

Chimeric Therapeutics Limited (ASX: CHM)

Portfolio of Autologus and Allogenic Cell Therapy
Prospects

Initiating Coverage

16 December 2021

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Company Information

Share price (\$) as at 15 December 2021	0.255
Valuation (\$ per share)	0.76
Issued capital:	
Ordinary shares (m)	333.4
Options (m)	29.7
Performance rights (m)	0.0
Fully diluted (m)	363.1
Market capitalisation (\$m)	85.0
12-month Share Price Low/High (\$)	0.24/0.44

Board and Management

Paul Hopper: Executive Chairman & Founder
Jennifer Chow: CEO & MD
Dr. George Matcham: Non-Executive Director
Dr. Lesley Russell: Non-Executive Director
Leslie Chong: Non-Executive Director
Cindy Elkins: Non-Executive Director
Dr. Syed Rizvi: Chief Medical Officer
Dr. Elliot Bourk: Vice President Corporate and Business Development
Dr. Ki Ren: Vice President Technical Operations

Largest Shareholders

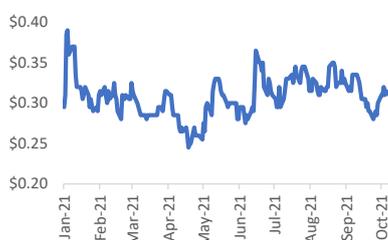
	%
Paul Hopper	24.7
City of Hope	3.6
Christine Brown	3.5
Michael Barish	3.5
Zerrin Investments Pty Ltd	1.4

Top 20 Shareholders

44.0

Source: IRESS

Share Price History



PORTFOLIO OF AUTOLOGOUS AND ALLOGENEIC CELL THERAPY PROSPECTS

Chimeric Therapeutics Limited (ASX: CHM) is a clinical stage cell therapy company that is seeking to develop novel cell therapies to potentially treat a range of cancers. The Company was listed in January 2021 and has a portfolio of autologous CAR-T candidates which it is seeking to develop and has recently expanded the portfolio with the option to licence an allogeneic CAR-NK platform.

KEY POINTS

Novel CLTX CAR-T Therapy in Phase I Clinical Trials: The Company has the world-wide exclusive license for City of Hope's (COH's) chlorotoxin (CLTX) CAR-T technology, a novel CAR-T therapy which is currently in Phase I clinical trials to determine its safety and efficacy. The study is seeking to enrol 18-36 patients. The first level of dose escalation has been completed with no dose limiting toxicity experienced by the four patients dosed. The trial is now moving into the dose escalation phase. Initial data released regarding the dose 1 level, showed that three of the four patients showed stable disease outcomes at the lowest possible dose. One patient experienced an adverse event commonly experienced by patients with glioblastoma. It is unknown at this point whether the CLTX CAR-T had any involvement in the adverse event. Initial data indicates that the CLTX CAR-T cells are not immunogenic, a key positive for the candidate.

Option to Acquire Allogeneic Platform Enhances Cell Therapy Portfolio & Provides Partnership Potential: CHM has secured the option to acquire the licence to the CORE-NK platform from Case Western Reserve University (CWRU). CORE-NK is an allogeneic (off the shelf) natural killer cell platform for the development of CAR-NK's for the treatment of both solid tumours and blood cancers. Preclinical studies showed the platform enabled the large scale proliferation of highly active NK cells with 10,000+-fold expansion over a five week period. The CORE-NK platform has completed a Phase I clinical trial in both blood cancer and solid tumours with the data expected to be released in mid-2022. The addition of the CORE-NK platform provides significant value potential for CHM as it provides for the potential to not only develop the CAR assets the Company currently licences but provides the potential to partner with large biotech firms to develop their CAR assets.

Significant Market Opportunity: Cell therapy is an attractive market with significant capital being injected into research and development of cell therapies on the back of the success of CAR-T cell therapy in blood cancer. These results have biotech companies seeking to develop the next generation of CAR-T cell therapy and the emerging CAR-NK therapy both in blood cancers and solid tumours. The interest in the market is highlighted by recent transactions that have taken place to secure cell therapy candidates by large biotech companies.

Capital Position: At 30 September 2021, CHM had \$17.4m cash on hand. The Company has not released the compensation details for the CORE-NK platform licence agreement, however has stated that the licence agreement will entail an upfront and milestone payments and royalties schedule in line with standard market practices. The upfront payment will be funded by existing cash reserves. With the addition of the CORE-NK platform we expect the Company will have to come to market sooner than expected to raise capital to fund the development of the portfolio of assets.

Valuation: We have assigned CHM a valuation of **\$0.76 per share**. We have valued CHM on a risk adjusted NPV basis for the CLTX candidate currently in a Phase 1 clinical trial for recurrent/progressive GBM. We have modelled sales in both Europe and US with a market penetration rate of 17% and peak sales of USD\$2.92b. We have assumed a launch date of 2027 and assigned an 8% probability rate of the candidate receiving approval. We have not incorporated value from other cancer indications nor the other assets given the structure of the Phase I trials is yet to be complete. Given the potential for other cancer indications for treatment by CLTX CAR-T, the CDH17 CAR-T and the addition of the CORE-NK platform, there is significant upside potential for CHM.

Short-term catalysts will likely be the completion of the Phase I trial of CLTX CAR-T and positive results from the trial that lead to the commencement of the Phase II trial. Any efficacy shown by CLTX CAR-T for the treatment of recurrent/progressive GBM will be of significant value given the significant unmet need. Further catalysts will likely be the commencement of the Phase I trials for the CDH17 CAR-T and the second Phase I trial in solid tumours for the CLTX CAR-T, which are expected to commence in 2022.

SWOT ANALYSIS

STRENGTHS

- ◆ CHM has a portfolio of autologous and allogeneic cell therapy assets that have the potential to be developed and treat a range of cancers. CAR assets are a valuable commodity with the amount of research and development for CAR therapies to treat solid tumours increasingly exponentially since the first CAR-T therapy was approved to treat blood cancer by the FDA in 2017.
- ◆ The Company has an experienced management team with the senior executives having significant experience in cell therapy development.
- ◆ The Company has appointed a cellular immunotherapy scientific advisory board to assist with identifying the best potential cell therapy candidates for the Company to continue to expand the portfolio.
- ◆ The Company has a number of irons in the fire. With the Company preparing for two additional Phase I trials in 2022 (Phase I trial for CLTX CAR-T in solid tumours leading with melanoma and a Phase I trial for CDH17 CAR-T in neuroendocrine tumours, colorectal, gastric and pancreatic cancer), the Company is expected to have two clinical stage assets in 2022 with three clinical Phase I trials as well as the next generation CAR-NK platform which is expected to enter Phase I trials in 2023.
- ◆ The Company has a number of patent applications pending and patents that have been granted providing the Company with intellectual property (IP) protection for its assets. The CLTX CAR-T cell therapy patents having an expiry of 2036.
- ◆ The Company has negotiated Sponsored Research Agreements with the creators of all the assets. This provides the Company with access to laboratory, facilities and the scientific team of the technology founders to further develop the technology.

WEAKNESSES

- ◆ CHM's assets are in the early stage of development and therefore there are significant risks associated with the development of the assets. Further to this, as with all early stage biotech companies, the Company will not generate revenue and therefore will be reliant on capital markets to fund the development of the assets.
- ◆ Of the 333.4m shares, 115.2m shares are classified as restricted and will be escrowed until 18 January 2023 (24 months post listing). As such there may be limited liquidity in the shares in the initial years.

OPPORTUNITIES

- ◆ CHM provides a unique opportunity in the Australian market, with there being only one other ASX-listed biotech company developing CAR-T therapy assets to treat solid tumours. There are limited opportunities on the domestic market to gain exposure to the emerging CAR-T market.
- ◆ Finding a CAR-T therapy solution for solid tumours is considered the search for the "holy grail," with CAR-T therapies essentially providing a cure for blood cancers for some patients. The ability to replicate this success in solid tumours would be a game changer for cancer patients. However, there are a number of roadblocks with the development of CAR-T therapies to treat solid tumours that need to be overcome. The life sciences community has invested significantly in research and development in an attempt to overcome these roadblocks.
- ◆ The Company will be seeking to undertake basket trials for its assets. Basket trials provide for expedited clinical trials with the therapy tested against multiple cancer targets at once as opposed to the traditional clinical trial mandate of testing potential therapy candidates on single targets, one at a time.
- ◆ There is the opportunity for expedited approval with CAR-T therapies receiving FDA approval to date, achieving approval from Phase II trials. Therefore, there is the potential for the assets to achieve approval faster than the typical process in the event the trials show promising outcomes.
- ◆ The acquisition of the CAR-NK platform, provides opportunities for not only development of CARs already licensed by CHM, but for the potential to partner with companies to develop their CAR assets.

THREATS

- ◆ Development of the Company's assets are in the early stage with the CLTX CAR-T asset the most advanced candidate, currently in Phase I trials to determine the safety profile at escalating dosage levels.

- ◆ The Company does not generate any revenue and is not expected to generate revenue in the near-term. As such the Company is reliant on capital raisings to fund development of the assets. The Company may not be able to raise sufficient capital to fully fund operations.
- ◆ The majority of patent applications for CLTX CAR-T are pending and there is no guarantee that they will be granted. Furthermore, another party may contest the patent applications which may result in the Company having to engage in a legal battle, which can be costly.
- ◆ Arbele Limited are also developing cell therapies targeting CDH17. Arbele are currently developing a CDH17 CAR-NK. This provides some competition for CHM, with first mover advantage and patent protection significant considerations.
- ◆ There are a number of barriers to overcome with the use of CAR-T therapies to treat solid tumours due to the heterogeneity of solid tumours when compared to blood cancers. In particular, glioblastoma is one of the more problematic cancers to treat due to the increased difficulties with penetrating brain cancer. This is highlighted by the lack of new treatments for GBM and the low survival rates.
- ◆ There has been a significant increase in research and development spend in cell therapy and an increase in the number of players seeking to make a breakthrough for the use of CAR-T therapy in solid tumours. Another organisation may beat CHM to the punch. First mover advantage will be significant to the commercial outcomes.
- ◆ The Company will likely have to raise capital in the near-term to fund the development of the portfolio of assets. The capital raising may dilute existing shareholder positions.
- ◆ There may be delays with the progression of the trials which may result in the Company requiring more capital than anticipated to complete trials. COVID-19 has resulted in widespread delays for clinical trials with increased difficulties sourcing participants and reduced capacity at research facilities.

COMPANY OVERVIEW

Chimeric Therapeutics Limited (ASX: CHM) is a clinical stage cell therapy company. CHM commenced trading on the ASX on 18 January 2021. The Company raised \$35m through the issue of 175m shares at an issue price of \$0.20. The Company currently has 333.4m shares on issue, 115.2m shares are classified as restricted and will be escrowed until 18 January 2023 (24 months post listing).

The Company was founded on the Chlorotoxin (CLTX) CAR-T licence and has since acquired the licence for an additional CAR-T candidate (CDH-17) which the Company will be seeking to develop with the goal of achieving approval and commercialisation. We note given the size and resources of the Company, if the clinical trials show promising outcomes we would expect the Company to seek to out-licence the technology to a large biotech company for further development and potential commercialisation or enter into a partnership.

What is cell therapy? Cell therapy is the transfer of intact, live cells into a patient to help lessen or cure a disease. CAR-T is a class of cell therapy used to treat cancer that involves the genetic engineering of a patient's T-cells. T-cells are immune system cells critical in orchestrating an immune response to the presence of cancerous cells. Essentially CAR-T cell therapy is designed to use a patient's immune system to combat cancer.

To deliver the therapy, blood is drawn from the patient from which the T-cells are separated. A gene is then added that makes the T-cells produce a protein called Chimeric Antigen Receptors (CARs) on their surface. Once the CAR-T cells multiply in the lab the CAR-T cells are given to the patient by infusion. The CARs allow T-cells to recognise and kill cancer cells with the specific antigen on their surface. The below graphic provides a visual representation of how CAR-T cell therapy works.

CAPITAL STRUCTURE

As at 17 November 2021, CHM had 333.4m fully paid ordinary shares on issue, 115.2m of which are restricted under escrow requirements. CHM also has 29.7m options on issue with various exercise prices and exercise dates. CHM currently has no debt and we would expect research and development activities to be funded by further capital raisings.

Capital Structure as at 17 November 2021	
Ordinary shares on issue	218,217,152
Ordinary Fully Paid Restricted	115,226,336
Options:	
Expiring 18 January 2024 - Restricted	4,957,897
Expiring 18 January 2025 - Restricted	5,500,000
Expiring 18 January 2025 - Exercise price \$0.20	6,280,002
Expiring 18 January 2026 - Exercise price \$0.20	6,280,002
Expiring 30 June 2026 - Exercise price \$0.29	4,265,444
Expiring 8 March 2026 - Exercise price \$0.29	695,552
Expiring 1 July 2026 - Exercise price \$0.29	700,000
Expiring 27 August 2021 - Exercise price \$0.32	1,000,000

Source: Chimeric Therapeutics Limited

CHM 1101 - CHLOROTOXIN (CLTX) CAR-T

CHM has a world-wide exclusive licence agreement with the City of Hope for the CLTX CAR-T technology. The CLTX CAR-T uses a peptide component of scorpion toxin called chlorotoxin (CLTX). The use of CLTX is novel with CHM the only company to incorporate a peptide toxin into a CAR-T cell therapy.

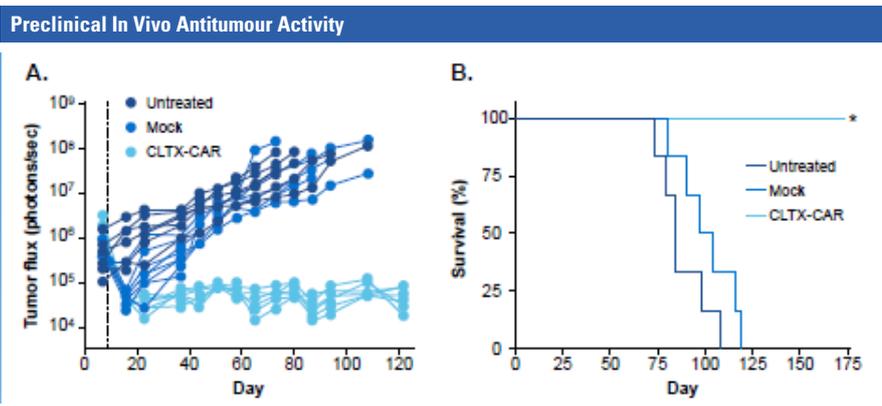
CLTX is a 36 amino acid peptide component of scorpion toxin which has shown to bind to cancer targets. CLTX has been used as an imaging agent primarily due to its superior binding abilities, particularly in brain cancer. CLTX is currently being used in "Tumour Paint", designed to make tumour cells glow providing surgeons greater visibility when surgically removing tumours. This is particularly important for brain tumours, which can be hard to distinguish from normal brain tissue. Blaze Bioscience is currently developing Tumour Paint (BLZ-100) which has received Orphan Drug status and fast-track designation from the FDA and is currently in the late stages of development for use in Paediatric Primary Nervous System Tumours. One of the key benefits of this for CHM and the CLTX CAR-T is that the use of CLTX has already been shown to be safe for use.

The scientists at COH determined that the cancer cells have to express matrix metalloproteinase -2 (MMP2). MMP2 has been shown to play an important role in promoting the invasion and metastasis of tumour cells, in particular brain cancer. A study done on the expression of MMP2 in brain glioma conducted on 104 patients determined that the positive rate of MMP2 expression in brain glioma was 73.8% while in normal brain tissue was only 12.5%. There was a significant correlation between the tumour diameter and grade and the level of MMP2 expression¹. Over expression of MMP2 has been detected in a range of cancers in addition to GBM including bladder cancer, lung cancer, prostate cancer, gastric cancer and melanoma.

COH evaluated CLTX binding for on patient derived brain tumour cell lines for the expression of three known cancer targets, IL13Ra2, HER2 and EGFR. Strong binding of CLTX to tumour cells was observed in the majority of primary GBM lines, independent of the three antigen targets.

Pre-clinical studies in mouse models showed significant promise for CLTX CAR-T. The key outcomes of the mouse model are highlighted in the below graphics. In addition to the binding capabilities of CLTX to the cancer cells, one of the key takeaways from the preclinical testing was that the CLTX CAR-T cells did not exhibit an observable effect on healthy cells.

1. ZHANG, H ET AL (2018), MMP-2 EXPRESSION AND CORRELATION WITH PATHOLOGY AND MRI OF GLIOMA, ONCOLOGY LETTERS.



Source: City of Hope Medical Centre

Licence Agreement

The upfront component of the licence agreement includes a cash payment of US\$10m over three years and CHM scrip. CHM will make payments based on development and sales milestones, tabled below. To date, the first milestone payment has been achieved with the Company completing the dosing of the first cohort of patients in the Phase I clinical trial.

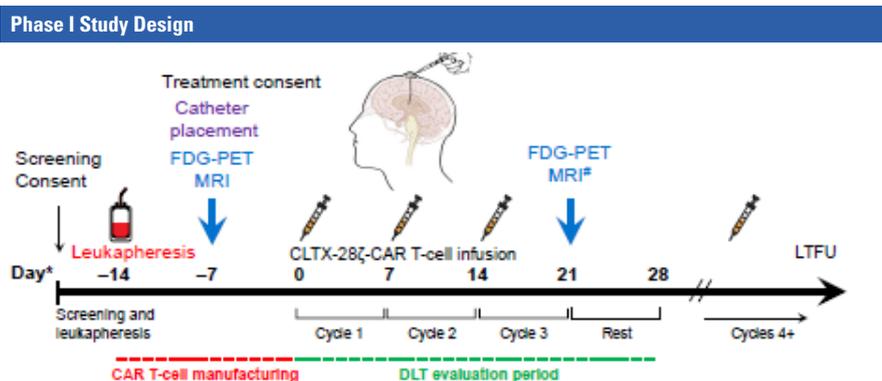
In addition to the below milestone payments, CHM is obliged to pay COH royalties on net sales. Royalties are based on industry standard single digit rates. Under the licence agreement, a non-refundable annual licence fee of US\$150,000 is payable to COH on or before 31 July each licence year, excluding the first and second licence years ending 31 December 2020 and 31 December 2021.

Development & Sales Milestone Payments		
Milestone	Payment Amount (US\$)	Pending/Achieved
Dosing of fifth patient in Phase I clinical trial	0.35	Achieved
Dosing of first patient in first Phase II clinical trial	0.75	Pending
Dosing of first patient in first Phase III clinical trial	2.0	Pending
Receipt of first Orphan Drug Designation for each licensed product or licensed service	1.0	Pending
Achievement of Marketing Approval in US	6.0	Pending
Achievement of Marketing Approval in Europe	6.0	Pending
Achievement of Marketing Approval in each of the first five jurisdictions other than the US and Europe for each licensed product or licensed service	1.0	Pending
Achievement of net sales of licensed products or services first totalling US\$250m in a license year	18.75	Pending
Achievement of net sales of licensed products or services first totalling US\$500m in a license year	35.5	Pending

PHASE I CLINICAL TRIAL FOR GLIOBLASTOMA

The Phase I clinical trial for the use of CLTX CAR-T in glioblastoma (GBM) has commenced with the first cohort of patients advancing past the 28-day follow up period with no dose-limiting toxicities experienced. This is a significant safety milestone and has seen the trial advance to the second dosing level.

The clinical trial is taking place at the City of Hope with the CARs being manufactured and delivered on campus. The trial will seek to enrol 18-36 patients with MMP2+ recurrent or progressive GBM across 4 dose levels. The objective of the trial is to evaluate the safety and maximum tolerated dose of the CLTX CAR-T in patients with recurrent or progressive GBM. This trial will determine the recommended dosing levels for a Phase II trial in the event the therapy is given clearance to advance to a Phase II trial.



Source: City of Hope Medical Centre

CHM is seeking to complete the Phase I trial within 24 months, with the trial commencing in September 2020. Following a successful Phase I trial, the Company will be seeking to move directly into a Pivotal Study comprising 50-75 patients.

In August 2021, the Company received IND clearance from the FDA for the CLTX CAR-T for patients with recurrent/progressive glioblastoma which enables the expansion for the Phase I clinical trial to additional sites.

In addition to the trial for glioblastoma, CHM is seeking to undertake a Phase I basket trial in solid tumours beyond GBM. A basket trial will allow for the therapy to be used to determine its success across multiple cancers as opposed to trialing the therapy in one cancer type at a time. Basket trials have the capacity to accelerate trials allowing a company to determine which cancers the therapy will likely be most successful at targeting.

CLTX-CAR-T is being delivered via intracranial intratumoral or intracranial intraventricular dosing methods. This means the therapy is being delivered directly into the tumour. This compares to other CAR-Ts which are delivered by intravenous infusion. The delivery of the therapy directly into the tumour has the potential to increase the success rate with the cells not having to navigate their way through the blood brain barrier to reach the tumour.

On 15 November 2021, the Company released the initial Phase I clinical trial data. The data focuses on the four patients enrolled in the dose 1 level of the trial, treated with 44×10^6 CLTX CAR-T cells through intratumoral administration. Dose escalation for this trial is planned across four dose levels administered through dual intratumoral and intraventricular routes of administration. For patients treated at dose 1 level, a disease control rate of 75% was shown with three out of the four patients treated achieving a stable disease result. Regional tumor control was also demonstrated through MRI showing tumor control where the CLTX CAR-T cells were administered and tumour progression where the cells were not administered. This observation gives Chimeric optimism for their dual routes of administration in higher dose levels. One patient experienced a grade 3 cerebral edema, which is possibly attributed to the CAR-T cells but the cause is yet to be determined. We note that cerebral edema is a commonly observed event in patients with glioblastoma. This gives us some level of confidence that the adverse event was not directly attributable to the CLTX CAR-T cells, however we await further information regarding the cause of the event.

A liquid biopsy detected persistent CLTX CAR-T cells in the tumour cavity throughout treatment, suggesting the CLTX CAR-T cells are not immunogenic, a key positive for the treatment.

PATENT APPLICATIONS

The Company has eight patent applications pending for CARs containing a chlorotoxin domain. The patent applications cover a range of jurisdictions. On 23 September 2021, the Company announced that the European patent has been granted. All remaining patent applications are pending. Patent protection is expected to 2036.

Patent Applications (as at 20 November 2020)

Country	Application No.	Filing Date	Status
US	15/767,960	13 October 2016	Pending
Europe	2016791158	13 October 2016	Granted
Japan	2018519030	13 October 2016	Pending

China	201680072823	13 October 2016	Pending
Israel	258670	13 October 2016	Pending
India	201817017511	13 October 2016	Pending
Korea	20187013153	13 October 2016	Pending
Canada	3001833	13 October 2016	Pending

ABOUT GLIOBLASTOMA (GBM)

GBM is the most common and one of the most aggressive brain cancers. There is an unmet clinical need in GBM with a five year survival rate of ~5%. There are some significant challenges with treating brain cancer which has resulted in very little progress with treatments to date. The current standard of treatment involves surgical removal followed with chemotherapy or radiotherapy.

GBM has an incidence rate of 3.19 per 100,000 persons in the US. More than 13,000 people were expected to be diagnosed with GBM in the US in 2020 with more than 10,000 people dieing from GBM in the US each year.²

The chemotherapy drug used most often for advanced gliomas is Temozolomide with sales in excess of \$1b and generic forms now being distributed in the market place. The last drug approved by the FDA for GBM was Bevacizumab which received approval to treat recurrent GBM in 2009. Bevacizumab is a targeted therapeutics antibody that binds and inhibits the vascular endothelial growth factor (VEGF) protein in tumour cells. Despite being approved, Bevacizumab showed no improvement to the overall survival rate of patients with advanced GBM. The approval of Bevacizumab highlights the unmet need for advancements in GBM treatments.

GBM CAR-T TRIAL LANDSCAPE

According to clinicaltrials.gov there are 11 CAR-T clinical trials being conducted to treat GBM, including the CLTX CAR-T clinical trial at COH. The CLTX CAR-T is the only CAR-T utilising a peptide and targeting MMP2+.

CAR-T GBM Clinical Trials			
Trial Name	Target	Clinical Phase	Sponsor
Brain-targeting Immune Cells (EGFRvIII-CAR T Cells) in Treating Patients With Leptomeningeal Disease From Glioblastoma.	EGFRvIII	Phase 1	Chembrain Ltd.
Immunogene-modified T (IgT) Cells Against Glioblastoma Multiforme	IgT	Phase 1	Shenzhen Geno-Immune Medical Institute
Study of NKG2D CAR-T in Treating Patients With Recurrent Glioblastoma	NKG2D	Not Applicable	UWELL Biopharma
Pilot Study of B7-H3 CAR-T in Treating Patients With Recurrent and Refractory Glioblastoma	B7-H3	Phase 1	BoYuan RunSheng Pharma (Hangzhou) Co., Ltd.
IL13Ra2-CAR T Cells With or Without Nivolumab and Ipilimumab in Treating Patients With GBM	IL13Ralpha2	Phase 1	City of Hope Medical Center, National Cancer Institute (NCI)
B7-H3 CAR-T for Recurrent or Refractory Glioblastoma	B7-H3	Phase 1 Phase 2	Bo Yuan RunSheng Pharma (Hangzhou) Co., Ltd.
Brain Tumor-Specific Immune Cells (IL13Ralpha2-CAR T Cells) for the Treatment of Leptomeningeal Glioblastoma, Ependymoma, or Medulloblastoma	IL13Ralpha2	Phase 1	City of Hope Medical Center, National Cancer Institute (NCI)
CAR-T Cells With a CLTX Tumor-Targeting Domain for the Treatment of MPP2+ Recurrent or Progressive Glioblastoma	CLTX	Phase 1	City of Hope Medical Center, National Cancer Institute (NCI)
CD147-CART Cells in Patients With Recurrent Malignant Glioma.	CD147	Early Phase 1	Xijing Hospital
Study of Autologous Anti-EGFRvIII CAR T Cells in Recurrent Glioblastoma Multiforme	EGFRvIII	Phase 1	Beijing Sanbo Brain Hospital, Marino Biotechnology Co., Ltd.
NKG2D-based CAR T-cells Immunotherapy for Patient With r/r NKG2DL+ Solid Tumors	NKG2D	Phase 1	Jiujiang University Affiliated Hospital, KAEDI

Source: Clinicaltrials.gov

CDH17 CAR-T

On 28 July 2021, CHM announced that it had obtained the exclusive license to the CDH17 CAR-T for solid tumours from the University of Pennsylvania (UPenn).

Under the terms of the license agreement CHM has acquired the rights to develop and commercialise the CDH17 CAR-T therapy for which it has agreed to pay UPenn licence fees, development milestones and royalty payments based on commercial net sales. The details of the license agreement have not been disclosed.

The CAR-T targets CDH17, a gene that is associated with poor prognosis and metastasis in neuroendocrine tumours as well as gastrointestinal tumours such as colorectal, pancreatic and gastric cancers.

Neuroendocrine cells are found throughout the body, but mainly in the gastro-intestinal tract (including large bowel and small bowel), pancreas and lungs. Neuroendocrine tumours (NET) are an uncommon type of tumour that forms in these cells.

While CDH17 has been identified as a cancer target, as with most cancer targets CDH17 is expressed on healthy cells as well as cancer cells. In normal cells, CDH17 is inaccessible as it is hidden beneath tight junctions. However, CDH17 upregulation results in exposure of CDH17 on the cancer cells allowing the CAR-T to bind to it. Of significance, preclinical studies of the CDH17 CAR-T only infiltrated the tumour cells expressing CDH17 and did not infiltrate healthy cells expressing CDH17, demonstrating no toxicity to normal tissues.

CDH17 CAR-T Cancer Targets		
Cancer	Estimated New Cases in US 2021	5 year Survival Rate*
Neuroendocrine	12,000	15%
Colorectal	149,500	14%
Pancreatic	60,430	3%
Gastric	26,560	6%

Source: Cancer.net, National Cancer Institute, Chimeric Therapeutics Limited
*5-year survival rate for metastatic disease.

The preclinical studies of CDH17 in mouse models has shown promising results. As detailed above the use of the CDH17 CAR-T only targeted cancer cells and did not infiltrate healthy cells. This is a significant positive for the treatment. We note that the full data from the preclinical trials is yet to be published so the full extent of the results is unknown at this stage.

The Company will be seeking to commence a Phase I clinical trial in 2022 for neuroendocrine tumours, colorectal, pancreatic and gastric cancer.

CDH17 CAR-T TRIAL LANDSCAPE

There are currently a number of clinical trials taking place for some of the cancers the Company is seeking to target, however there is only one other company targeting CDH17, Arbele Limited. Arbele, is a biotech firm located in Hong Kong and is currently developing a CAR-NK targeting CDH17 with the CAR-NK currently in the preclinical phase.

CHM management has confirmed that an extensive patent search was undertaken and there is currently no overlapping patent applications between the two companies and their CDH17 candidates, however, patent disputes remains a risk in future.

CORE-NK PLATFORM

CHM has obtained the option to acquire the exclusive licence to the CORE-NK platform, an allogenic (off the shelf) Natural Killer (NK) cell platform, from Case Western University (CWRU) in Ohio, USA. The platform was developed by Dr. David Wald at CWRU and activates and expands health donor naked NK cells to provide an off the shelf NK cell platform.

Like T cells, NK cells can be engineered to better recognise a specific tumour. NK cells are the latest development in cell therapy and have a number of advantages over CAR-T cells including: (1) they can detect more chemical signals of tumours than T cells; and (2) they are less prone to attacking healthy tissue than T cells. As such, the platform provides significant development opportunities for CHM.

NK cells, comprising 10%-15% of peripheral blood lymphocytes, play an important role in immune surveillance due to their innate ability to kill cancer and virally infected cells.³ NK cell function is largely controlled by families of cell surface activating and inhibitory receptors. Activation signals are promoted by activating receptors such as NKG2D that recognize ligands including the stress-induced protein MICA. Inhibitory receptors recognise molecules, such as MHC class I, that are universally expressed on normal cells and frequently downregulated on cancer cells.³

The adoptive transfer of NK cells is considered a promising therapeutics strategy given the high cytotoxic activity against cancer cells. However, the widespread clinical success of NK cell therapy has been limited partially due to challenges in manufacturing large doses of NK cells that are likely to be required for clinical efficacy.³

The CORE-NK platform uses a novel mbIL-21 based NK cell feeder Cell line that can support the generation of large doses of highly activated NK cells.

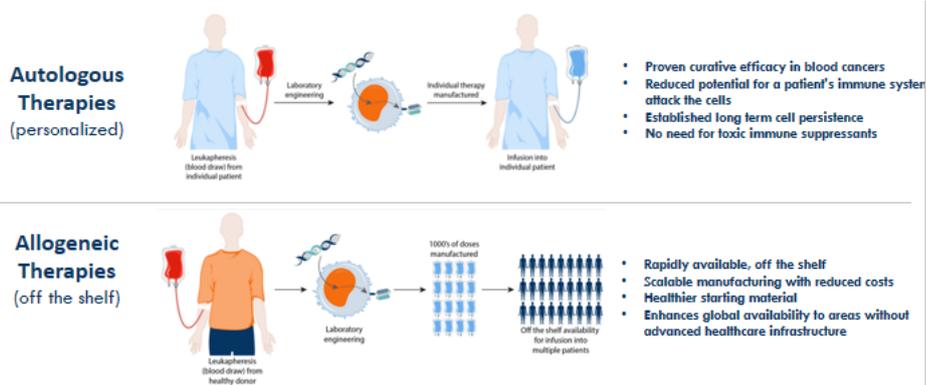
The CORE-NK platform has been de-risked to a certain degree with the platform already having completed a Phase I trial targeting both solid tumour and blood cancer cells. While the clinical trial data is yet to be published, early indications suggest the platform shows some promise. The platform will open up the opportunity for the Company to use the platform to develop CAR-NK'S to potentially treat both blood cancers and solid tumours.

Why an Allogeneic Platform?

CAR-T cell therapy has proven very successful in the treatment of blood cancers, however there are a number of drawbacks with the treatment as it currently stands. The current autologous CAR-T treatment means that the patients own T-cells are used in the treatment. This requires a significant amount of time and infrastructure to collect and deliver the altered T-cells back to the patient for treatment, contributing to the significant expense of the treatment.

Allogeneic cell therapies use cells from a healthy donor to attach the CAR to and deliver to the patient. Using "off the shelf" cells, allows for a provider to scale up manufacturing, reducing the time for delivery of the treatment and the cost. The concept of allogeneic cell therapy is of interest to large biotech companies because it is expected to be more commercially viable than autologous treatments, however, a key roadblock to date has been developing a platform that can provide for the necessary NK cell expansion required for clinical efficacy.

Autologous vs. Allogeneic Cell Therapies



Source: Chimeric Therapeutics Limited

CLINICAL DEVELOPMENT

Dr. Wald and his team have developed a platform that seeks to support large scale expansion of highly active NK cells. The team created a NK cell feeder line (NKF) through over expressing membrane bound IL-21 that is capable of inducing robust and sustained proliferation of highly cytotoxic NK cells. Preclinical studies found that the expanded NK cells exhibit increased cytotoxic function against a panel of blood cancer and solid tumour cells as compared to IL-2-activated non-expanded NK cells. The NKF-expanded NK cells also demonstrate efficacy in mouse models of human sarcoma and T cell leukaemia. Mechanistic

3. Evelyn O. Ojo, et al, Membrane bound IL-21 based NK cellfeeder cells drive robust expansion and metabolic activation of NK cells, Nature Research.

studies revealed that membrane-bound IL-21 leads to an activation of a STAT3/c-Myc pathway and increased NK cell metabolism with a shift towards aerobic glycolysis.

Pre-clinical studies found that the NK cell feeder cell line enables the large scale proliferation of highly active NK cells. NK cells were shown to enable long-term NK cell proliferation - after 5 weeks of expansion there was an average of 10,973-fold expansion. The NK-NK cells also reduced the tumour burden in mouse models and improved survival using both a lung cancer model and a blood cancer model.³

A Phase I clinical trial has been completed using the platform to for both blood cancer and solid tumours. The trial was completed in June 2021 with data expected to be released in mid-2022. 11 patients were enrolled and 9 patients were dosed with three levels of dose escalation, which included: (1) 10×10^6 ; (2) 25×10^6 ; and (3) 50×10^6 . All 9 patients dosed completed all three dose levels.

A key point that was made in the published preclinical studies was that further developments in NK cell manufacturing is warranted to support large scale, universal clinical studies. While the existing methods can support the manufacture of tens of billions of cells, higher capacity culture systems will be necessary to efficiently and cost effectively generate hundreds of billions or more NK cells from single donor expansions. Researchers commented that based on an average expansion of over 10,000-fold at 5 weeks, it should be feasible to manufacture greater than 4×10^{12} NK cells starting from a single donor apheresis sample.³ According to CHM, this amount of NK cells would treat 100 patients.

CAR-NK DEVELOPMENT PLAN

The Company will be seeking to move into Phase I clinical trials of the platform using the two existing CAR's and attaching them to NK cells in addition to an undisclosed CAR. These are expected to be developed in 2022 with the Phase I trials to commence in 2023. While not disclosed, we would anticipate the Company to seek to undertake a basket trial if possible, treating for a number of cancer indications to determine which, if any, provides the best outcomes to pursue for further development.

The company is also planning to develop a next generation CORE-NK platform that they plan to take into phase 1 clinical trials as a combination therapy in 2023 in Acute Myeloid Leukemia (AML), Multiple Myeloma (MM) and B cell malignancies.

While the platform has completed a Phase I trial, the platform remains in the early stages of development as does the use of NK cells for the treatment of cancer. The platform will provide significant development and partnership opportunities, however requires further validation.

CAR-NK CLINICAL TRIAL LANDSCAPE

According to clinicaltrials.gov, there are currently 23 clinical trials being undertaken with CAR-NKs. The clinical trials are seeking to target a mixture of targets and indications across both blood cancer and solid tumours. All trials are relatively early stage with only one Phase II trial being conducted in recurrent/metastatic gastric, head and neck cancer.

CAR-NK Clinical Trials			
Trial Name	Target	Clinical Phase	Sponsor
Study of Anti-PSMA CAR NK Cell in Castration-Resistant Prostate Cancer	Anti-PSMA CAR-NK cells	Early Phase 1	Allife Medical Science and Technology Co., Ltd.
Immunotherapy Combination: Irradiated PD-L1 CAR-NK Cells Plus Pembrolizumab Plus N-803 for Subjects With Recurrent/Metastatic Gastric or Head and Neck Cancer	N-803	Phase 2	National Cancer Institute (NCI)
Study of Anti-Mesothelin Car NK Cells in Epithelial Ovarian Cancer	Anti-Mesothelin Car NK Cells	Early Phase 1	Allife Medical Science and Technology Co., Ltd.
Clinical Research of ROBO1 Specific BiCAR-NK Cells on Patients With Pancreatic Cancer	BiCAR-NK cells (ROBO1 CAR-NK cells)	Phase 1 Phase 2	Asclepius Technology Company Group (Suzhou) Co., Ltd.
Clinical Research of ROBO1 Specific CAR-NK Cells on Patients With Solid Tumors	ROBO1 CAR-NK cells	Phase 1 Phase 2	Asclepius Technology Company Group (Suzhou) Co., Ltd.
Pilot Study of NKG2D-Ligand Targeted CAR-NK Cells in Patients With Metastatic Solid Tumours	NKG2D ligands	Phase 1	The Third Affiliated Hospital of Guangzhou Medical University

Clinical Research of ROBO1 Specific BiCAR-NK/T Cells on Patients With Malignant Tumor	BiCAR-NK/T cells (ROBO1 CAR-NK/T cells)	Phase 1 Phase 2	Asclepius Technology Company Group (Suzhou) Co., Ltd.
NKX019, Intravenous Allogeneic Chimeric Antigen Receptor Natural Killer Cells (CAR NK), in Adults With B-cell Cancers	NKX019	Phase 1	Nkarta Inc.
Cord Blood Derived Anti-CD19 CAR-Engineered NK Cells for B Lymphoid Malignancies	CD19 Cells	Phase 1	Shanghai Simnova Biotechnology Co.,Ltd.
Umbilical & Cord Blood (CB) Derived CAR-Engineered NK Cells for B Lymphoid Malignancies	iC9/CAR.19/IL15-Transduced CB-NK Cells	Phase 1 Phase 2	M.D. Anderson Cancer Center
Universal Chimeric Antigen Receptor-modified AT19 Cells for CD19+ Relapsed/Refractory Hematological Malignancies	CD19 Cells	Phase 1	Chengdu USino Technology Biology Co., Ltd
Anti-BCMA CAR-NK Cell Therapy for the Relapsed or Refractory Multiple Myeloma	Anti-BCMA CAR-NK Cells	Early Phase 1	Sichuan Kelun-Biotech Biopharmaceutical Co., Ltd.
NKX101, Intravenous Allogeneic Engineered Natural Killer Cells, in Adults With AML or MDS	NKX101	Phase 1	Nkarta Inc.
Anti-CD33 CAR NK Cells in the Treatment of Relapsed/Refractory Acute Myeloid Leukemia	Anti-CD33 CAR NK cells	Phase 1	Sichuan Kelun-Biotech Biopharmaceutical Co., Ltd.
CAR-pNK Cell Immunotherapy for Relapsed/Refractory CD33+ AML	Anti-CD33 CAR-NK cells	Phase 1 Phase 2	PersonGen BioTherapeutics (Suzhou) Co., Ltd.
Clinical Research of Adoptive BCMA CAR-NK Cells on Relapse/Refractory MM	BCMA CAR-NK 92 cells	Phase 1 Phase 2	Asclepius Technology Company Group (Suzhou) Co., Ltd.
Study of Anti-CD22 CAR NK Cells in Relapsed and Refractory B Cell Lymphoma	Anti-CD22 CAR NK Cells	Early Phase 1	Allife Medical Science and Technology Co., Ltd.
Study of Anti-CD19 CAR NK Cells in Relapsed and Refractory B Cell Lymphoma	Anti-CD19 CAR NK Cells	Early Phase 1	Allife Medical Science and Technology Co., Ltd.
Anti-CD19 CAR NK Cell Therapy for R/R Non-Hodgkin Lymphoma.	Anti-CD19 CAR NK	Early Phase 1	Chongqing Precision Biotech Co., Ltd
Clinical Study of HLA Haploidentical CAR-NK Cells Targeting CD19 in the Treatment of Refractory/Relapsed B-cell NHL	Anti-CD19 CAR-NK	Phase 1	Second Affiliated Hospital, School of Medicine, Zhejiang University
Study of Anti-CD19/CD22 CAR NK Cells in Relapsed and Refractory B Cell Lymphoma	Anti-CD19/CD22 CAR NK Cells	Early Phase 1	Allife Medical Science and Technology Co., Ltd
PCAR-119 Bridge Immunotherapy Prior to Stem Cell Transplant in Treating Patients With CD19 Positive Leukemia and Lymphoma	Anti-CD19 CAR-NK cells	Phase 1 Phase 2	PersonGen BioTherapeutics (Suzhou) Co., Ltd.
Study of CAR.70- Engineered IL15-transduced Cord Blood-derived NK Cells in Conjunction With Lymphodepleting Chemotherapy for the Management of Relapse/Refractory Hematological Malignancies	CAR.70/IL15-transduced CB-NK cells	Phase 1 Phase 2	M.D. Anderson Cancer Center

Source: clinicaltrials.gov

ONCOLOGY & CELL THERAPY MARKET

The oncology market is significant with cancer being the second leading cause of death globally, accounting for nearly 10 million deaths in 2020⁴, with an estimated 19.3 million new cancer cases. The global incidence rate is expected to grow to 28.4 million new cases in 2040⁵.

The increasing prevalence of cancer has resulted in the global oncology market being valued at US\$97.4b in 2017 and is expected to reach \$176.5b by 2025⁶.

There has been an increasing amount of capital spend on R&D in the oncology space with companies and institutions continuing to seek to advance the technology and improve efficacy of cancer treatments. Immunotherapies have emerged as a significant area of growth for cancer treatments with immunotherapies looking to harness a patients immune system to fight the cancer.

4. World Health Organisation (WHO)

5. Hyana Sung PhD, et al., Global Cancer Statistics 2020: GLOBOCAN Estimated of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries, February 2021.

6. Chimeric Therapeutics Limited Prospectus, January 2021.

As is highlighted below, cancer is the dominant area when it comes to transactions with the total deal value from 2008-2020 far surpassing the next therapeutic area being neurologic therapies.



A form of immunotherapy that has emerged as a significant area of interest is CAR-T and now CAR-NK cell therapies. There are currently five CAR-T therapies approved by the FDA for use in blood cancers with the first CAR-T therapy approved in 2017. The first approved CAR-T therapy was Kymriah, which was approved for the treatment of Acute Lymphoblastic Leukaemia (ALL). This was followed by Yescarta, which is approved for the adult non-Hodgkin Lymphoma. Both these treatments rely on the incorporation of CD19 receptor into the T cell. Both therapies showed very positive results with Kymriah reporting a complete remission rate of 81% from clinical studies and Yescarta reporting a complete remission rate of 54%. As with all immunotherapy cancer treatments they come with a significant price tag - US\$475,000 for Kymriah and US\$370,000 for Yescarta. In 2020 sales of Yescarta grew to US\$607m and Kymriah sales were US\$474m.

The approval of these CAR-T therapies has spurred on a significant investment in R&D of CAR-Ts given the impressive efficacy of the treatment. A number of companies and institutions are seeking to improve on the therapy as well as finding the ability to treat solid tumours with CAR-T therapies, which would be a game changer for cancer treatment if it can be achieved. There is yet to be a CAR-T therapy approved for the treatment of solid tumours. One of the key reasons for this is that solid tumours tend to be much more complicated than blood cancer and there are a number of biomarkers that are prevalent for solid tumours. Blood cancers in this regard are quite linear. This is just one of the barriers to the use of CAR-T therapies in solid tumours.

The potential market for CHM's assets is significant as is highlighted by the sales of the CAR-T therapies that have been approved by the FDA. The sales reflect the significant success that CAR-T therapies have had in treating blood cancers. However, this is an increasingly competitive area of the market with more and more companies and institutions seeking to find the breakthrough to treat solid cancers through the use of cell therapy.

RECENT MARKET TRANSACTIONS

Below we have detailed a selection of recent transactions regarding early stage cell therapy assets that we consider relevant to CHM. There are a wide variety of transactions with upfront payments ranging from \$40m-\$150m and milestone payments ranging from up to \$300m to up to \$2.3b. These numbers show the level of interest in developing cell therapies is high and these assets are considered valuable, despite the early stage of clinical development. We note that while some of these compensation amounts are eye watering high, most of the assets are in the early stages of development with milestone payments typically back-ended. As such, on a probability and risk adjusted NPV basis, the current value of these compensation amounts is significantly reduced.

Recent Transactions					
Date	Companies Involved	Assets	Stage	Upfront	Milestone Payments
Feb-21	Caribou and AbbVie	Development of CAR-T therapies		\$40m upfront in cash and equity investment	Up to \$300m in development, regulatory and launch milestones
Apr-20	Fate Therapeutics & Janssen	Collaboration for novel CAR-T and CAR NK candidates	Discovery	\$50m cash upfront and \$50m equity investment plus full funding for R&D.	Fate eligible for payments of up to \$1.8b in development and regulatory milestones and \$1.2b in commercial milestone payments plus royalties
Jan-20	Astellas and Adaptimmune	CAR-T platform	Discovery	Upfront US\$50m	Development milestones up to \$147.5m per product and up to \$110m in sales milestones
Dec-20	Bayer & Atara Boptherapeutics Allogeneic T cell and CAR-T technologies	Collaboration will be used to test mesothelin expressing solid tumours	Discovery	US\$60m	Up to \$610m for development and regulatory and commercial milestones plus royalties on net sales.
Jun-21	Kite & Shoreline Collaboration	Collaboration to develop novel allogeneic cell therapies	Discovery	\$60m upfront	Up to \$2.3b
Sep-21	Adaptimmune & Genentech	Allogeneic T cell therapies for up to 5 cancer targets	Discovery	\$150m	\$150m over the next five years plus milestone payments that could value the deal at \$3b
Aug-21	Kite & Appia Bio, Inc	Allogeneic T cell therapies for blood cancers. Looking to develop CAR-iNKT cells using Appia Bio's allogeneic cell therapy platform		Undisclosed	Up to \$875m plus tiered royalties
Jan-20	Astellas & Xyphos Inc	Acquired Xyphos and its five preclinical CAR-T candidates		\$120m	Up to \$545m

Source: Company websites

VALUATION

We have assigned CHM a value of **\$0.76 per share (\$0.70 per share fully diluted)**. The valuation is based on a risk adjusted NPV basis for the CLTX CAR-T candidate currently in a Phase 1 clinical trial for recurrent/progressive GBM. We have modelled sales in both Europe and US with a market penetration rate of 17% and peak sales of US\$2.92b. We have assumed a launch date of 2027 and assigned an 8% probability of the candidate receiving approval. The launch date takes into account that approval will likely be fast tracked post the Phase II trials in the event the outcomes are positive.

We have made a number of assumptions in the model regarding timing and costs based on industry standards. In the event of delays or costs are above those forecast, this will likely have an adverse impact on the valuation.

We have applied a discount rate of 11.4% which comprises a risk-free rate of 1.82% (the Australian 10-year government bond yield at the time of the valuation was done), a beta of 1.6 and a market risk premium of 6.0%. We note that any change to these inputs may result in a change to the valuation outcome.

We have not incorporated value from other cancer indications or the other assets given the Phase I trials are yet to commence. Given the potential for other cancer indications for CLTX CAR-T, CDH17 CAR-T expected to move into Phase I clinical trials for neuroendocrine tumours, colorectal, pancreatic and gastric cancers in 2022 and the addition of the CORE-NK platform and development of the next generation COE-NK platform, we view there to be significant potential upside for CHM. While we view there to be significant potential upside there remains significant development risk with the Company's assets.

The Company has limited cash reserves and with the addition of the CORE-NK platform will likely have to raise additional capital in the near-term to fund the development of the portfolio of assets.

CHM Valuation Summary							
Candidate	Indication	Status	Peak Sales	Price per Treatment	Launch Date	Probability of Approval	AUDUSD FX Rate
CLTX CAR-T	GBM	Phase I	US\$2.92b	US\$400,000	2027	8%	0.75
NPV (\$m)	235.4						
Debt (\$m)	0.0						
Cash (\$m)	\$17.4						
Total Value (\$m)	\$252.8						
Share on issue (m)	333.4						
Options (m)	29.7						
Fully Diluted shares on issue (m)	363.1						
Value per share (basic)	\$0.76						
Value per share (fully diluted)	\$0.70						

Source: Iress, Company websites

FINANCIALS SUMMARY

The Company is not expected to generate any revenue in the near-term with the Company's candidates in the early stages of clinical development. Given the expected spend on R&D, increased general and administration costs, licence fees and the acquisition of additional assets, the Company will have to raise additional capital in the near-term.

Profit & Loss					
AUD\$m	FY21A	FY22F	FY23F	FY24F	FY25F
Revenue	0	0	0	0	0
COGS	0	0	0	0	0
Gross Profit	0	0	0	0	0
Operating Expenses:					
R&D	(3.8)	(3.9)	(13.6)	(13.6)	(10.9)
General & Administrative Costs	(9.0)	(7.2)	(7.6)	(7.9)	(8.3)
Other	(2.1)	0	0	0	0
EBIT	(14.8)	(11.3)	(21.4)	(21.7)	(19.5)
Net Finance costs	0.0	0	0	0	0
Tax	0	0	0	0	0
Profit After Tax	(15.1)	(11.3)	(21.4)	(21.7)	(19.5)

INVESTMENT VIEW

We view there to be significant upside potential for CHM given the portfolio of cell therapy assets and the potential market for the candidates in the event they are commercialised. As is highlighted by some of the recent transactions, these assets can be valued highly by the market. While we view there to be significant potential upside value, this value is dependent on the success of the clinical trials.

The initial data from the CLTX CAR-T Phase I trial in recurrent GBM has provided some encouraging initial data at the dose 1 level. We expect the completion of this trial and positive results from the escalating dose levels which then prompt a Phase II trial to be a catalyst for the share price. Given the low survival rates in GBM any efficacy shown by CLTX CAR-T will be a considerable positive, although we note that there are additional complexities associated with brain cancers that have resulted in a lack of progress of treatment and low survival rates.

BOARD AND MANAGEMENT

BOARD OF DIRECTORS

Paul Hopper - Executive Chairman: Paul is the Executive Chairman and Founder of Chimeric Therapeutics. Paul is an inspired bioentrepreneur that has been instrumental in founding several successful biotechnology companies including Imugene, Viralytics, Prescient and now Chimeric Therapeutics.

Paul has over 25 years of experience in the biotech, healthcare and life sciences sectors serving as the Chairman, non-executive director or CEO of more than fourteen companies in the United States, Australia and Asia.

Paul has extensive experience fund raising in Australia, Asia, the US and Europe along with proven expertise in corporate governance, risk and strategy. Paul was the former Chairman of Viralytics when it was acquired by Merck in 2018 and is currently on the board of three ASX-listed companies.

Dr. George Matcham - Non-Executive Director: Dr. Matcham is a cell therapy expert with over 30 years experience at Celgene Corporation where he championed the introduction of cellular immunotherapy and led the establishment of cell therapy and biologics technical development.

Dr. Matcham joined Celgene in 1988 when the company was a 30-person startup and after 3 decades of successful leadership retired in 2018 with the company shortly thereafter being acquired for \$74B by Bristol-Myers Squibb (BMS). Dr. Matcham was vital to the growth of cell therapy at Celgene holding several leadership positions, including Chief Operations Officer of Celgene Cellular Therapeutics and Senior Vice President of CART CMC Development, where he oversaw clinical supply.

Dr. Matcham holds a Ph.D in Biochemistry from Cardiff University and currently serves on the board and as an advisor at Instil Bio.

Dr. Lesley Russell - Non-Executive Director: Dr. Russell has over 25 years of international operational and leadership experience with established and emerging biotechnology companies including Amgen, Eli Lilly, Teva, and Cephalon.

Dr. Russell previously served as the Chief Medical Officer at Cephalon Inc. prior to its acquisition and as the Global Head of R&D at Teva Pharmaceuticals. Dr. Russell medical training and extensive experience in the area of hematology/oncology and has submitted more than a dozen NDAs or sNDAs to the US Food and Drug Administration over the course of her career.

Dr. Russell currently serves as a Non-Executive Director of Enanta Pharmaceuticals and Imugene Ltd in addition to Chimeric Therapeutics.

Leslie Chong - Non-Executive Director: Leslie has over 20 years of experience in clinical development in oncology. Leslie is currently the Chief Executive Officer and Managing Director of Imugene (ASX:IMU) and a Non-Executive Director of Cure Brain Cancer Foundation (CBCF)

Leslie began her career in oncology clinical development at GSK and Exelixis before taking a role at Genentech as a Senior Clinical Program Leader where she focused on therapies for brain cancer. Leslie has deep development experience with small molecules, immunotherapies, cancer vaccines, oncolytic viral therapies, epigenetics and monoclonal antibodies.

Cindy Elkins - Non-Executive Director: Cindy Elkins was Executive Vice President and Chief Information Officer at Juno Therapeutics, one of the pioneers in CART technology focused on blood cancers.

After the acquisition of Juno, Cindy served as the Global Head CART Patient Experience at Celgene Corporation and Bristol-Myers Squibb (BMS) where she was responsible for connecting patients with their personalized therapy through world leading service and technology. Prior to Juno, Ms. Elkins was Vice-President of Pharma Informatics at Genentech/Roche, where she was instrumental in ensuring all technology systems/processes were ready as soon as the FDA approved new medicines such as Zelboraf®, Gazyva®, Cotellic® and Tecentriq®.

Cindy currently serves as the Board Chair at the Foundation for Art and Healing in addition to as a non-executive director for Chimeric.

MANAGEMENT

Jennifer Chow - Chief Executive Officer and Managing Director: Jennifer joined CHM as the CEO and MD in September 2021. Jennifer is a cell therapy pioneer and expert with experience developing and commercializing FDA approved CART cell therapies, Abecma™, Breyzani™, Yescarta™ and Tecartus™. Jennifer also has experience leading the commercial development for more than 15 pipeline cell therapies.

Jennifer joined Chimeric from Kite Pharmaceuticals where she was the Head of Global Marketing, Analytics and Commercial Operations and was responsible for optimizing the commercial development of all Kite pipeline therapies.

Prior to Kite, Jennifer was the Global Cell Therapy Commercial Lead at Celgene Corporation defining the global commercial strategy and operating model for Celgene cell therapies. Jennifer has developed over 10 oncology therapeutics for launch and has more than 20 years' experience in the biotech and pharmaceutical field.

Paul Hopper - Executive Chairman and Founder: See above.

Dr. Syed Rizvi - Chief Medical Officer: Dr. Syed Rizvi is the Chief Medical Officer of Chimeric Therapeutics. Syed has over 25 years of biotechnology and pharmaceutical industry experience leading global and US medical affairs and clinical teams.

Syed is a cell therapy pioneer with extensive development and commercialization experience. Dr. Rizvi was one of the founding executive team at Legend Biotech where he was head of the CART program serving as VP Clinical Development and Medical Affairs and responsible for the development of the Ciltacabtagene Autoleucl BCMA CART program.

Prior to Legend, Syed was the head of global medical affairs for the CART and immunology programs at Celgene Corporation and the head of hematology, US medical affairs.

Dr. Elliot Bourk - Vice President, Corporate and Business Development: Dr. Bourk is the Vice President, Corporate and Business Development at Chimeric Therapeutics. Elliot is a cell therapy expert with over 5 years leadership experience in the development and commercialization of cell therapies from early to late stage.

Dr. Bourk joined Chimeric from Kite Pharmaceuticals where he led early commercial strategy, responsible for the optimization of a portfolio of early-stage cell therapy pipeline assets and for guiding business development strategies and transactions.

Prior to joining Kite, Dr. Bourk was a founding member of the cell therapy commercial team at Celgene Corporation and was the commercial lead for the development of next generation CART platforms. Dr. Bourk has worked on the development and commercialization of the majority of the leading CART therapies including Abecma™, Breyzani™, Yescarta™ and Tecartus™.

Dr. Li Ren - Vice President Technical Operations: Dr. Ren has nearly 20 years of experience developing and advancing cell therapy drug candidates from the pre-clinical stage through to commercial licensure.

Dr. Ren has led the process and analytical development of multiple allogeneic & autologous cell therapy products over her career, including CART cells, TCR cells, NK cells and mesenchymal-like stem cells.

Dr. Ren joined Chimeric from Bristol-Myers Squibb (BMS) where she most recently oversaw the technology transfers of Juno cell therapy pipeline products to BMS manufacturing facilities. Over the course of her career Dr. Ren has supported multiple IND submissions for pipeline products to enable clinical trials and designed and led process & analytical validation programs in support of commercial registration filing.

CELLULAR IMMUNOTHERAPY SCIENTIFIC ADVISORY BOARD

Dr. Yi Lin: Dr. Lin is currently the Chair of the Cellular Therapeutics Cross Disciplinary group at Mayo Clinic Cancer Center, an Associate Professor of Medicine, and a consultant in the Division of Hematology and the Division of Experimental Pathology at the Mayo Clinic in Rochester, MN.

Dr. Lin is a pioneer in cellular immunotherapy having participated in many of the first in human CART cell therapy trials and multiple phase 2 cellular immunotherapy clinical trials. Dr. Lin is also the author of over a hundred publications, including many pivotal cell therapy consensus statements and practice guidelines.

Dr. Lin is a key committee member of SITC (Society for Immunotherapy for Cancer), the IMWG (International Working Group on Myeloma), CIBMTR (Centre for International Blood and Marrow Transplant Research) and iwCART, the International Workshop on CART.

Dr. Lin completed her medical training at the Northwestern University Feinberg School of Medicine in Chicago, IL. Dr. Lin completed a residency at the Mayo Clinic College of Medicine in Rochester, MN, followed by a hematology and medical oncology fellowship.

Dr. Michael Bishop: Dr. Bishop is currently Professor of Medicine and Director, the David and Etta Jones Center for Cellular Therapy at the University of Chicago, a leading cellular therapy program in the United States.

Dr. Bishop is widely recognized as an expert in hematopoietic stem cell transplant and cellular therapy research and patient care, with a focus on leukemias and lymphomas. Dr. Bishop has a specific interest in managing patients that have not responded to first-line treatments and is working with his team to address the unique social, economic, physiological and biological issues that these patients face while undergoing treatment.

Dr. Bishop has served as an investigator for multiple clinical trials investigating novel cellular immunotherapies. Dr. Bishop is also an active contributor to medical literature, authoring more than 200 peer-reviewed articles, in addition to more than 35 book chapters and two books on cancer treatment and research. He also serves on the editorial board of numerous scientific journals, including *Biology of Blood and Marrow Transplantation*.

Dr. Bishop previously served as the Director of the Hematopoietic Stem Cell Transplantation Program at the University of Chicago and as a senior investigator and the clinical head of stem cell transplantation for the National Cancer Institute at the National Institutes of Health.

Dr. Eric Smith: Dr. Smith is the Director of Translational Research, Immune Effector Cell Therapies, head of the Eric Smith Lab for Synthetic Biology and Cellular Engineering at the Dana-Farber Cancer Institute and a member of the Faculty of Medicine at the Harvard Medical School in Boston, Massachusetts.

Dr. Smith specializes in cellular immunotherapy and hematological malignancies with a focus in multiple myeloma. Dr. Smith utilizes the latest advances in gene engineering and cellular manipulation to design and screen novel cellular therapy strategies which, working in close partnership with the Dana Farber technical operations team, he then translates to the clinic.

Dr. Smith spent the early part of his career in New York where he earned his MD and PhD (Genetics and Genomic Sciences) from the Mount Sinai School of Medicine, where he also trained as a research track resident in internal medicine. Dr. Smith then moved to Memorial Sloan Kettering Cancer Center for his medical oncology fellowship and further research training. Dr. Smith went on to serve as faculty and Director of Translational Development at the MSKCC Cellular Therapeutics Center before joining the Harvard Medical community at the Dana Farber Cancer Institute in mid-2020.

Dr. Smith's pre-clinical work has resulted in nine awarded or pending patents, multiple products stemming from his lab work have been translated to the clinic and he is an author of many seminal publications in the field.

Dr. David Maloney: Dr. Maloney is a Full Member of the Clinical Research Division, the Medical Director, Cellular Immunotherapy and the Bezos Family Immunotherapy Clinic and he holds the Leonard and Norma Klorfine Endowed Chair for Clinical Research at the Fred Hutchinson Cancer Research Center in Seattle, Washington.

Dr. Maloney is a renowned clinician-scientist who has been at the forefront of cellular therapy research and development with a primary focus in the development of chimeric antigen receptor (CAR) T cell therapy for a wide variety of cancers. Dr. Maloney has been a clinical investigator in over 15 cellular therapy clinical trials ranging from phase 1, first in human trials to commercially approved CART cell therapies.

Dr. Maloney's long-standing research interest is in the development of immunotherapies for lymphoma, myeloma, CLL, and ALL. Dr. Maloney was instrumental in the development and testing of rituximab, the first antibody-based cancer drug on the market that transformed the treatment of certain leukemias and lymphomas.

Dr Maloney has amassed greater than 265 publications in peer-reviewed journals and has received the Presidential Award from the Society for Biological Therapy (now the Society for Immunotherapy of Cancer).

Dr Maloney received his MD and PhD in cancer biology from Stanford University, completed internship and residency in internal medicine at Brigham and Woman's Hospital and a fellowship in oncology at Stanford. In 1994 he joined the faculties of Fred Hutchinson Cancer Research Center and the University of Washington where he is currently a Professor of Medicine.

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