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Daily news on ASX-listed biotechnology companies

Dr Boreham's Crucible: Immutep

By Tim BOREHAM

ASX code: IMM; **Nasdaq code:** IMMP

Share price: 39.5 cents; **Shares on issue:** 866,239,815; **Market cap:** $342.2 million

Chief executive officer: Marc Voigt

Board: Dr Russell Howard (chair), Pete Meyers, Marc Voigt, Lucy Turnbull*****
***** Ms Turnbull re-joined the board after the sudden death of director Grant Chamberlain on January 28, 2022

Financials (December half 2021): revenue (research material sales) $21,408 (previously $193,533), net loss $16.2 million (previously $19.8 million deficit), cash of $99.7 million up 64%

Identifiable major shareholders: FIL Ltd (Fidelity) 7.3%, Australian Ethical 4.8%, Marc Voigt 1%, Dr Frederic Triebel 0.9%.

As a developer of a new cancer drug, Immutep knows that it's gaining traction when the world's luminaries gather - virtually at least - to discuss that mode of treatment and nothing else.

Such was the case with immunotherapy play Immutep at the January 26, 2022 confab, the inaugural lymphocyte activation gene-3 (LAG-3) Drug Development Summit.

Immutep CEO Marc Voigt was honored with delivering the opening remarks, while Immutep chief scientific officer Dr Frederic Triebel – a.k.a. the godfather of LAG-3 – gave a keynote speech alongside heavy hitters from Roche, Bristol Myers Squibb and Regeneron.

As Basil Fawlty said in a different context: “There’s enough material for an entire conference.”

Immutep’s lead compound is called eftilagimod alpha (efti to friends) and targets the LAG-3, a protein that regulates immune responses. The compound is better known as IMP321.

Mr Voigt says there’s a high likelihood the first LAG-3 therapy will win approval this year, with Bristol Myers Squibb eyeing a March 19 ‘target action date’ for a biologics application to the US Food and Drug Administration (FDA).

Bristol Myers Squibb is seeking approval for its LAG-3 antibody relatlimab, to be used in combination with nivolumab (Opdivo) for unresectable or metastatic melanoma.

“As LAG-3 becomes commercial there will be more noise around it,” Mr Voigt says. “We are the only LAG-3 pure play with more programs than anyone else, including big pharma.”

But to get this far, Immutep’s path has been anything but smooth, with some clinical results failing to meet their primary endpoints.

Turnbull wins second term

And now a potted history:

The LAG-3 protein was discovered by French immunologist and now Immutep chief scientific officer Dr Frederic Triebel. In 2001, Dr Triebel founded Immutep SA.

In 2014, ASX plodder Prima Biomed acquired Immutep for $US10.8 million in cash and shares.

In May 2016, Prima divested its original CVac ovarian cancer vaccine program to Sydys Corp of the US, for 9.8 percent of Sydys and $400 million of potential milestones and royalties. Sydys had $US856.00 in the bank at the time.

Nothing has eventuated from that tie-up.

The original CVac program attracted former Sydney lord mayor Lucy Turnbull to the board, which she chaired between October 2010 and November 2017.

(Ms Turnbull’s spouse, Malcolm, was Australia’s Prime Minister during some of that period.)

Ms Turnbull has now re-joined the board, the catalyst being January’s sudden death of Grant Chamberlain, an Immutep director since August 2017.

Immutep has been listed on the Nasdaq for the last decade, with the American depository receipts accounting for 28 percent of total shareholders.

What's all the fuss about?

Immutep's platform is being furthered as a combination therapy with immune checkpoint inhibitors (such as the blockbuster drug Keytruda).

The idea is that efti (IMP321) "pushes the gas" while the inhibitors release the "brakes" of the immune system.

Immutep's key program is called Aipac and relates to metastatic breast cancer patients.

Aipac, by the way, stands for "active immunotherapy paclitaxel".

Aipac tests a new class of products called antigen-presenting cell activators, which the company hopes will be relevant for other solid tumors.

The $20 million phase IIb trial tested IMP321 in combination with paclitaxel - brand name Taxol - a standard-of-care chemotherapy.

The randomized, double-blinded and placebo-controlled trail enrolled 227 hormone receptor positive (HR+) and human epidermal receptor 2 negative (HER2-) metastatic breast cancer patients across 30 sites in Europe.

In March 2020, the company revealed first data from the 227-patient trial, which showed a 63 percent progression-free survival, relative to 54 percent for the control group (paclitaxel plus placebo).

In December 2020, the company followed-up with overall survival data showing a media benefit of 2.7 months, relative to placebo.

In short, the results missed the primary endpoints on progression free survival and overall survival.

But - as you do - the company stressed a "statistically significant overall survival benefit across pre-determined patient sub groups".

These included those aged under 65 (median benefit 7.1 months) and those with a low starting monocyte count (9.4 months).

Monocytes are a type of white blood cell.

In November last year, Immutep presented at a 'late breaking' slot at the Society for the Immunotherapy of Cancer (SITC) pow-wow.
(If management really does burst into these forums screaming 'hold the front page' - Jimmy Olsen like - please get us a ticket).

In front of its learned peers, management outlined a revised overall survival benefit of 19.6 months for the under-65s, 19.6 months for the low monocytes and 4.2 months for those with luminal B type cancers.

Constructive feedback

Immutep's quest to develop efti (IMP321) received a boost earlier this month, with the US FDA providing "constructive feedback" on the company's plans for a phase III registrational trial for metastatic breast cancer.

In October 2021, the European Medicines Agency also said 'go for it' - although not using that exact wording.

Mr Voigt says the new trial will optimize the design of the global trial, focusing on patients most likely to benefit.

"We have learned from Aipac and would not go with the European scheduling of giving paclitaxel for six months and then stopping," he says. "Instead, the drug will continue to be administered, if tolerated, until the cancer progresses."

Tacti-002

As in 'two active immune-therapeutics', Tacti-002 tests efti in combination with the checkpoint inhibitor Keytruda (pembrolizumab) for non-small cell lung cancer (NSCLC) and head and neck squamous cell carcinoma (HNSCC).

Done in collaboration with Merck & Co of the US, the open label, single-arm trial has recruited 185 patients across 20 centres in the US, Europe and Australia.

Part A relates to a first-line treatment for NSCLS and part B for a patient-derived xenograph refractory version (the tissue containing the non-responsive tumors are taken from the body for treatment in mice). Part C relates to a second-line HNSCC treatment.

So far, two phase II trials have been completed for both indications. In the case of NSCLC, the company reported an overall response rate of 41.7 percent and two complete responses (the tumors disappeared).

Reported at last November's SITC chinwag, the HNSCC effort showed an overall response rate of 29.7 percent compared with 14.6 percent for pembrolizumab (for the general patient population).

Recruitment of a 74-patient expansion of part A was completed last year and the company plans to present data in the current half.

Recruitment of part B was also completed last year, with the company due to tell all at the European Lung Cancer Congress that kicks off on March 30.

Tacti-003

Tacti-003 evaluates efti in the "commercially more relevant" setting of a first-line treatment for recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) "in a randomized setting".

In April 2021, the company won fast-track designation from the FDA, for use of the compound for this purpose.

Immutep has started recruiting a 154-patient randomized, open-label trial across 35 clinical sites in the US, Europe and Australia.

Intriguingly, one of the first sites to open was in Kapitanivka in central Ukraine, where first-line concerns are more about dodging bullets and bombs at one of the front lines of the Russian invasion.

“It’s terrible for people living there and especially terrible for the patients and their families,” he says. “We support the very few patients in Tacti-003 as much as we can.”

Czech out this Covid research

Is there a Covid-19 angle in all of this. Yes, of course!

And with the latest variant of the blight causing renewed problems in China, cracking a genuine treatment remains a lucrative prize. In Immutep’s case, a Czech research centre asked for some efti to carry out its own Covid trial.

“We are happy to provide that but we are not actively investing. We can’t do oncology as well as infective diseases,” Mr Voigt says.

“But efti is an immune booster, so as a therapeutic against Covid it could make sense.”

For reasons unknown, the Czech program is called ‘Eat Covid’ - and only if it were that easy.

Finances and performance

Following a $67 million raising in June last year, Immutep had a healthy December-end cash balance of just under $100 million.

Immutep’s main financial commitment is of course the efti phase III trial, with the other programs largely funded by partnering deals.

The cost of the registration trial is not mentioned but it could be ‘efti.

“Our funding is strong. The company is in a better financial position than it has ever been since inception in 2001,” Mr Voigt says.

He says Immutep won’t be going back to the market for more dosh any time soon, with the funding ‘runway’ prolonged with a prudent approach to spending.

“I review every invoice, whether it is 50 cents or $500,000,” Mr Voigt says. “We spend investors’ money very wisely.”

Immutep shares are at a similar level to 12 months ago, which is a reasonable performance given the punishment meted out to biotechs in recent months.

Trading has been volatile over the last two years and at one point the stock was the most heavily traded on the Nasdaq.

Immutep shares tumbled to a low of 11 cents in March 2020 after the initial disappointing Aipac results.

Last year, the shares ran up to 70 cents in early June and then again in November, ahead of the SITC prezzo - after which the stock fell again.

Mr Voigt says the shares corrected after a “phenomenal” period of growth: “to take a break from time-to-time is healthy.”

Dr Boreham’s diagnosis

Mr Voigt says checkpoint inhibitors are typically a “big boy’s game”, which means that Immutep has discarded its junior school bumfreezers* for proper daks**.

Immutep also has the attention of the institutional big boys, with Blackrock, Fidelity, Karst Peak and local hero Australian Ethical all gracing the register.

With a $300 million market capitalization, Immutep is on the cusp of graduating from junior classes to Big School, having endured the corporate equivalent of Chinese burns, wedgies, nipple cripple and the ‘typewriter’*** over the years.

In the next couple of months, investors should look out for further data from the Tacti-002 and updates on Tacti-003 recruitment. Later in the year the company hopes to deliver interim results from Insight-003, the first triple-combination efti trial.

But despite the company’s multi-pronged clinical efforts, the Aipac breast cancer trial is likely to determine its fortunes in the rough-and-tumble biotech playground.

* Shorts; ** long trousers; *** advanced juvenile torture techniques

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort, but retains his faculties. Despite the junior school torment of the school bully literally stealing his marbles, he still has some in an idiomatic sense.