



Biotech Daily

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Daily news on ASX-listed biotechnology companies

Dr Boreham's Crucible: Imugene

By TIM BOREHAM

ASX code: IMU

Share price: 37 cents

Shares on issue: 4,936,304,190

Market cap: \$1.83 billion

Chief executive officer: Leslie Chong

Board: Paul Hopper (executive chair), Ms Chong, Dr Axel Hoos, Charles Walker, Dr Lesley Russell, Dr Jens Eckstein

Financials: (March quarter 2021): revenue nil, cash outflows \$4.64 million, cash on hand \$29.4 million (a further circa \$30 million of listed and unlisted options are expected to be converted within the next two years)

Identifiable major holders: Richard John Mann & Family 5.93%, Paul Hopper 4.09%, Dr Nicholas Smith 2.7%, Leslie Chong 1.56%, Private Portfolio Management 1.35%.

Trick question: excluding CSL, which ASX drug developer boasts the biggest market capitalization?

The answer is not the \$1.3 billion stem cell play Mesoblast, which at one stage was worth north of \$2 billion. And it's not the cancer diagnostics and therapeutics house Telix Pharmaceuticals (with a current worth of \$1.26 billion).

What about the rare skin disorders group Clinuvel, which has an approved drug and is revenue producing?

Sorry - no cigar. Since the start of April, Imugene has risen fourfold and is now valued at \$1.73 billion, having briefly been worth \$2.3 billion.

“Our investors have been very happy of late,” trills chief executive Leslie Chong, who joined the company in late 2015 from big pharma Genentech.

The Imugene scene over time

Led by the aptly-monikered Dr Warwick Lamb, Imugene started out as an animal health company in the 1990s and then dabbled in enhanced generics including vitamin D and ibuprofen formulations.

In late 2013, the company acquired the private Biolife Science Queensland, an immunology play based on Medical University of Vienna know-how.

This introduced Imugene’s lead molecule HER-Vaxx, which targets HER-2, as in human epidermal growth factor receptor-2.

The deal also introduced legendary biotech wheeler-and-dealer Paul Hopper to Imugene and he was duly appointed chair.

In August 2018, Imugene acquired the rights to B-cell peptide vaccines (notably the PD1 checkpoint inhibitor) from Ohio State University and Mayo Clinic.

In 2019, Imugene acquired the global licence for CF33, a chimeric vaccinia (pox) virus developed by City of Hope’s ebullient chair of surgery, Prof Yuman Fong.

The tech was owned by the private Vaxinia, in which Mr Hopper and Prof Fong were major investors.

In May 2021, the company announced that it had licenced a novel oncolytic virus called CD19 (as in cluster differentiation) from California’s City of Hope cancer centre. The terms were undisclosed but involved an immaterial cash payment.

The facts on HER-vaxx

HER-Vaxx is Imugene’s oldest and most advanced program.

Aimed at gastric cancer, a phase II gastric cancer trial, with sites in Eastern Europe and India, enrolled its first patient in March 2019.

As opposed to the mechanism of action of ready-made antibody treatments such as the top-selling Herceptin, HER-Vaxx activates the patients’ own immune system to produce its own HER-2 antibodies.

HER-2 is overexpressed in 10 to 30 percent of breast, gastric, ovarian and pancreatic cancers.

In an interim analysis last November, Imugene reported a “statistically significant” benefit.

There were 27 evaluable patients in the interim analysis which resulted in an overall survival (the primary endpoint) of 14.2 months for patients on HER-Vaxx plus chemotherapy, versus 8.8 months for chemo alone.

In January, 2021 Imugene completed the recruitment of 36 advanced gastric cancer patients.

In April, the company reported a statistically significant number of events had occurred - that is, data on 24 patients - to establish the secondary endpoint of PFS was met.

The company is now awaiting nature to take its course (yep - the patients to die) in order to log the overall survival results.

Of course, the longer the patients live, the better the data.

As for the B-cell peptide program, Imugene is also developing a checkpoint inhibitor called PD-1 (as in programmed cell death-1).

Imugene’s PD1-Vaxx targets non-small cell lung cancer (NSCLC), the most common lung cancer. The program centres on phase I high-strength dosing of patients who have failed checkpoint inhibitor drug therapy.

What alpha is better?

Some eyebrows were raised about the company’s use of a ‘one-sided’ P (probability) value in the gastric cancer study, which produced a flattering ‘hazard ratio’ of 0.418.

The ‘one sided’ P value refers to the company setting a probability factor of 10 percent (for the nerds: $\alpha = 0.1$). A registrational study (aimed at drug approval) requires a two-sided alpha of five percent ($\alpha = 0.05$).

This means that in the Imugene’s case there is less than a 10 percent risk that the effect they saw was purely by chance, as opposed to less than five percent.

The use of a one-sided alpha meant the trial designers expected a positive treatment effect, so the probability bar was lowered.

Ms Chong says setting alpha at 0.1 is normal in phase II or signal seeking proof-of-concept studies, while the measure is also acceptable worldwide for phase II immunotherapy studies.

Why? A smaller number of patients or events are required to complete the study at a lower cost, while providing “meaningful and significant statistics that could well lead to further development” of a drug.

Unleashing the CF33 armoury

As with other oncolytic viruses, CF33 causes tumor cells to rupture and then trains the immune system to recognize the diseased cells and exterminate them.

Pre-clinical work suggests that CF33 infiltrates all kinds of solid tumors and replicates rapidly, spreading easily to other malignant cells

Imugene's CF33 program centres on Check-Vacc (CF33 plus the PD-L1 transgene), targeting triple negative breast cancer.

Imugene hopes to get US Food and Drug Administration clearance by early July, with enrolment targeting 30 patients starting shortly after.

Then there's Vaxinia, the most potent oncolytic virus in the company's armoury.

After the usual toxicology work, the company plans an "ambitious" study of 86 patients with solid tumors that have metastasized despite previous treatment.

These include head neck and shoulder cancers, advanced melanoma, and gastric, breast, lung, renal, bladder and colorectal cancers.

Throw in pancreatic cancer (potentially) and that's pretty much the A-Z of tumors.

The latest pickup

Coupled with CF33, CD19 is intended to enable CAR-T (as in chimeric antigen receptor T-cell) therapies.

Chimeric antigen receptor T-cells are T-cells that have been genetically engineered to produce an artificial T-cell receptor for use in immunotherapy.

The proposed combination therapy has been dubbed onCARlytics – geddit? Basically it involves souping up the virus to include CD19 (CD19 transgene).

The oncolytic virus (CF33) infiltrates solid tumors and expresses CD19 on the cell surface, so that a CD19 directed target (such as a CAR-T drug) would work in combination.

As we noted in our recent piece on Mr Hopper's freshly listed Chimeric, CAR-T is a sexy new area of immunotherapy attracting hot investor interest.

But Ms Chong stresses that CD19 is not a CAR-T play, per se.

What CD19 does - or what it's hoped to do - is tag cancer cells for CAR-T or other CD19 directed therapies in destruction of solid tumors.

To date the US Food and Drug Administration has approved four CD19 CAR-T therapies, but only for blood cancers (B-cell lymphomas and acute lymphoblastic leukaemia).

Ms Chong says “supercharging” CF33 and CD19 is a “revolutionary new paradigm in combination therapy” allowing combination use with CAR-T drugs.

Under the City of Hope deal, Imugene has been bestowed the global rights to develop CF33-CD19. This is in return for the upfront fee, annual maintenance fees, milestone payments and royalties.

Lucrative options

It's never a good look when a company's top brass lighten their personal holdings, as Messrs Chong and Hopper recently did.

But the duo was selling ordinary shares to exercise wildly in-the-money options before they expired at the end of June.

Ms Chong sold a tad over 4.48 million shares to convert 50 million options, at a cost of \$2.14 million (approximately 4.2 cents apiece). At the time of disposal in late May the shares were worth \$1.8 million, give or take a few bob.

Mr Hopper sold 1.5 million to convert 25 million options at a cost of \$1.07 million.

Post transaction, Ms Chong retains 77 million shares (current market value \$29 million) and Mr Hopper has 201.4 million (\$76 million).

“Paul has sold 1.01 percent of his holdings and he has never sold in seven years,” she says of her chairman.

Ms Chong adds that she didn't exactly have \$2 million under her couch cushion; hence the need to sell the shares to buy the options.

The upshot is that Imugene has \$3.2 million of funds - the option exercise proceeds - it did not have previously.

But the disclosure could have been better: a laudatory statement mentioned the options purchase, but not the accompanying share sales (which were disclosed in the standard ASX release).

Finances and performance

Thanks to in-the-money options, Imugene won't be short of a dollar as the options are exercised over the next two years.

All in all, there are circa \$30 million of options out there and -not surprisingly - holders are converting them sooner rather than later given the bonanza gains on offer.

The company has listed options that will bring in \$9.9 million this year and a further \$12.3 million in 2022. These are exercisable at 4.5 cents to 5.4 cents.

Then there are \$11 million of unlisted options - held by board and management - exercisable from 4.0 cents to 4.5 cents.

As of the end of March the company had just over \$29 million in the bank.

Imugene shares hit a record of 47 cents on May 26, having changed hands for as low as one cent in mid-2013.

Northern Queensland beef baron Jack Mann accounts for just over five percent of the register.

Dr Boreham's diagnosis:

Two years ago, Ms Chong declared that the conductor had blown the whistle and the Oncolytic Express was about to leave the station.

Well move over, Fat Controller: Imugene's spectacular valuation uplift since then suggests the Oncolytic Express has been upgraded from Puffing Billy to bullet train.

"That train has certainly got a lot bigger," Ms Chong says. "We have basically five trials that are in the clinic, or will be in the clinic this year or next."

Given the early nature of Imugene's programs it's hard to know on which track the company will end up, and it's unlikely to be an express service to drug development.

The company may well be shunted off the ASX line by being acquired.

Ms Chong notes the blood cancers targeted by the four approved CAR-T drugs account for only 10 percent of all cancers, with the therapies working 60 to 90 percent of the time.

"Imagine if we could get solid tumors to react in that way," she says.

"That would be revolutionary and the most significant drug [discovery] you could imagine."

Disclosure: There's a strong one-sided probability that Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort.