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Bioshares

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

Companies covered: **CYP, IMU, HMD**

	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)	18.9%
Cumulative Gain	828%
Av. Annual gain (18 yrs)	16.0%

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Extract from Bioshares –

Imugene To Expand Portfolio With License of Oncolytic Virotherapy

Imugene (IMU:$0.019) will expand its oncology program by acquiring Vaxinia Pty Ltd and acquire a license from the City of Hope (COH) comprehensive cancer centre (Los Angeles) for an oncolytic virotherapy (OV), CF33.

CF33 was selected from ~100 evolved (chimeric) variants of different strains of the pox virus that were screened for their ability to stimulate an immune response by recruiting CD8-positive T-cells, as well as their ability to activate immune blockade molecules. Such activation helps make checkpoint inhibitor drugs such as Keytruda and Opdivo more effective. They were also screened for their cell-killing power (lysis).

The CF33 program commenced in 2016, with CF33 itself identified in 2017.

Vaxinia employs staff experienced in developing oncolytic virotherapies who were formerly employed at Viralytics. Viralytics developed CAVATAK, a picornavirus OV, which was acquired by Merck in 2018 for $502 million.

Features of CF33

Studies of CF33 have found that it is capable of killing cancer cells with as little as 1,000 PFUs (plaque forming units). CF33 was also tested against the National Cancer Institute's panel of 60 types of tumour cells, demonstrating success in killing all 60 types.

Animal studies have shown than CF33 can be dosed at $1x10^7$ PFUs with no evidence of major toxicity, but also be effective at $1x10^3$ PFUs, indicating that CF33 may have a very high therapeutic index, or a wide safety margin for dosing.

Other data that has emerged from preclinical studies is that CF33 is more effective in reducing tumour volume than several other leading OVs (Amgen's T-Vec and Genelux's GLV-1h68), when each was administered at $1x10^3$ doses in lung cancer xenografts in mice. Of note was that CF33 alone showed an effect on non-injected tumours (abscopal effect).

Poxviruses are large DNA viruses, which gives them a large capacity for the insertion of other genes (more than 25 kb), and are easy to manipulate. In the case of CF33, this capacity could be applied to the inclusion of the genetic sequence of an immune checkpoint inhibitor.

Evidence is growing that shows that OV therapy combined with immune blockade inhibitors leads to improved treatment outcomes. A 198 patient trial of T-Vec with the CTLA-4 inhibitor ipilimumab in unresectable melanoma patients showed that T-Vec plus ipilimumab achieved an objective response rate of 39% versus 18% for ipilimumab alone.

Cont'd over

Deal Terms

Vaxinia

The transaction will see Imugene acquire 100% of Vaxinia for an upfront payment of $462,500 and shares valued at $1.619 million, based on the 7-day VWAP (approximately 3% of issued capital post-transaction).

Other equity-based milestone payments are based on the granting of an IND by the FDA, dosing of the first patient in a Phase I trial and demonstration of safety from the Phase I trial.

The shareholders of Vaxinia include Imugene chairman Paul Hopper, CF33 inventor Professor Yuman Fong and an ex-Viralytics executive.

City of Hope

Imugene will license CF33 from COH for an upfront fee, annual maintenance fees credited against future royalty payments, payments related to development and commercial milestones, as well as single digit royalties on net sales.

Existing Programs

Imugene will continue the development of its existing programs, which include HER-Vaxx, PD1-Vaxx, B-Vaxx and a HER2/PD1 combination vaccine. However, Imugene CEO Leslie Chong said that "while all programs are equal for now, (the company) will have to see where it will all settle when (CF33) hits the clinic," an event anticipated for 2020.

Competitive Position - IP

According to Professor Fong, many competitor virotherapies are coming to the end their patent lives. The patent application for CF33 is titled "Chimeric Poxvirus Compositions And Uses Thereof", with an estimated expiration date of 2037.

The patent claims the sequence of CF33 and one or more anticancer nucleic acid sequences, such as for a PD-L1 inhibitor or a sodium iodide symporter (SIS). The SIS is responsible for iodine uptake in the thyroid, saliva, gut, intestines and breasts. Its inclusion in the design of CF33 opens up the possibility of using iodine tracers to monitor the location and distribution of CF33.

Analysis

Imugene's proposed acquisition of Vaxinia and license of CF33 has the potential to transform the company, create significant shareholder value, and potentially eclipse the value of its existing programs.

The investment appeal of the proposed transaction stems from the potential for a rapid entry into human clinical trials, anticipated to begin with a monotherapy, dose-finding Phase I study in 2020.

An expedited clinical pathway exists because of the resources and advanced infrastructure available at the City of Hope cancer centre. The COH manages a GMP biologics manufacturing facility where virus material for the planned Phase I trial is nearing manufacturing completion.

Furthermore, the availability of staff at Vaxinia experienced with the regulatory and clinical demands for OV development will help ensure the development of CF33 is managed competently.

One major hurdle ahead for the clinical program will the acceptance of an Investigational New Drug application for CF33 by the FDA. (The NIH's Recombinant DNA Advisory Committee has been replaced by the Novel and Exceptional Technology Advisory Committee, and approval for gene therapy programs no longer require NIH approval.)

Imugene is capitalised at $61 million and retained cash of $21 million at March 31, 2019.

Bioshares recommendation: **Speculative Buy Class A**

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Oncolytics Virotherapies and the Poxvirus

Oncolytic virotherapies involve the adminstration of either wild-type or engineered viruses, delivered directly into tumours or intravenously.

There are nine families of viruses that are being investigated for oncolytic virotherapy. However, these nine types can be better categorised as either RNA or DNA viruses. These two groups can be divided again according to whether they carry single or double stranded RNA or DNA.

Poxviruses are double stranded DNA viruses, as are adenoviruses and herpesviruses.

Poxviruses have been selected for development of oncolytic virotherapies because they can infect many different types of tumours and, being bigger DNA viruses, are very amenable to genetic engineering.

Other poxviruses in development include Sillagen's Pexa-Vec (formerly Jennerex's JX-594) and Genelux's GL-ONC1 (GLV-1h68). Genelux's Phase I/II trial of GL-ONC1 (with or without Avastin) in 64 ovarian cancer patients is expected to be completed towards the end of 2019, with PFS one of four primary endpoints.

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