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Daily news on ASX-listed biotechnology companies

Dr Boreham's Crucible: Chimeric Therapeutics

By TIM BOREHAM

ASX code: CHM

Share price: 3.9 cents; **Shares on issue**: 425,278,237*; **Market cap:** $16.6 million

Chief executive officer: Jennifer Chow

Board: Mr Hopper (executive chair), Ms Chow, Leslie Chong, Dr Lesley Russell, Cindy Elkins, Dr George Matcham

Financials (March quarter 2023): revenue nil, loss of $687,000, cash of $2.82 million

Identifiable major holders*: Paul Hopper 21%, Dr Christine Brown 2.75%, Dr Michael Barish 2.7%

***** Ahead of capital raising, which if fully subscribed would add an extra 153,913,040 shares

The imperative for cash-strapped ASX biotechnology companies to get money through the door has been highlighted by oncolytic drug developer Chimeric's quest to raise up to $6.25 million, by way of a placement and a follow-on share purchase plan (SPP).

Chimeric listed in January 2021 after raising $35 million at 20 cents to fund its CLTX Car-T immune-oncology programs, acquired from the City of Hope Hospital in Los Angeles (see below).

In those buoyant times investors had oversubscribed for $60 million in the initial public offer (IPO), which was put together by legendary biotech entrepreneur Paul Hopper.

Reality has since bitten with the venom of a deadly scorpion (see below).

As the company announced on Monday, May 15, share plan subscribers are invited to subscribe at four cents a share, a 13 percent discount on the undisturbed closing price on Friday May 12.

The placement is subscribed by board and management, which Mr Hopper describes as a sign of confidence in the potential of the company's programs.

Meanwhile, other ASX biotechs raising equity include Dimerix and 4D Medical, while Mesoblast has just done so.

Kiss of the scorpion

CLTX refers to chlorotoxin, while Car-T is short for chimeric antigen receptor T-Cell.

Initially, Chimeric's main program involved a treatment for the difficult-to-treat glioblastoma, a form of brain cancer.

In an exotic vein, the active ingredient derives from the venom (peptide) of the deathstalker scorpion - chlorotoxins that bind to unique targets in the body.

This scorpion juice is worth something like $9,000 a gram, but fortunately for researchers the active ingredient is derived synthetically and they don't have to chase the arachnids across the Sahara Desert.

The toxin is familiar to the oncolytic community, because for years it has been used as an imaging agent to detect cancers.

"Logically if you have something that will tell you where cancer cells are, it will attach to these cells," says Chimeric chief executive Jennifer Chow.

Search and destroy

Car-T therapies work by 'supercharging' the body's T-cells to fight cancers. The genetically-engineered cells are grown by the millions in a laboratory and then re-injected, resulting in the patient getting a turbo-charged version of their own T-cells.

Car-T treatments are known to be effective with blood-based cancers such as leukaemia, with six drugs approved in the US.

Formally known as a 36 amino acid peptide, the scorpion toxin recognizes a cancer marker called membrane-bound matrix metallo-protease-2 (MMP2). The healthy cells are unharmed.

Ms Chow says Chimeric has focused on "first-in-class assets with novel design".

Chimeric's work has also expanded into so-called 'natural killer' cells, based on assets derived from Case Western Reserve University in Ohio (a state hitherto better known for its Rock 'n Roll Hall of Fame).

It’s all about the people

A former executive at Car-T specialist Kite Therapeutics, the Toronto-born Ms Chow was Chimeric’s chief operating officer before being anointed in the top job in August 2021.

She had also held roles at Roche, Nycomed/Takeda and Schering Canada.

Ms Chow says the Chimeric team has 75 years’ collective experience in the space, having been involved elsewhere in taking four of six of the approved Car-T drugs to market.

Chimeric’s foundation intellectual property was devised by City of Hope researchers Prof Christine Brown and Dr Michael Barish. The former chairs Chimeric’s scientific advisory board.

Mr Hopper has founded - or been involved in - no fewer than 14 drug companies, including fellow ASX-listed immuno-oncology play Imugene. We only mention this because Imugene chief Leslie Chong moonlights as a Chimeric director.

The board also includes Cindy Elkins, an erstwhile Juno Pharmaceuticals heavyweight.

Don’t mention the C word

While the C (cure) word is still only mentioned in hush tones in the oncolytic community, Ms Chow cites the example of a 33-year-old US woman undertaking Car-T-cell therapy for aggressive acute myeloid leukaemia (AML) at an Ohio research centre.

Within days, the patient’s condition had stabilized and within 33 days the cancer had disappeared. More than two years later, she was still cancer-free.

“I have worked in cancer for my whole career and have never seen outcomes like this before,” Ms Chow says.

She says cancer treatment had developed incrementally over decades, with the advent of chemotherapy and targeted and immune therapies.

“It wasn’t until the introduction of Car-T therapies that we measured the improvement in term of years, the outcomes have been really dramatic.”

Unrelated to Chimeric, an early-stage Italian Car-T clinical paediatric trial has shown encouraging results in the solid tumor neuroblastoma, a nerve tissue cancer that affects the adrenal glands.

Carried out at Rome’s Bambino Gesù Children’s Hospital, the study showed that nine of the 27 enrolled children exhibited no sign of cancer after six weeks.

It wasn’t entirely a feel-good story in that two later relapsed and died, bearing in mind that all the kids were in a bad way.

Natural born thriller

Chimeric's 'natural killer' platform - CHM0201 - was developed by Dr David Wald of Ohio's Case Western Reserve University. The parties are jointly developing the program through an exclusive global licence.

The autologous (off-the-shelf) therapy involves a healthy donor providing the material, from which the natural killer (NK) cells are isolated, enhanced and made into thousands of doses and frozen.

The patient's blood is sent to a facility where the T-cells are supercharged. The claret is then shipped back to the same patient.

In March 2022, the company said a previous nine-patient, phase I study established safety across three dosing levels, with no sign of graft-versus-host disease (rejection).

Six of the patients enrolled had colorectal cancer, with disease control evident in two. The other three were acute myeloid leukaemia patients including the aforementioned 33-year-old lady. The other two showed disease stabilization, but not a complete response.

Chimeric is undertaking a trial combining its therapy with the existing agent inhibitor Vactosertib, for advanced colorectal and blood cancers.

"Because it's an off-the-shelf therapy, this one can move a bit quicker," Ms Chow says.

"We expect enrolment to be completed by the end of this calendar year and it will take another six months to get the data."

Tackling glioblastoma

The asset on which Chimeric's IPO was based, CHM1101 (CLTX-Car-T) is in a phase I clinical trial at City of Hope, as a potential glioblastoma treatment.

"Glioblastoma is a disease for which next to nothing works," Ms Chow says.

"Sadly, the drug approval bar is very low because there has been no new drug for 10 years."

Enrolling 18 to 36 patients, the ongoing phase I dose escalation trial involves four dose strengths.

The third cohort was dosed in December 2022, with all patients progressing beyond 28 days without any toxicity issues.

In early March, the fourth cohort was dosed, with results pending.

"If the data is good enough, we will want to expand the trial and engaging other sites puts us in a good position to do that," Ms Chow says.

And gastro-intestinal tumors …

Bought in from the University of Pennsylvania, CHM2101 targets CDH17, an antigen expressed on tumors.

CHM2101 was developed by the university's Dr Carl June, who in 2018 was nominated by Time magazine as one of the world's most 100 influential people for his earlier work in developing the first FDA-approved Car-T therapy, tisagenlecleucel, marketed as Kymriah.

Kymriah initially was approved for paediatric acute lymphoblastic leukaemia, with the indication later expanded to non-Hodgkin's lymphoma in adults.

Pre-clinical data from the CHM2101 program showed "strong evidence of efficacy, with complete eradication of eight different types of gastrointestinal tumors with no relapse or toxicity".

Chimeric held an investigation new drug meeting with the US Food and Drug Administration in March, in view of paving the way for a clinical trial at the university.

Finances and performance

The Chimeric board has done the shareholder-friendly thing by pitching the share purchase plan at a better price than the placement.

The placement was struck at 4.6 cents, equal to the previous Friday' May 12 'undisturbed' closing value.

The share plan will be at four cents, a 13 percent discount to the May 12 close and a whopping 25 percent discount to the 10-day volume weighted average price (VWAP) leading up to May 12.

The entry price could be even cheaper: a five percent discount to the five-day VWAP leading up to - and including - the June 2 closing date for the share plan.

The placement is subject to shareholder approval at an extraordinary general meeting, likely to be held in late June.

Chimeric reported cash of $2.82 million at the end of the March 2023 quarter, having burnt through $687,000 in the three months. Given the company had outflows of $13.3 million for the first nine months of the financial year, this implies a considerable improvement.

The raising is not Chimeric's first post-IPO top-up.

In February 2022, the company tried to raise $18.1 million in an institutional and retail rights issue, at 17 cents a share. After some struggle, it banked $14.4 million.

Chimeric also has another funding mechanism: in June last year it entered an equity placement agreement with the Melbourne-based L1 Capital, by which the boutique fundie provides up to $30 million of equity over 24 months.

Struck at a five percent discount to the prevailing price, the drawdowns are at the company's discretion and the facility need not be used at all. Self-evidently, the facility does not preclude the company from raising funds elsewhere.

Chimeric shares shot to a high of 41 cents from the 20 cents listing price, but since then reality has bitten (or stung, given we're talking about scorpion venom).

With a circa 21 percent Chimeric stake pre-placement, Mr Hopper has plenty of skin in the game and is about to add some more dermis.

Dr Boreham's diagnosis:

While Chimeric has a few clinical irons in the fire to pique investor interest, any hopes of a lucrative short-term payday have been dashed.

Chimeric certainly doesn't look like being a repeat of Mr Hopper's immune-oncology play Viralytics, acquired by Merck & Co in 2018 for $502 million.

(By the way, last October Merck quietly ditched Viralytics' key drug candidate, the melanoma treatment Cavatak as part of its "routine pipeline prioritization.")

Ms Chow notes that cell therapies are expected to be the fastest-growing cancer sector in the next decade, growing from a $US1 billion market in 2020 to around $US22 billion by 2030 (a compound annual growth rate of 21 per cent).

Martin Luther King Jr once said: "We must accept finite disappointment but we must never lose infinite hope."

And while he probably wasn't talking about the Australian biotechnology sector, Chimeric holders should draw some comfort from the longer-term potential.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. We only mention that because a 'fake medico' accusation would really sting.