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: 11 cents

Shares on issue: 7,164,974,859

Market cap: $788.15 million

Chief executive officer: Leslie Chong

Board: Paul Hopper (executive chair), Ms Chong, Dr Lesley Russell, Dr Jens Eckstein, Dr Jakob Dupont, Kim Drapkin

Financials: (September quarter 2023): revenue nil, operating cash outflows $22 million, cash balance $163.3 million*****, quarters of available funding: seven

Year to June 30, 2023: revenue nil, grant income $11.78 million (down 9%), loss of $39.7 million (previous loss $37.9 million)

***** After capital raising of $51 million (net of costs)

Identifiable major holders: Paul Hopper 4.47%, The Vanguard Group, Inc. 4.35%, Mann Family 4.03%, Dr Nicholas Smith 1.65%, Blackrock Inc 1.51%.

Amid ongoing industry debate about the merits of off-the-shelf (allogeneic) therapies versus autologous ones that tweak an individual patient's cells, Imugene chief Leslie Chong is quite the convert to the former.

She says that the autologous approach involves patients sitting for several hours during the leukapheresis process to remove white blood cells, with the T-cell regeneration taking 19 to 42 days.

“In the meantime, the patient is deteriorating and they have to give them more chemo just in order for them to get the drug.”

In contrast, off-the-shelf drug is sourced from healthy donors, frozen and can be shipped to clinics in multiple batches, which means multiple drugs for multiple patients. Because the cells are from healthy folks, they are more potent and robust.

Imugene has good reason to advocate the off-the-shelf approach: the cancer immune-therapy house has just acquired an allogeneic program from the Nasdaq-listed Precision Biosciences.

The program, azer-cel is in the new-ish field of CAR-T therapies (chimeric antigen receptor T-cells), which involves souping-up patients’ T-cells for a better immune response. Azer-cel is now the company’s most advanced business.

To date, the four approved CD19 CAR-T therapies have been autologous, so Imugene could make history by getting the first allogeneic one to market.

These approved therapies are all for blood cancers, with solid cancers proving more challenging.

“We are in the sweet spot because autologous therapies are failing,” Ms Chong says.

Meanwhile, Imugene shares had a stellar November, on the back of four quick-fire announcements pertaining to the company’s azer-cel and oncolytic virus programs (see below).

A cancer cure? Imagene that

Imugene has an - er - interesting history, having started out as an animal health company in the 1990s and then dabbling in enhanced generics including vitamin D and ibuprofen formulations.

Currently, the company has six assets over four platforms, covering allogeneic CAR-Ts (azer-cel), Oncarlytics (oncolytic virotherapy), the CF-33 oncolytic virus (Checkvacc and Vaxinia) and B-cell immunotherapies (HER-Vaxx, PD1 Vaxx).

Targets include blood, breast, lung, gastric and head and neck cancers, as well as melanomas, glioblastomas and other solid tumors.

A decade ago, the company acquired the private Biolife Science Queensland, an immune oncology play based on Medical University of Vienna know-how.

This introduced Imugene's then 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.

Ms Chong joined the company in late 2015 from big pharma Genentech.

In August 2018, Imugene acquired the rights to B-cell peptide vaccines (notably the programmed death or 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 licenced a novel oncolytic virus called CD19 (as in cluster differentiation) from City of Hope, for an immaterial cash payment.

Then there's last August's azer-cel deal.

Phew!

Thanks a million - or three

Under the deal terms, Imugene paid $US8 million upfront in cash to Precision Biosciences, with $US13 million in deferred cash or shares (at Imugene's discretion).

A further $US8 million is payable at the end of the phase Ib trial - once again in cash and shares - with a further $US198 million in performance-based payments. Imugene also pays "industry standard royalties" on commercialization.

The company assumes the lease on a modern 9,700 square metre (2.4 acres) manufacturing facility in Durham, North Carolina.

Imugene can thank fellow immune-therapy house Chimeric for landing the deal - and did so by way of a $3 million 'spotter's fee'.

The story goes that Precision Biosciences CEO Michael Amoroso was close to Chimeric CEO Jennifer Chow, given the duo worked together at CAR-T champ Kite Pharmaceuticals.

Precision did not have the money to develop the drug so elicited Ms Chow's interest, to which she replied that Chimeric was a bit small - but why not chat to Imugene?

Mr Hopper is the executive chair of both Imugene and Chimeric.

Azer-cadabra – it's a new cancer drug!

Formally known as azercabtagene zapreleucel, azer-cel "supercharges" T-cells so that they seek and destroy malignant cells expressing CD19.

An ongoing phase I trial, so far has treated 84 patients with either non-Hodgkin lymphoma (NHL) or B-cell lymphoblastic leukemia (B-ALL).

On November 10, this year Imugene said it has dosed the first of 10 patients in its phase Ib azer-cel trial for advanced non-Hodgkin lymphoma, following "strong safety and efficacy signals" in the 84-patient, phase I trial.

The first phase Ib patient (with a difficult form of non-Hodgkin lymphoma) was dosed at Banner Health in Phoenix, Arizona.

The company expects that 10 patients will comprise a confirmatory study as support for FDA approval of a phase II registrational trial and - ultimately – the marketing nod for what would be the first approved allogeneic CAR-T cancer therapy.

These patients will have failed previous autologous CAR-T therapies for diffuse large B-cell lymphoma (DLBCL). Ms Chong describes DLBCL as "rare, but not as rare as folks would want it to be".

With an average cost of $US375,000 ($A566,600) per treatment, the company estimates a US market of $US2.5 billion a year. As the autologous CAR-T market grows, the incidence of failed CAR-T cases will also grow.

"Given what I have seen from the study results, we could potentially receive accelerated approval as early as the end of 2026," Ms Chong says. "It's not that far away."

Nailed to the MAST

Imugene's other November tidings related to its clinical program for Vaxinia, a.k.a. the novel cancer-killing virus CF33-hNIS.

The study is known as MAST, as in metastatic advanced solid tumours. hNIS stands for human sodium iodine symporter, but we all knew that already.

This week, the FDA accorded the program fast track status, for bile duct cancer if the company chooses to pursue that indication.

On November 2, the company said it had cleared cohort four of the intravenous monotherapy dose escalation study, as well as cohort two of the intravenous combination study of Vaxinia with pembrolizumab (Keytruda). The company has opened cohort five of the monotherapy arm and cohort three of the combination arm of its phase I trial.

The study started in May 2022 and aims to recruit up-to 100 patients at 10 trial sites in the US and Australia, and is expected to run for about 24 months.

On November 8, the company said 34 patients dosed to date had achieved “positive early signals”, including one complete response for bile duct cancer (cholangio-carcinoma) and one partial response for melanoma. A further 16 patients showed disease stabilization.

An expansion study of 10 bile duct cancer patients is planned.

“We were especially pleased about the bile duct complete responder because it is a true unmet need,” Ms Chong says. “There is not much else out there - none of the immune-therapies have really touched [the disease].”

A “beautiful pipeline”

Ms Chong says the azer-cel program enhances a “beautiful pipeline” across four platforms and 10 trials. Limits with space - and your columnist’s sanity - preclude a full rendition.

In May 2023, Imugene received FDA approval to start a human CAR-T trial, targeting advanced or metastatic solid tumors with their Oncarlytics program

Known as Oasis but not involving either Liam or Noel, the dose-escalation study will involve Imugene’s Oncarlytics being administered alongside an approved drug against the CD19 target, blinatumomab (branded Blincyto).

Oncarlytics combines the oncolytic virus CF33 with the transgene CD19. The mechanism of action involves CF33 infiltrating solid tumours and expressing CD19 on the cell surface.

“There are no CD19s or autologous CAR-T therapies approved in solid tumors, so the idea here is revolutionary,” Ms Chong says.

On the HER-Vaxx front, a phase II trial dubbed Next Horizon has enrolled HER-2 positive gastric cancer patients.

Finances and performance

To fund the azer-cel purchase, Imugene passed the hat around for $35 million in a placement at 8.4 cents and then raised $18.2 million in a share purchase plan (it was aiming for up to $30 million). The shares come with an attached option exercisable at 11.8 cents by August 2026.

As if any investor needs to be reminded about the huge cost of developing a drug, in September 2020, Imugene raised $80 million. With more than $160 million in the bank, Imugene is one of the most cashed-up ASX biotechs.

Ms Chong says the company has an open mind about funding the azer-cel trial to commercialization, noting that Imugene’s management has been involved in taking 13 cancer drugs to market in previous roles.

Imugene shares have had a rollicking November, up 150 percent including a 10 percent leap on the back of the fast-track designation tidings alone.

Over the last 12 months the shares have traded between four cents (November 1 this year) and 20 cents (mid-December last year). They stock hit an all-time high of 59 cents in early November 2021 and in April 2020 it plumbed the depths of two cents.

Dr Boreham's diagnosis:

Ms Chong says while the biotech sector has been hit hard over the last couple of years, sentiment towards the former 'golden child' of CAR-T therapies has declined even more.

"But it looks like it is making a comeback," she says, noting last month's successful $US280 million Nasdaq listing of autologous CAR-T developer, Cargo Therapeutics.

Despite November's stellar share surge, Imugene's $620 million market cap is still well shy of its eyebrow-raising $3 billion-plus peak four years ago, when the trials were less advanced.

"I never know how the market will react to any announcement," Ms Chong muses.

Along the way, investors might have become confused by the company's multiple evolving programs and priorities. Bell Potter says the company plans to "pause" further program acquisitions and focus on what it has.

"This is eminently sensible given the high bar set by equity markets for new capital, especially for early-stage biotech assets," says the broker, which values Imugene shares at 15 cents each.

Courtesy of azer-cel and the prospect of early approval, Imugene looks to be closer to the Holy Grail of drug commercialization than it has ever been.

In chair Paul Hopper's words: "We are steadfast in the view Imugene is positioned more strongly than ever before; and in time the company and shareholders will see the benefits."

Let's Hop-per to it!

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. But one day he may grasp the Holy Grail of becoming proficient at something … or be CAR-T-ed away.