
Manufacturing: Spodoptera frugiperda expression system (Sf9/BV), which expresses large properly folded proteins and particles
Trial: Set to commence 131 patient trial on May 15
Trial Completion: December 2020

Oxford University

Technology: Adenoviral vector vaccine
Vaccine Design: ChAdOx1 - replication-deficient chimpanzee adenovirus Oxford 1 encoding SARS-CoV-2 Spike protein
Manufacturing: HEK293 cell lines containing the adenoviral E1 gene
Trials: A safety, tolerability and reactogenicity Phase I/II trial in 1,090 subjects commenced on April 23
Trial Completion: May 2021

Sinnovac Biotech

Technology: Bifidobacteria monovalent DNA oral vaccine
Design: An orally administered, genetically modified probiotic bacteria which is designed to release DNA molecules in the gut which encode for antigenic transgenes and neutralizing nanobodies
Manufacturing: N/A
Trial: An 144 subject safety and immunogenicity trial commenced on April 16, to be followed by a Phase II component in 600 subjects.
Trial Completion: August 2020

CanSino Biologics

Technology: Adenoviral vector (replication defective) vaccine
Vaccine Design: Ad5-NCoV - expresses SARS-CoV-2 Spike protein
Manufacturing: N/A
Trials: A safety and immunogenicity, 108 subject Phase trial commenced on March 16; an antibody response, 500 subject Phase II trial commenced on April 12
Trials Completion: December 2020/ January 2021

Innovio / CEPI

Technology: Adenoviral vector vaccine to produce T-cell response, delivered using electroporation
Vaccine Design: Drug INO-4800 and electroporation device CELLECTRA 2000. The device enables intradermal administration. INO-4800 encodes for the SARS-Cov-2 Spike protein
Manufacturing: N/A
Trial: A safety and immunogenicity Phase I trial in 40 subjects commenced on April 3, with subjects having received their first dose (day 0). Second dose follows at week 4.
Trial Completion: Interim results expected late June 2020, with completion by April 2021.

Continued over

NCT Number	Title	Sponsors / Collaborators	Start Date	Primary Completion Date
NCT04380701	A Trial Investigating the Safety and Effects of Four BNT162 Vaccines Against COVID-2019 in Healthy Adults	Biontech	April 23, 2020	Aug-20
NCT04352608	Safety and Immunogenicity Study of Inactivated Vaccine for Prophylaxis of SARS CoV-2 Infection (COVID-19)	Sinovac Biotech	April 16, 2020	13-Aug-20
NCT04313127	Phase I Clinical Trial of a COVID-19 Vaccine in 18-60 Healthy Adults	CanSino Biologics and others	March 16, 2020	30-Dec-20
NCT04368988	Evaluation of the Safety and Immunogenicity of a SARS-CoV-2 rS (COVID-19) Nanoparticle Vaccine With/Without Matrix-M Adjuvant	Novavax	May 15, 2020	31-Dec-20
NCT04341389	A Phase II Clinical Trial to Evaluate the Recombinant Vaccine for COVID-19 (Adenovirus Vector)	CanSino Biologics and others	April 12, 2020	31-Jan-21
NCT04324606	A Study of a Candidate COVID-19 Vaccine (COV001)	University of Oxford	April 23, 2020	01-May
NCT04334980	Evaluating the Safety, Tolerability and Immunogenicity of bacTRL-Spike Vaccine for Prevention of COVID-19	Symvivo	April 30, 2020	31-Aug-21
NCT04283461	Safety and Immunogenicity Study of 2019-nCoV Vaccine (mRNA-1273) for Prophylaxis of SARS-CoV-2 Infection (COVID-19)	Moderna/ NIAID	March 16, 2020	20-Sep-21
NCT04368728	Study to Describe the Safety, Tolerability, Immunogenicity, and Potential Efficacy of RNA Vaccine Candidates Against COVID-19	Biontech, Pfizer	April 29, 2020	27-Jan-23
NCT04276896	Immunity and Safety of Covid-19 Synthetic Minigene Vaccine	Shenzhen Geno-Immune Medical	March 24, 2020	31-Jul-23
NCT04299724	Safety and Immunity of Covid-19 aAPC Vaccine	Shenzhen Geno-Immune Medical	February 15, 2020	31-Jul-23

Bioshares Model Portfolio (11 May 2020)

Company	Code	Price (current)	Price added to portfolio	Recommend-ation	Cap'n ($M)	Date added
Opthea	OPT	$3.020	$0.160	Spec Buy A	$813	November 2014
Telix Pharmaceuticals	TLX	$1.500	$0.910	Spec Hold A	$380	May 2019
Volpara Health Technologies	VHT	$1.330	$0.375	Spec Hold A	$291	June 2017
Cyclopharm	CYC	$1.250	$1.35	Spec Buy A	$98	September 2019
Somnomed	SOM	$1.090	$0.94	Spec Hold B	$68	January 2011
Immutep	IMM	$0.145	$0.320	Spec Hold A	$56	March 2019
Cogstate	CGS	$0.320	$0.24	Spec Buy A	$52	April 2019
Micro-X	MX1	$0.140	$0.38	Spec Buy A	$43	May 2017
Dimerix	DXB	$0.250	$0.09	Spec Buy A	$40	December 2018
Pharmaxis	PXS	$0.088	$0.260	Spec Buy B	$35	December 2016
Acrux	ACR	$0.135	$0.31	Spec Hold A	$22	July 2017
Rhinomed	RNO	$0.080	$0.24	Spec Hold B	$14	Jun-19

Portfolio Changes – 11 May, 2020

IN:
No changes

OUT:
No changes

Stocks Removed from Bioshares Portfolio in TTM

Date removed	Stock
September 2019	1AD, ALC, BCT
June 2019	CUV

Commentary

The SARS-CoV-2 vaccine candidates now in clinical trials may be confirmed as safe and possibly effective in the latter half of 2020. However, they may become redundant if SAR-CoV-2 mutates to the extent that the antibodies the vaccines elicit to neutralise SARS-CoV-2 target proteins become ineffective. This is a risk.

Vaccines that target more than one SARS-CoV-2 proteins, such as Biontech's BNT162 may provide more durable protection against future mutations of SARS-CoV-2.

Another important consideration for investors to note is that the manufacturing capacity exists to supply millions of doses has yet to established and validated, even though fermentation systems for genetically-engineered products confer some scalability advantages. (Some steps such as purification may be more rate limiting than others.) The pairing of mRNA vaccine developer Biotech with Pfizer, a company with substantial resources and experience in large scale vaccine development and manufacturing, marks the BNT162 program as one to monitor closely.

Bioshares

Stock Updates

Somnomed Sales Down Over 80%

Somnomed (SOM: $1.09) finished the March quarter with $26 million in cash, including funds raised in April.

The company announced in late March that it was raising $15.5 million at a steep discount of 60% at $0.80 per share. The raise was to provide the company with sufficient funds to ride out the impact of the coronavirus pandemic.

For the March quarter the company reported a reasonable result, with sales up 9% compared to the previous corresponding period, to $15.6 million. However, this was due to a very strong January and February (up 17%) before the pandemic impact in March which saw revenue fall by 11% for that month.

On a cashflow basis, the company registered a positive cashflow from operations and investment (in property, plant and equipment) of $1.5 million for the quarter.

Current sales (at the end of April) for the company have fallen by 80%-85% due to restrictions in dental visits and sleep clinics during the pandemic.

The company has downsized its manufacturing and installed a company-wide reduction in costs and salaries. Further downsizing may occur if the pandemic has a prolonged and severe impact on its business.

Somnomed is capitalised at $90 million.

Bioshares recommendation: **Speculative Hold Class B**

Clinuvel Pharmaceuticals – Sitting on $62 Million

Clinuvel Pharmaceuticals (CUV: $22.83) is, in terms of cash resources, is one of the healthiest ASX listed biotechs. At the close of the March quarter it retained $62 million in cash.

The company recorded a positive cash flow from operations of $2.2 million, in what is generally its second quietest period across the year.

In the March Quarter, receipts from customers were down 9% on the previous corresponding period, to $5.4 million.

Sales in the March quarter were all from Europe. Population movement controls imposed in March appear to have had some impact on revenue.

In the previous December quarter, which sees the least demand for the company's photoprotective drug (leading into the northern hemisphere winter), receipts from customers increased by 43% to $3.7 million over the PCP.

Last month Clinuvel started selling its Scenesse product in the US with coverage now accepted by at least 30 insurers and at least three treatment centres providing the therapy (delivered by a depot injection for two months of treatment).

In the US there are around 2,300 people living with EPP, the sunlight intolerance disorder for which Clinuvel's drug Scenesse is approved to treat. Scenesse sells for around €14,000 per injection, with injections given on average around four times a year and up to six times a year.

Sales can be expected to grow significantly from the addition of the US market. However the effect from the coronavirus pandemic will impact the initial growth trajectory.

Clinuvel's chairman Willem Blijdorp stated recently that Clinuvel needs to have a minimum of two years of cash in reserve to survive any crisis. With $62 million in funds and a lean spending set up with annual costs of around $16 million, Clinuvel is securely positioned.

Clinuvel has also taken its first major step to commercialise its drug in China. In collaboration with HK Winhealth Pharma Group Co, Clinuvel is seeking to supply its therapy to 10 patients with EPP under a Named Patient Program, whereby local subsidies might be available to pay for the treatment. It is the first step of its commercial program in China.

The company is also progressing its second application for Scenesse in the US, that being for the treatment of vitiligo. A formal meeting was recently held with the FDA and clinical experts to discuss the clinical development pathway for vitiligo treatment with Scenesse in the US. Clinuvel's objective is to file a supplemental NDA for the drug for treatment of vitiligo, once a pivotal study can be completed.

Clinuvel is capitalised at $1.13 billion.

Bioshares recommendation: **Hold**

Cogstate Secures Funding from Multiple Sources

Cogstate (CGS: $0.32) has secured a US$2.44 million loan under the US Coronavirus Aid, Relief and Economic Security Act. The loan can be forgiven, which means it does not need to be repaid.

The aim of the program is to keep US employees in their jobs during the coronavirus pandemic through the Paycheck Protection Program. Cogstate has 128 US-based staff, all of whom are working remotely now. At least 75% of the loan needs to be used for employee salaries.

Cogstate also recently secured US$1.3 million in funding from the Alzheimer's Drug Discovery Foundation. The funding will be used to apply its International Shopping List Test to a smartphone. The ADDF is eligible to receive royalties from revenue of between 2.5%-4%.

The coronavirus pandemic provides a mixed environment for Cogstate. There will very likely be an impact from a drop in the commencement of clinical studies during the pandemic.

However, there is an increasing need now to provide remote cog-

Cont'd over

nitive testing using the company's software, rather than the traditional pencil and paper tests such as ADAS-Cog and CDR-SB. It represents an opportunity for companies such as Cogstate to introduce more computerised cognition tests that complement or can replace the incumbent, more rudimentary tests.

Cogstate is capitalised at $54 million. The company held cash of US$7.3 million, with US$42 million in future work secured. In the first nine months of this year, the company signed contracts worth US$37.6 million, including US$10.7 million in the March Quarter.

Bioshares recommendation: **Speculative Buy Class A**

Correction:
In *Bioshares* 841, the Survival Index for Cogstate was incorrect. The correct figure is 2.7 .

Rhinomed to Raise $6.5 Million

Rhinomed is in the process of raising $6.5 million through a fully underwritten renounceable rights issue. The issue is being conducted at $0.077 per share, which is a 2.3% discount to its 10 day VWAP.

The company's largest shareholder, Whitney George, who currently owns 29% of the company, will be underwriting the offer.

Assuming a 50% take up in the rights issue excluding the shares to be issued to George under his entitlement, it may see George end up with a 39% stake in the company. However, the deal is subject to approval by the Australian Foreign Investment Review Board.

George is President of Sprott Inc and CIO of Sprott Asset Management which has US$10.7 billion in funds under management.

Bioshares recommendation: **Speculative Hold Class B**

Imugene – Well Positioned With $34 Million in Cash

Imugene (IMU: $0.029) completed the March quarter retaining $33.7 million in cash, after a very timely funding round in December last year which raised just under $25 million.

The company's Phase II HER-Vaxx trial has passed an important review by the Independent Data Monitoring Committee, which did not raise any safety issues with the therapy, and recommended that the trial continue following a risk-benefit assessment.

The trial is enrolling 68 patients with metastatic gastric cancer, where those tumours overexpress the HER-2 protein.

The aim of the therapy is to induce patients' immune systems to produce their own antibodies to bind to the cancer protein, as opposed to treatment with injected monoclonal antibodies such as Herceptin and Perjeta.

The study is being conducted in India and Eastern Europe where the expensive antibody therapies are not always available to patients.

Imugene plans to commence a second study this year with a similar approach, but the therapeutic vaccine will induce patients to produce PD-1 antibody inhibitors, rather than injected monoclonal PD-1 antibody therapies such as Keytruda.

The aim is not necessarily to replace these therapies, but to offer an additional treatment approach that may result in a different outcome than that achieved with monoclonal antibodies. In this checkpoint inhibitor market, there are many more options with respect to cancer indications that may benefit from such a treatment. Toxicology and manufacturing has been completed with high levels of the PD-1 antibodies shown to be generated in preclinical studies.

A third clinical trial with its third technology, CF33 which is an oncolytic virotherapy, is expected to move into Phase I studies also this year. In combination with checkpoint inhibitors, oncolytic virotherapy is believed to significantly increase the abundance of checkpoint inhibitor targets as the virus breaks up (lyses) tumour cells.

A recent study was published showing such a benefit in a preclinical model of triple negative breast cancer when CF33 was delivered with a PD-L1 inhibitor.

Imugene is capitalised at $125 million.

Bioshares recommendation: **Speculative Buy 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 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

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