Biotech Daily

Friday July 26, 2019

Daily news on ASX-listed biotechnology companies

Dr Boreham's Crucible: Imugene

By TIM BOREHAM

ASX code: IMU

Share price: 2.4c

Shares on issue: 3,609,847,749

Market cap: $86.6 million

Chief executive officer: Leslie Chong

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

Financials (Year to June 30, 2019): revenue nil, cash outflows $7.6 million, cash balance $19.05 million, estimated September quarter outflows $8.6 million.

Identifiable holders: Private Portfolio Managers 6.2%, Platinum Asset Management 3.6%, Dr Nicholas Smith 3.2%, Paul Hopper 2.1%, Sarah Cameron 1.7%.

Move over Thomas the Tank Engine - the Oncolytic Express is about to leave the station!

The railway analogy is not our own, but the work of Imugene chief Leslie Chong after the company signed a deal to buy an immuno-oncology drug developer from Vaxinia, a private company linked to Imugene executive chairman Paul Hopper.

Yes! That's the Paul Hopper who early last year sold the ASX-listed Viralytics to Merck for $502 million.

“The Oncolytic Express is fuelled up and the conductor has called all aboard,” Ms Chong writes in the company’s normally staid newsletter. “It’s full steam ahead.”

The lowdown on the deal

Imugene has acquired the global licence for CF33, a chimeric vaccinia (pox) virus developed by Professor Yuman Fong, the chair of surgery at California’s City of Hope Comprehensive Cancer Centre.

The technology in effect is held by the unlisted Australian private entity Vaxinia, of which Mr Hopper is the chairman and major shareholder. Also a former Viralytics executive, Prof Fong is also a Vaxinia investor and your columnist is also running out of “alsos”.

CF33 shows early promise in inciting a “local and systemic’’ tumor response in mice, in standard xenograft models of breast, pancreatic and colorectal cancers.

Of course, everything works in mice. As the former Prime Minister might have said “There’s never been a better time to be a mouse with cancer.” Or his replacement: “How good are mice?”

The virus is known as chimeric because it was formed from several other viruses. Normally, a virus attacks only one kind of cell, such as hepatitis on liver cells and meningitis on brain cells.

“I took nine different vaccine strains, put them into a cancer cell and allowed them to combine and make brand new viruses,” Prof Fong says. “I picked out hundreds of new viruses that never existed in nature. Instead of trying to be smart and genetically engineering them, we let nature do that.”

Like other oncolytic viruses in development, CF33 multiplies in tumor cells, causing them to rupture. The virus then trains the immune system to recognize the cells and attack them. With extreme prejudice.

Prof Fong says the use of cancer viruses has been hampered to date because cautious regulators have demanded an initial single-dose approach.

As a result, viruses are “just too safe” and it may take a decade for drug developers to be allowed to increase the dose.

“Not only are viruses barely able to kill cancer, [the owners] are running out of [intellectual property],” he says. “We have turned out products that were good for working papers but few have reached man [approval stage].”

A feature of CF33 is that it has a higher potency, which means its works at a much lower dosage than other viruses.

CF33’s potency was compared - favorably of course - with that that of Amgen’s approved oncolytic virus T-vec, as well as a vaccinia-based virus being developed by Genelux.

Value combo pack

Imugene intends to develop CF33 as a combination treatment with existing checkpoint inhibitors on the market (such as the skin cancer drug Keytruda).

Checkpoint inhibitors target immune checkpoints, which devious tumors use to protect themselves from attacks by the immune system.

“We are in the age of combination [therapies] because a single agent is not doing the work is needs to do,” Ms Chong says.

She says checkpoint inhibitors might produce a 20 to 30 percent response, “but when you add something like an oncolytic virus, that can increase [the response] three to four-fold”.

Ms Chong describes CF33 as “especially impressive” as it can shrink multiple types of cancer at low doses.

The mice models also have showed the bizarre, but apparently well-known, ‘abscopal effect’, in which untreated tumors shrink when tumors are treated elsewhere in the body.

The CF33 virus is considered safe because it’s a tricked-up version of the active constituent of the vaccine that eradicated smallpox.

“Therefore, it’s been given to millions of people in the world,” Prof Fong says.

“It’s arguably the most important therapy ever produced by man because it wiped out smallpox.”

Other deals

The Vaxinia compact is the second in-licencing deal for Imugene in the last 12 months, with the company acquiring the rights to a line of B-cell peptide vaccines from Ohio State University and Mayo Clinic, in August last year.

Both deals build on Imugene’s existing work originating from the Medical University of Vienna.

Imugene’s lead molecule HER-Vaxx targets HER-2, as in human epidermal growth factor receptor, which is over expressed in 10 to 30 percent of breast, ovarian and pancreatic cancers.

The blockbuster cancer drug Herceptin also targets HER-2, but Imugene hopes that it can do so more cheaply and with more efficacy.

HER-Vaxx is a mimotope: a small molecule, often a peptide, which mimics the structure of an epitope (the specific target the antibody binds to).

The mimotopes cause the B-cells to produce millions more antibodies to fight the cancer.

Imugene is also developing a checkpoint inhibitor called PD-1 (programmed cell death-1, for those who really want to know) which is in preclinical stage.

What's next?

With CF33, Imugene plans to knock on the door of the US Food and Administration by the end of 2019, ahead of a planned investigational new drug application.

If the FDA is favorably inclined, Imugene will initiate a phase I trial next year, covering 30-patients with mixed advanced solid tumors (including lung, melanoma, bladder and gastro-intestinal).

The trial is budgeted at $US4.5 million ($A6.4 million).

An ensuing phase I/II trial would select tumor types from the first phase and enroll about 30 patients across four cohorts. Envisaged to start in late 2021, the trial would cost around $US18 million.

Separately, a phase II trial of HER-Vaxx - targeting gastric cancer - is in progress.

A second phase II trial, B-Vaxx also targets HER-2 for a broad range of tumors, funded by Ohio State University, has enrolled patients who want to forego chemotherapy.

Depending on how the data is cut and patient survival factors, Imugene may be able to post interim results later this year.

Finance and performance

Being a related-party transaction, the Vaxinia deal is subject to shareholder approval at a meeting to be convened on September 9 (the date is subject to change).

We'll assume Mr Hopper left the Imugene board room for some urgent errands when the deal was being thrashed out.

The deal involves an upfront cash payment of $462,500 and the issue of $1.6 million of Imugene shares.

Vaxinia's shareholders are also entitled to payments on milestones including an investigational new drug application to the FDA, dosing the first phase I patient and the trial meeting its safety endpoint.

California's City of Hope is also entitled to undisclosed upfront licence fees, annual maintenance fees and royalties, as well as milestones. All upfront licence payments will be funded through Imugene's existing cash reserves.

Speaking of which, Imugene held cash of $19 million at June 30 - enough to fund the company's activities for at least the next 12 months.

Imugene raised a collective $28.8 million in three capital raisings, two in December 2017 and another in July last year.

The company will seek partnerships post any phase I success with CF33, or alternatively will raise more capital at that stage.

Imugene shares have traded between 1.4 cents and 2.4 cents over the last 12 months. They slowly gained favor since the July 14 Vaxinia announcement, before which the stock traded at 1.6 cents.

Dr Boreham's diagnosis:

Imugene is not shy about highlighting the similarities between CF33 and Viralytics' lead product Cavatak that was central to the Merck deal.

Viralytics was at a similar (phase II) stage when Big Pharma came a knockin'.

In a company-sponsored analysis, Edison Investment Research cautions the immuno-oncology field is crowded as well as promising.

"While the transaction gives Imugene a foothold in a space that has attracted a lot of pharma interest, it is also an area where there a large number of competing products in development," the report says.

"Therefore, we suspect that Imugene will need to demonstrate superior efficacy in the clinic in order to attract a pharma partner."

As reflected in Imugene's humble $87 million valuation, Imugene is still at an early stage and, returning to the choo-choos analogy, any number of loose tracks could derail this one.

But if CF33 - or indeed, any other Imugene programs - attracts Big Pharma's gaze, shareholders are in for an upgrade from the caboose to the first-class carriage.

"I hope you're on board," Ms Chong tells investors.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. When it comes to decent investment proposition, he tends to be left on the platform while the train steams away.