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# CHIMERIC THERAPEUTICS LTD (ASX:CHM)

## A cutting edge oncology company with an all-star management team

Chimeric Therapeutics Ltd listed on the ASX January 21, 2021, raising A$35m with a market capitalisation at IPO around A$40m (20 cent issue price).

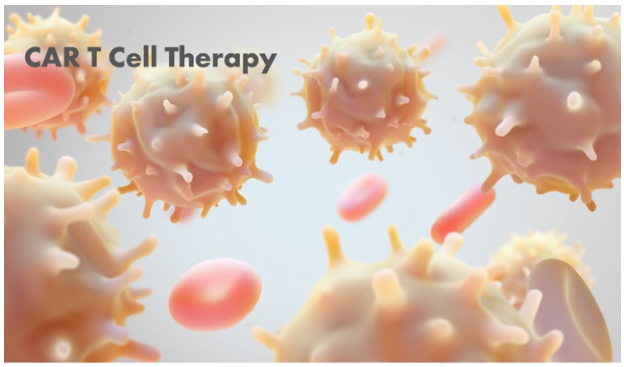
*"The best, most experienced management team in Australia for CAR T cell therapy" - **Paul Hopper***

Given the demand of Chimeric's primary asset, chlorotoxin, and its star studded management team, the company's share price shortly after listing reached its 52 week high of 44 cents. Chimeric currently trades at 34 cents (market capitalisation A$64m). As at June 30, the company reported a cash balance of A$22.4m and is well funded for the foreseeable.

### Chimeric acquires an exclusive licence to novel CDH17 CAR T from the University of Pennsylvania (UPENN)

New technology, novel CDH17 CAR T, originates from one of the greatest CAR T therapy universities globally, the University of Pennsylvania (UPENN), an organisation considered the originator of CAR T cell therapy.

*"I have looked at many deals over the years and this is one of the most promising that I've seen. We've gotten it at a very attractive price, and it's within a stone's throw of going into a clinical trial - which is pretty amazing because at the moment there is a land grab around the world, with people trying to get their hands on cell therapy CAR T assets. To find something not so far away from dosing humans is a real gem" - Paul Hopper*



CAR T cell therapy restores a T cell's ability to recognize and destroy cancer.

### What is CAR T?

Chimeric antigen receptor T-cell therapy, or CAR T, is a type of treatment in which a patient's T cells (a type of immune system cell) are changed in the laboratory so they will attack cancer cells. After T cells are taken from a patient's blood, the gene for a special receptor that binds to a certain protein on the patient's cancer cells is added to the T cells in the laboratory. The special receptor is called a chimeric antigen receptor (CAR). Large numbers of the CAR T cells are grown in the laboratory and given to the patient by infusion. CAR T cell therapy, is currently being used to treat certain blood cancers, however, its use in the treatment of other types of cancer is now being studied.

### What is CDH17

CDH17 is a novel third generation asset which has been in development for over a decade. Pre-clinical models have shown potent efficacy, with no tumour relapse, and it is highly anticipated it will move into the clinic by 2022.

Chimeric has signed a three-year sponsorship agreement, and will continue to collaborate and further develop the asset at UPENN. CDH17 has a robust intellectual property portfolio, and long-life patent potential through to 2039. The company has negotiated attractive licensing fees, funded through existing cash reserves, with industry standard commercialisation royalties. Chimeric will continue to build and leverage their in-house cell therapy expertise to take the asset through rapid development and commercialisation.

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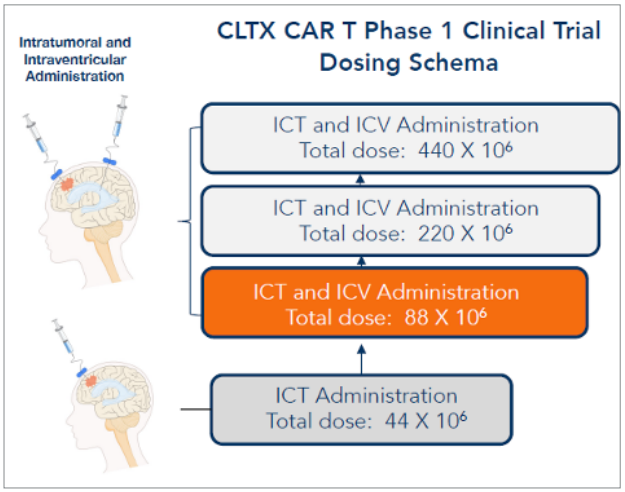
Chimeric is committed to bringing the promise of cell therapy to life for more patients. Traditional drug development and oncology has focused on delaying disease progression and improving survival by three or four months. Novel cell therapies have brought the promise forward to cure cancer, having demonstrated a curative impact. Chimeric's mission is to develop and commercialise a drug that can bring curative potential to patients more rapidly.

During 2021 Chimeric has focused on three specific areas:

1. To explore methods to accelerate chlorotoxin development (with data read-out expected by the end of Q4 2021).
2. To advance the company's pipeline (which is what CDH17 brings).
3. To expand the company's in-house cell therapy expertise to continue to grow and aid the rapid development of these assets, highlighted by the company's most recent appointment, Dr Yi Lin, a recognised leader and pioneer in the development of cellular immunotherapies.

### The Holy Grail

Chlorotoxin, is the asset Chimeric was founded on, and is a novel first-in-class CAR T designed for patients with glioblastoma (currently in Phase 1 clinical trials at the City of Hope Hospital in California). This diagram shows the dosing scheme for the trial:




In April 2021, Chimeric announced the completion of the lowest dose cohort at 44 million cells. The dosage was well tolerated with no safety concerns. Shortly after, the company advanced to the second dose cohort, and is currently midway through (highlighted in orange above), receiving 88 million cells through intratumoural and intraventricular administration.

As the company advances to third and fourth dose cohorts, Chimeric will expand clinical sites. The company is confident work performed thus far should allow for rapid progression into pivotal Phase 2 trials, enabling Chimeric to register the asset commercially around the world. Additionally, Chimeric has discovered chlorotoxin (originally designed to treat glioblastoma) binds to a number of other types of tumours, and will therefore plan a Phase 1 basket trial in other solid tumours, such as metastatic melanomas (primary), as well as prostate and colorectal cancer.

### Strategic pipeline

Chimeric has focused on enhancing its pipeline for two reasons:

1. Improve value to patients - as cancer diagnoses continues to increase, the company believes cell therapies will offer more to patients with curative intent.
2. Increase market opportunity - as the oncology market continues to grow, Chimeric aims to have several assets in the pipeline to bring through to commercialisation.

Chimeric has focused on discovering transformative innovation with therapies they believe will have the best chance of curing cancer.

The company focuses on both solid tumours and 'in blood' cancers, and remains focused on oncology, with cell therapy development catogorised into three buckets:

1. Novel CAR designs with antigen targets like chlorotoxin, third generation constructs, and dual antigen targets.
2. Looking at allogeneic cell sources (therapies that don't use a patient's own cells), allowing for off-the-shelf therapy.
3. Alternative cell types - cell therapies in development that don't use T cells like currently approved CAR T therapies, but instead, use a type of microphage.

Chimeric was incredibly fortunate to licence CDH17 CAR T with UPENN as the asset falls squarely into the top bucket. CDH17 is a novel CAR design (novel antigen target), but also a third generation construct (*see image below*). What this means is, in the intracellular part of the construct, CD3 zeta activation domain, a 41BB co-stimulatory domain, and a CD28 co-stimulatory domain is evident, making this a third generation construct (having all three present on the one construct). Chimeric believes this will enhance the activation, purification, and expansion of this particular CAR T. CDH17 in pre-clinical trials has shown a complete eradication of tumour cells with no relapse, and no toxicity.

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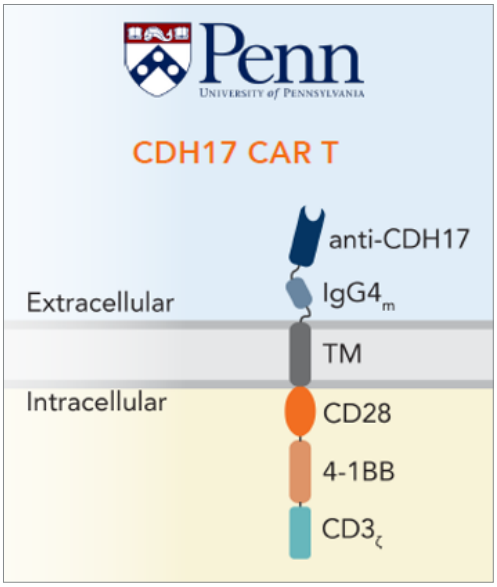



Chimeric will work with UPENN on all pre-clinical activities required to be able to file an application for an investigative new drug (IND) and move into a Phase 1 clinical trial for multiple tumour areas by 2022.

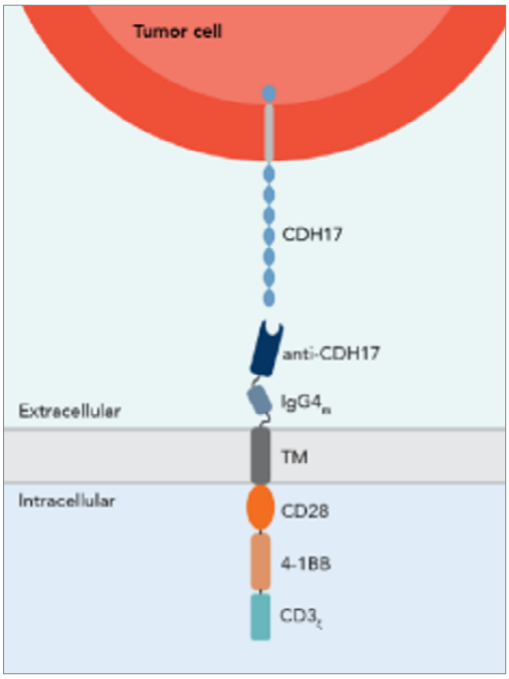
This is an exciting time for Chimeric as it's a rare chance to collaborate with one of the world's best CAR T professors, Dr Xianxin Hua. UPENN is a globally recognised leader in cellular immunotherapy, and widely known for being home to the first FDA approved CAR T therapy - much of which was done under the work of Dr Carl June, who continues to collaborate with the inventor of CDH17, Dr Hua.

UPENN ranks first amongst global universities for cell therapy patents (according to **Nature**), and has launched more than 10 start-ups in cell and gene therapy, therefore ranking in the top 10 cancer research centres in the world. Dr Hua has been with UPENN for 20 years, is a full Professor of Cancer Biology, Investigator at the Abramson Family Cancer Research Institute, and Harrington Scholar Innovator.

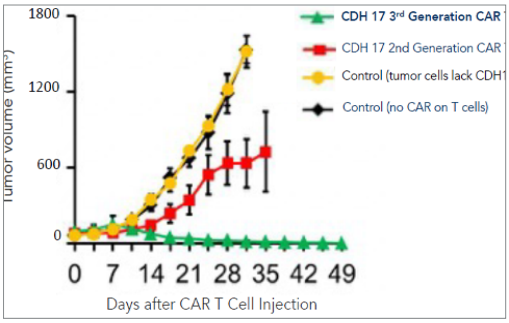
Dr Hua leads a team who are focused on antibody and CAR T development. The doctor and his team have worked together for 10 years developing CDH17 and amassing an incredible amount of data. Dr Hua began trying to identify the optimal antibody, in this case a nanobody, that specifically binds to neuroendocrine tumour cells. Dr Hua was able to validate this nanobody to be very specific to CGH17 on tumour cells, and spent further time developing the construct.

What can been seen in the following image are different pieces to the construct, the targeting domain, co-stimulatory domains, and lines in-between called linkers.

Dr Hua experimented with shorter and longer linkers, more or less co-stimulatory domains, and was able to observe what combination delivers the most potent efficacy, whilst remaining safe for clinical trials.




Further, Dr Hua was able to show incredible pre-clinical efficacy. The following image (Y Axis / vertical line) shows the tumour volume (in mice) continuing to grow over a period of time (X Axis / horizontal). Both the yellow and black lines illustrate that when there is no therapy, the tumour grows freely. The red line (CDH17 2nd generation), is an earlier construct Dr Hua and his team developed, however, was discontinued due to a lack of efficacy. As is shown, the tumour does not grow as quickly, nor is it eradicated. Chimeric has licenced the green line (CDH17 3rd generation CAR T), as pre-clinical trials show a complete eradication of the cancer with no relapse. These models are recorded over a 25 day period. In separate trials, CDH17 3rd generation has shown to have efficacy to day 49.

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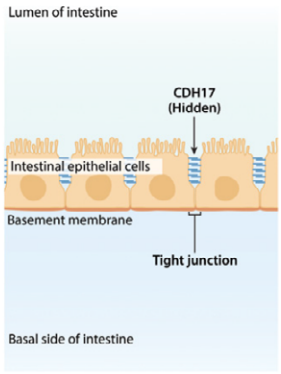
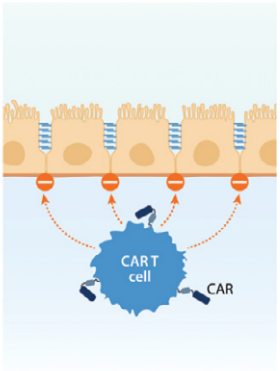
Chimeric is confident, based on pre-clinical findings, that CDH17 3rd generation (CDH17 3G) is safe and satisfies regulatory approval criteria for Phase 1 clinical trials. CDH17 3G is expressed on normal tissues, critically confirming that CAR T 3G does not bind to normal tissues. If it did, CAR T 3G would kill normal tissue, resulting in serious adverse effects. Fortunately, Dr Hua has been able to show this doesn't happen.



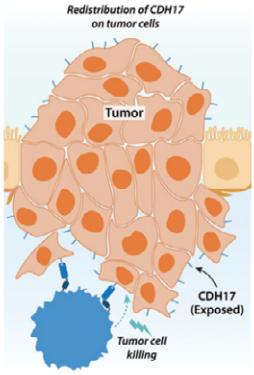

In normal cells, CDH17 is inaccessible as it is hidden beneath tight junctions that reinforce the barriers of normal cells.

In the image above, normal tissues and normal cells, with the blue lines showing CDH17 3G expressed in normal cells, are hidden behind tight junctions of the cells and are inaccessible, reinforcing the barriers of normal cells.
The next image below illustrates CAR T cells are not able to reach CDH17 3G on normal cells, with normal healthy cells unable to pass the tight junctions to find CDH17 3G to bind - therefore, no damage is caused to normal healthy cells.




CAR T cells are not able to reach the CDH17 on normal cells due to the tight junctions.

The next image illustrates what happens when cancer exists. The healthy cell is disrupted, the cancer cell has CDH17 3G exposed and the CAR T cells are able to find cancers with CDH17 3G bound to them, sending a signal to kill those cancer cells. This example provides Chimeric a great deal of confidence leading into Phase 1 clinical trials, as both efficacy and safety are apparent.

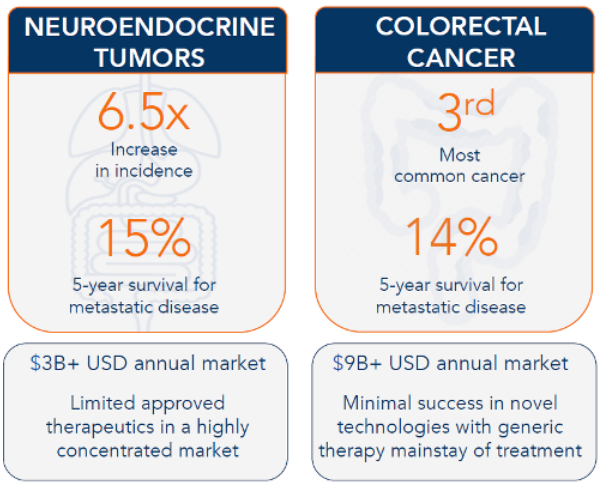



In cancer CDH17 upregulation results in exposure of the CDH17 on the cancer cell surface allowing the CAR T to detect and bind to it.

## Management is key

CDH17 3G is an important tumour targeting antigen due to its oncogenic deriver. When CDH17 3G is expressed on a cancer cell, it accelerates tumour formation, metastatic disease, and cancer. When there is over expression of CDH17 3G, patients have poorer prognosis and move faster to metastatic disease. The ability to inhibit CDH17 3G over-expression in tumour cells reduces proliferation of the cancer cells, whilst seeing increased apoptosis of cancer cells, resulting in more cancer cells dying.

Based on pre-clinical data, Chimeric has decided to progress with CDH17 3G on four other tumour types with a high unmet medical need, in two markets that have a high expression level of CDH17 (diagram I& J). Chimeric will place all four tumour types in a basket trial, ranging from Neuroendocrine tumours, with an expression over 95% of CDH17 3G (at the high end), to pancreatic cancer at the lower end, having over 50% of CDH17 3G expressed cells. None of these therapies have greater than a five year survival period for patients with advanced disease (above 15%), thus, there is a desperate need for new therapies and treatments.

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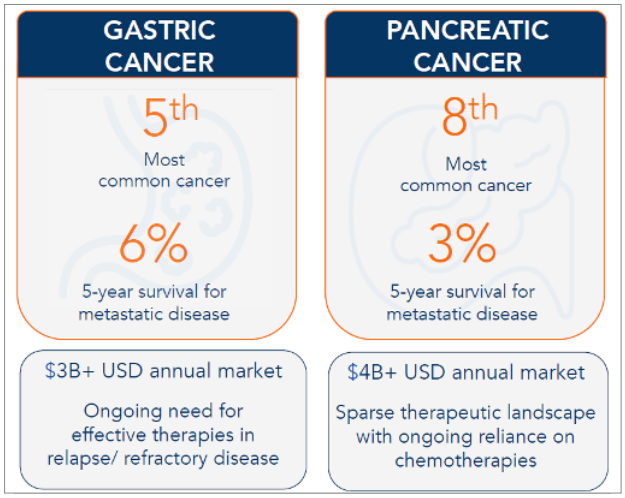
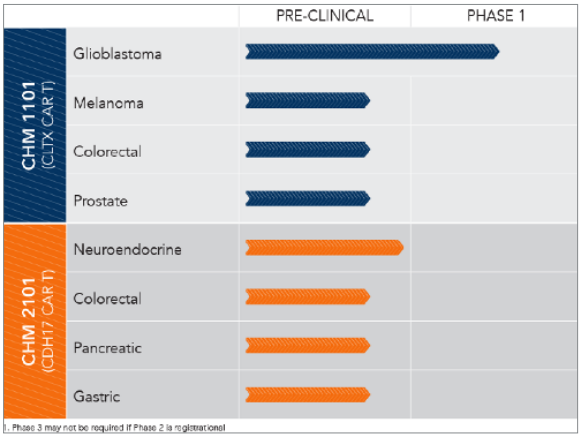



Chimeric's team is crucially important, and arguably the most experienced in CAR T therapy globally (certainly in Australia). Dr Syed Rizvi and Jennifer Chow joined in late 2020, with Dr Eliot Bourk joining in March 2021. Dr Li Ren and Dr Yi Lin both joined recently. Dr Bourk leads corporate and business development, with Dr Li Ren having over 20 years experience in technical and cell manufacturing therapy. Combined, all team members have developed over 25 cell therapies and have worked on four of the five FDA approved cell therapies through the entire development processes to commercialisation. We believe this experience and knowledge will combine well with the UPENN team.

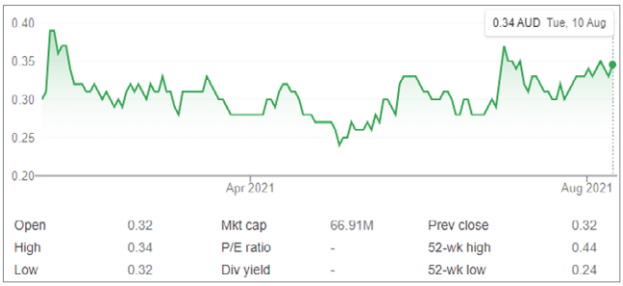
For the remainder of 2021, Chimeric will focus on pre-clinical validation of all four tumour types, seeking aproval from the FDA to advance to Phase 1 clinical trials in 2022. The company will work towards securing **vector**, and a drug product manufacturing strategy. Chimeric will submit an investigative new drug (IND) for all four tumour types to open a Phase 1 basket trial at UPENN, and shortly after will expand to additional clinical trial sites. This is an exciting time for the company to take the next step and develop their highly anticipated pipeline.

Chimeric's founding asset, chlorotoxin (*shown in blue in the image below*) is well into its Phase 1 glioblastoma clinical trial, followed by pre-clinical work on a basket of chlorotoxin indications. Highlighted in orange, is work currently performed on UPENN's basket of cancers, neuroendocrine, colorectal, pancreatic, and gastric cancers.




## Outlook

The remainder of the year and into 2022 will see the advancement of chlorotoxin through phase 1 dose escalation, expansion into solid tumours, the opening of new sites, and ensuring manufacturing conditions are satisfied ready to move CDH17 3G into phase 1 clinical trials at the University of Pennsylvania. The company's board and management will continue to expand in line with the development of assets CLTX CAR T, and CDH17 3G. We look forward to hearing updates as Chimeric continues to move through the rest of CY21 and beyond. An investment in Chimeric is highly speculative and we recommended speaking to an adviser prior to making a decision.

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