EDISON

Chimeric Therapeutics

Initiation of coverage

Scorpion venom CAR-T stalking GBM

Pharma & biotech

Chimeric Therapeutics is a newly formed Australia-based biotechnology company with a focus on oncology that has recently gone public on the ASX. In September, Chimeric announced that it in-licensed CLTX-CAR T, currently in Phase I, from the City of Hope National Medical Center for US$10m (payable over 30 months) as well as milestones and royalties. The initial focus of the programme will be glioblastoma multiforme (GBM) but it can be applied to other tumours, such as melanoma.

Year end	Revenue (A$m)	PBT* (A$m)	EPS* (A$)	DPS (A$)	P/E (x)	Yield (%)
06/20	0.0	(0.1)	(63.02)	0.0	N/A	N/A
06/21e	0.0	(16.3)	(0.05)	0.0	N/A	N/A
06/22e	0.0	(11.3)	(0.03)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding amortisation of acquired intangibles, exceptional items and share-based payments.

Using scorpion venom to target cancer

CLTX-CAR T uses a 36-amino acid peptide sequence first isolated from deathstalker scorpion venom chlorotoxin to help target the GBM tumour cells. This chlorotoxin has been shown to bind to a wide variety of GBM cells in preclinical testing, which may make it a better GBM-targeting mechanism than others currently being tried.

GBM remains an unmet medical need

GBM accounts for 60% of brain tumours in adults and continues to have a poor prognosis with five-year survival of only 5.1%. Surgery, radiation and temozolomide are the current standards of care but patients typically recur due to the infiltrative nature of the GBM tumours.

Phase I has begun

The Phase I study dosed its first patient in September 2020 (two patients total have been dosed so far) and expects to enrol approximately 18 patients with recurrent/progressive glioblastoma. The goal of the study will be to determine a maximum tolerated dose schedule and a recommended dosing plan for the Phase II trial as well as to get initial evidence of efficacy and assess safety.

Valuation: A$307m or A$0.93 per basic share

We value Chimeric at A$307m or A$0.93 per basic share (A$0.87 per diluted share) using a risk-adjusted net present value (NPV) model. Key assumptions of our model include A$3,210m in peak sales, a launch in 2027 and a 10% probability of success due to the fact the programme is in Phase I. Following an IPO on the ASX, the company had A$36.9m in net cash and we estimate a need to raise an additional A$52.5m through 2026 to fund operations based on the current business plan, which, while modelled as illustrative debt, may lead to significant dilution if raised through equity depending on the prevailing stock price of such issuance(s).

19 January 2021

Price	**A$0.30**
Market cap	**A$97m**
	A$1.29/US$
Net cash (A$m) at 30 June 2020 (pro-forma)	36.9
Shares in issue	330.5m
Free float	N/A
Code	CHM
Primary exchange	ASX
Secondary exchange	N/A

Share price performance

N/A

%	1m	3m	12m
Abs	N/A	N/A	N/A
Rel (local)	N/A	N/A	N/A
52-week high/low		N/A	N/A

Business description

Chimeric Therapeutics is an oncology-focused Australia-based company that recently went public on the ASX. The lead programme is CLTX-CAR T, currently in Phase I for the treatment of GBM. This is an innovative approach for an unmet medical need. Beyond GBM, the technology may have applicability for other tumours such as melanoma.

Next events

Initial Phase I data	H1 CY21

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Edison profile page

Chimeric Therapeutics is a research client of Edison Investment Research Limited

Investment summary

Company description: A focus on oncology

Chimeric Therapeutics is an Australia-headquartered healthcare company formed in 2020 that is focused on CLTX-CAR T, a Phase I programme in GBM that it licensed from the City of Hope National Medical Center in September 2020. CLTX-CAR T uses a 36-amino acid peptide sequence first isolated from deathstalker scorpion venom chlorotoxin. This chlorotoxin has been shown to bind to a wide variety of GBM cells in preclinical studies, which may make it a better GBM-targeting mechanism than others currently being tested. The Phase I study dosed its first patient in September 2020 (two total so far) and expects to enrol approximately 18 patients with recurrent/progressive glioblastoma.

Valuation: A$307m or A$0.93 per basic share

We are initiating coverage of Chimeric Therapeutics at A$307m or A$0.93 per basic share (A$0.87 per diluted share) using a risk-adjusted NPV model focusing strictly on the CLTX-CAR T programme. We attribute a 10% chance of success to CLTX-CAR T, our standard probability of success for a programme in Phase I. We are also modelling peak sales of A$3,210m and launch in 2027. We will adjust our assumptions as CLTX-CAR T advances through clinical studies.

Financials: IPO provides funds into FY23

Chimeric reported pro-forma cash and cash equivalents of A$36.9m following its IPO on the ASX. Based on our estimates for burn rates (operating cash burn of A$16.2m and A$11.2m for FY21 and FY22, respectively), this cash should last the company into FY23. We project a need to raise an additional A$52.5m through 2026 to fund operations based on the current business plan, modelled as illustrative debt. As the company has little operating history, we may need to adjust our operating expense estimates when the company reports its semi-annual financials in the coming months.

Sensitivities: Development and commercial risk

There is significant development risk for the CLTX-CAR T programme as it is targeting a historically intractable cancer and we have not yet seen human efficacy data for it. However, chlorotoxin has been shown to bind to a wide variety of GBM cells, which may make it a better GBM-targeting mechanism than others that have been examined. Further, CAR T therapies to date have been approved for hematologic tumours only and there may be additional delivery challenges associated with generating efficacy in solid tumours such as GBM. With regards to commercial risk, it is hard to predict what the GBM treatment paradigm will look like in 2027 and whether other therapies may be approved by then, though the lack of treatment options may mean it will look a lot like today as GBM is a very difficult disease to find an effective treatment for. Also, while there are a lot of CAR T programmes ongoing for GBM, most are sponsored by academia and not by well-funded corporates that can develop the medicines to approval. Additionally, if the data is strong enough, the approval timeline may be accelerated due to the high unmet medical need in GBM. There is also operating risk as the company was only recently founded in 2020, with the management team joining in Q4. However, management is experienced, with the chief operating officer coming from Kite Pharma/Gilead and the chief medical officer coming from Legend Biotechnology, a US$3.7bn Nasdaq-listed firm. They provide Chimeric with a greater level of experience than for many other firms at the same stage. The company also faces financing risks, which could lead to potentially significant dilution if funding needs are met through equity issuances. Share issuance over the next few years may be higher than current shares outstanding, depending on the prevailing stock price at the time of such raise(s).

Company description: Innovation in oncology

Chimeric Therapeutics is a relatively new company that in-licensed the CLTX-CAR T programme from the City of Hope National Medical Center in September 2020. The initial focus of the new programme will be GBM, but it could potentially also be applied to other tumour types, especially those of neuroectodermal origin (primarily brain but also including melanomas and small cell lung cancer).

Exhibit 1: Chimeric Therapeutics pipeline

Programme	Indication	Status	Partners	Comments
CLTX-CAR T	GBM	Phase I	None	Licensed from City of Hope. Phase I initiated in Q320. Clinicaltrials.gov NCT04214392

Source: Chimeric Therapeutics

Targeting GBM with scorpion venom

In September 2020, Chimeric announced it had in-licensed the worldwide rights to develop and commercialise the CLTX-CAR T programme from the City of Hope National Medical Center. Under the terms of the agreement, Chimeric will pay US$10m in six instalments over 30 months. There are also potential development, regulatory and commercial milestones as well as a single-digit royalty and a 5% equity stake in the company.

Exhibit 2: City of Hope licence agreement milestones

Event	Milestone type	Milestone
Dosing of fifth patient in Phase I	Development	US$0.35m
Dosing of first patient in Phase II	Development	US$0.75m
Dosing of the first patient in Phase III	Development	US$2m
Receipt of the first Orphan Drug Designation	Regulatory	US$1m
Marketing approval in the United States	Regulatory	US$6m
Marketing approval in Europe	Regulatory	US$6m
Marketing approval in each of the first five jurisdictions other than the United States and Europe	Regulatory	US$1m (US$5m total)
Upon net sales of US$250m in a year	Commercial	US$18.75m
Upon net sales of US$500m in a year	Commercial	US$35.5m

Source: Chimeric Therapeutics Prospectus

With regards to the technology, typically, CAR T therapies use a monoclonal antibody sequence in their targeting domain, which enables the CAR T cells to recognise antigens and kill the tumour cells. In contrast, CLTX-CAR T uses a 36-amino acid peptide sequence first isolated from deathstalker scorpion (Leiurus quinquestriatus) venom chlorotoxin to help target the GBM tumour cells. Chlorotoxin has been used as an imaging agent as it has been established to bind broadly and specifically to GBM and other neuroectodermal tumours, while minimally binding to non-cancerous cells both in the brain and elsewhere in the body (see Exhibit 3) based on preclinical testing. This ability to bind specifically to tumour cells while leaving normal cells largely alone should help limit the toxicities associated with the therapy while maintaining efficacy. In mouse models, CLTX-CAR T injection showed little to no evidence of adverse reactions such as neurological symptoms or loss of body weight while demonstrating robust anti-tumour activity.[1]

Chlorotoxin is able to target GBM tumour cells by binding to matrix metalloproteinase-2 (MMP-2), which is also expressed in a variety of tumours including melanoma, breast cancer and lung cancer. MMP-2 is not significantly expressed in surrounding or healthy brain tissue but may be expressed more heavily in other tissues (such as the lung, bladder and female organs), although the data to date suggests that chlorotoxin binds minimally to non-cancerous cells both inside and outside the

1 Wang et al., Chlorotoxin-directed CAR T cells for specific and effective targeting of glioblastoma. *Science Translational Medicine*. 12, eaaw2672 (2020)

brain. Further, any risk for off-target effects would likely be mitigated by the very localised employed drug delivery approach for CLTX-CAR T (details below).

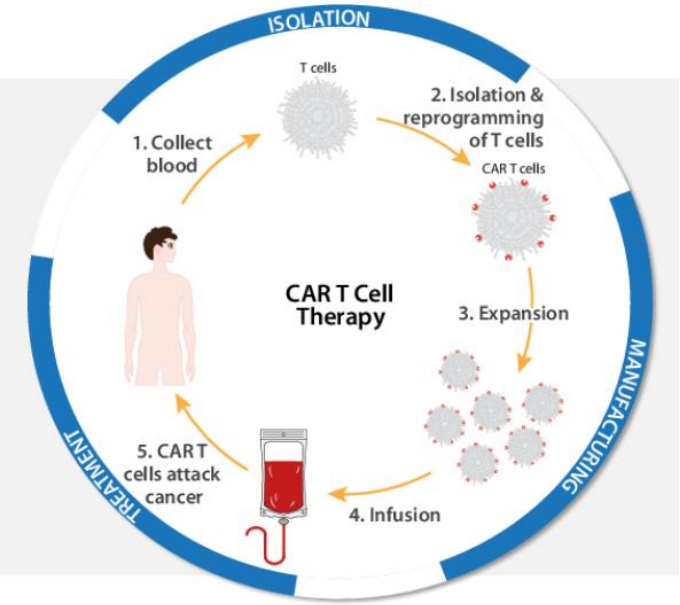
Exhibit 3: Reactivity of chlorotoxin to different cell types

Cell type	Type	% positive
Glioblastoma grade IV	Primary brain tumour	100
Anaplastic astrocytoma grade III	Primary brain tumour	100
Medulloblastoma	Peripheral neuroectodermal tumour	100
Melanoma	Peripheral neuroectodermal tumour	100
Pilocytic astrocytoma Grade I	Primary brain tumour	93
Neuroblastoma	Peripheral neuroectodermal tumour	89
Ewing's Sarcoma	Peripheral neuroectodermal tumour	83
Other gliomas	Primary brain tumour	80
Normal brain or uninvolved tissue of brain cancer patients	Noncancer	28
Epilepsy/gliosis/stroke/Parkinson's/Alzheimer's brain tissue	Noncancer	0
Cells from various parts of the body outside the brain	Noncancer	0

Source: Lyons et al., Chlorotoxin, a Scorpion-Derived Peptide, Specifically Binds to Gliomas and Tumors of Neuroectodermal Origin. *GLIA* 39:162–173 (2002)

CLTX-CAR T is currently in a Phase I trial, run at the City of Hope Medical Center (Duarte, California) in 18 patients with recurrent or progressive glioblastoma. CLTX-CAR T is an autologous therapy developed from the patient's own cells (see Exhibit 4). Patients receive the therapy via dual delivery (via intratumoral and intraventricular injection, both of which are local, which should help limit systemic side effects) for three weekly cycles over 28 days on an outpatient basis. Each treatment cycle begins with one or two CLTX-CAR T cell infusions (one at each catheter site) and lasts for one week. There will be three dosing cohorts ranging from 44m to around 440m cells. Patients will be able to continue with CLTX-CAR T treatment per principal investigator and participant discretion. Besides initial indications of efficacy, it will be important to learn more about the safety, especially the neurotoxicity profile of the treatment, given that CAR T therapies have frequently been associated with neurological toxicity. Additionally, key objectives of the study will be to determine a maximum tolerated dose schedule and a recommended dosing plan for the Phase II trial.

Exhibit 4: Illustration of autologous CAR T cell therapy process



Source: Chimeric

With regards to the timing of the development programme, the Phase I trial dosed its first patient in September and is scheduled to complete in 2023. However, we believe the programme can be accelerated once initial patient responses are seen. If the programme yields positive data, the FDA

may grant a breakthrough therapy designation (BTD), which would help accelerate programme development. Gilead's Yescarta (axicabtagene ciloleucel), also a CAR T programme, was approved on the basis of a single-arm, open-label trial in 101 patients. Contingent on study results, Chimeric believes accelerated approval may be possible from a pivotal Phase II study with 50–75 patients (fewer patients than Yescarta mainly due to the level of unmet medical need and relative size of the market compared to Yescarta's approved indication in large-B-cell lymphomas).

We currently assume approval for CLTX-CAR T in GBM in 2027 though there is potential for acceleration if the data are strong enough. We also expect the company to begin development in additional cancers (such as melanoma, breast and lung), potentially as early as CY21.

The CAR T landscape

CAR T therapies have helped revolutionise the treatment of certain cancers. CAR T therapies work by engineering the body's immune T-cells to recognise cancer cells as they would invading or diseased cells. Novartis's Kymriah (tisagenlecleucel) was the first CAR T therapy approved in the US and was approved for relapsing B-cell acute lymphoblastic leukemia in children and young adults, who account for 60% of such cases. Kymriah consisted of a one-time treatment that had an 83% complete response rate in clinical trials with patients who did not respond to standard treatments. Like many revolutionary cancer therapies, Kymriah was priced at a premium of US$475,000 for the treatment. Kymriah sales in 2019 were US$278m. A second therapy, Yescarta, was approved later that year in patients with large-B-cell lymphomas whose cancer has progressed after receiving at least two prior treatment regimens. The therapy demonstrated a 51% complete response rate and has a price of US$373,000 per treatment (though without a performance-based component). Sales in 2019 for Yescarta were US$456m. It is important to note that Gilead acquired Yescarta through its purchase of Kite Pharmaceuticals for US$11.9bn.

With the success of CAR T in hematologic cancers, there has been a surge in development across all cancer indications. Within GBM there appear to be 15 separate active trials (see Exhibit 5) using a variety of targets.

Exhibit 5: CAR T pipeline for GBM

Trial name	Phase	Patients	Target	Sponsor
B7-H3 CAR T for Recurrent or Refractory Glioblastoma	I/II	40	B7H3	BoYuan RunSheng Pharma
Autologous CAR-T/TCR-T Cell Immunotherapy for Solid Malignancies	I/II	50	EGFRvIII	Shenzen BinDeBio
CD147-CART Cells in Patients With Recurrent Malignant Glioma.	I	31	CD147	Xijing Hospital
CART-EGFRvIII + Pembrolizumab in GBM	I	7	EGFRvIII	University of Pennsylvania
Chimeric Antigen Receptor (CAR) T Cells With a Chlorotoxin Tumor-Targeting Domain for the Treatment of Recurrent or Progressive Glioblastoma	**I**	**18**	**CLTX**	**City of Hope/Chimeric**
IL13Ralpha2-Targeted Chimeric Antigen Receptor (CAR) T Cells With or Without Nivolumab and Ipilimumab in Treating Patients With Recurrent or Refractory Glioblastoma	I	60	IL13Rα2	City of Hope
NKG2D-based CAR T-cells Immunotherapy for Patient With r/r NKG2DL+ Solid Tumors	I	10	NKG2D	Jiujiang University Affiliated Hospital
Intracerebral EGFR-vIII CAR T Cells for Recurrent GBM	I	24	EGFRvIII	Duke
Genetically Modified T-cells in Treating Patients With Recurrent or Refractory Malignant Glioma	I	92	IL13Rα2	City of Hope
Memory-Enriched T Cells in Treating Patients With Recurrent or Refractory Grade III-IV Glioma	I	42	HER2	City of Hope
Brain Tumor-Specific Immune Cells (IL13Ralpha2-CAR T Cells) for the Treatment of Leptomeningeal Glioblastoma, Ependymoma, or Medulloblastoma	I	30	IL13Rα2	City of Hope/Mustang Bio
C7R-GD2.CAR T Cells for Patients With GD2-expressing Brain Tumors (GAIL-B)	I	34	C7R-GD2	Baylor
EGFR806-specific CAR T Cell Locoregional Immunotherapy for EGFR-positive Recurrent or Refractory Pediatric CNS Tumors	I	36	EGFR806	Seattle Children's Hospital
HER2-specific CAR T Cell Locoregional Immunotherapy for HER2-positive Recurrent/Refractory Pediatric CNS Tumors	I	48	HER2	Seattle Children's Hospital
Personalized Chimeric Antigen Receptor T Cell Immunotherapy for Patients With Recurrent Malignant Gliomas	I	100	CD133/ EGFRvIII	Beijing Mario Biotech

Source: Clinicaltrials.gov

Out of those 15 only five are sponsored by companies (the rest are academic) with Chimeric and Mustang Bio being the only sponsors outside of China. Mustang Bio announced the initiation of its Phase I trial in December 2020, however the company does not appear to emphasise its GBM programme as much as its others. This indicates that Chimeric has the opportunity to be a leader in this area if it is able to advance the CLTX-CAR T programme.

The GBM market

GBM is the most common and aggressive brain tumour and accounts for approximately half of all gliomas.[2] According to the National Cancer Institute there are approximately 23,820 cases per year of brain and other nervous system cancers in the US, and another 64,600 in Europe according to the International Agency for Research on Cancer. We estimate around 12,000 of these are GBM in the US with another 32,000 in Europe. The survival rate of GBM is especially poor with a five-year survival rate of only 5.1% and a median overall survival of 10 months.[3]

Therapeutic options are limited. Since 2005, only three new treatments have been approved for GBM: temozolomide, bevacizumab and tumour-treating fields (TTFields). The current standard of care for newly diagnosed GBM is a combination of surgery, radiation and temozolomide with recurrence occurring due to resistance to temozolomide.

GBM is a difficult indication for all therapies for two key reasons. First the cells are heterogeneous so that the expression of different targets can vary greatly between tumours (see Exhibit 6). And second, due to antigen escape (loss or downregulation of the target antigen), recurrent tumours may have far different expression patterns than the original tumour. With regards to CAR T, both of these are issues that affect constructs that target EGFR, HER2 and IL13Rα2, but so far do not seem to greatly affect CLTX-CAR T, at least not in the preclinical setting.[4]

Exhibit 6: Common mutations in GBM

Name	Function	Expression status	Prevalence	Prognosis
EPHA3	Regulation of adhesive and repulsive mechanisms including cell motility and adhesion	Overexpressed	40–60%	Poor; over-expression common in recurrent GBM
EGFR	Regulation of processes involved in cell growth, division and survival	Overexpressed	40–60%	Poor; over-expression common in recurrent GBM
MGMT	Prevention of mismatch errors	Methylated	40–60%	Favourable
CDKN2A	Regulation of cell cycle and retinoblastoma activation	Decreased	49–52%	Poor
PTEN	Regulation of cell signalling, involved in cell proliferation and survival	Deleted and/or mutated	34%	Poor
PIK3CA	Regulation of processes involved in cell growth, division and survival	Overexpressed and/or mutated	15%	Poor
PDGFRA	Regulation of processes involved in cell growth, division and survival	Overexpressed	13%	Poor
IDH1	Production of NADPH	Mutated	5–10%	Favourable
MDM2	Regulation of p53 activity	Overexpressed	8–9%	Unclear
MET	Regulation of proliferation, survival and motility	Overexpressed and/or mutated	4–6%	Poor
SF/HGF	Activating ligand for HGFR/c-MET tumour growth and angiogenesis	Overexpressed	1.6–4%	Poor

Source: Taylor et al., Glioblastoma Multiforme: An Overview of Emerging Therapeutic Targets. *Frontiers in Oncology*. September 2019, Volume 9, Article 963

Outside of CAR T, there are some other potentially interesting therapies in development for GBM. One is marizomib, which is being developed by Bristol Myers for newly diagnosed GBM (note CLTX-CAR T is intended for recurrent GBM so they would not be necessarily competing therapies).

2 Hanif et al., Glioblastoma Multiforme: A Review of its Epidemiology and Pathogenesis through Clinical Presentation and Treatment. *Asian Pacific Journal of Cancer Prevention*. 18 (1), 3–9

3 Taylor et al., Glioblastoma Multiforme: An Overview of Emerging Therapeutic Targets. *Frontiers in Oncology*. September 2019, Volume 9, Article 963

4 Wang et al., Chlorotoxin-directed CAR T cells for specific and effective targeting of glioblastoma. *Science Translational Medicine*. 12, eaaw2672 (2020)

It is an irreversible proteasome inhibitor that crosses the blood brain barrier and is in a 749-patient Phase III trial for newly diagnosed GBM patients in combination with temozolomide and radiotherapy. It has limited monotherapy efficacy (3.3% objective response rate in the monotherapy arm from the Phase I/II) but may have some efficacy in combination (34.3% objective response rate in combination with bevacizumab compared to 21.9% historically for bevacizumab alone). Another therapy under development is regorafenib, a multikinase inhibitor that is approved under the brand name Stivarga for hepatocellular carcinoma, colorectal cancer and gastrointestinal stromal tumour. First approved in 2012 and marketed by Bayer, it had US$460m in sales in 2019. Data from a Phase II trial indicated it was able to increase median overall survival in recurrent GBM from 5.6 months to 7.4 months. It is in a Phase II/III 550-patient in newly diagnosed and recurrent GBM patients.

Our estimates for CLTX-CAR T in GBM are based on the assumptions that around half of the approximately 12,000 GBM patients in the US and 32,000 patients in Europe will be eligible for therapy following recurrence. There is no hard data on the size of this market but this is around where Roche, the manufacturer of bevacizumab, has estimated the market size. We then estimate that at peak the market share for CLTX-CAR T will be 20% of these patients in the US and 15% in the EU (slightly lower than the US due to cost). This may prove conservative if the therapy fulfils its promise of being as effective as the currently approved CAR Ts but with minimal toxicity, as it would be one of the only therapies available for GBM if approved. Also, there is the potential for CLTX-CAR T to move to frontline therapy in GBM as the indication as a whole is an unmet medical need, not just the segment in patients with recurrence. However, as we currently have no human clinical data, approval is not likely until 2027 (and hence we do not know what the competitive landscape may look like at that point) and as the mode of administration is rather invasive, we believe conservatism is prudent.

Using a US$375,000 price per patient per course of therapy (which is currently a discount to what Novartis is charging for Kymriah and approximately in line with Gilead's Yescarta) we arrive at peak sales (globally, including both the US and Europe) of US$1,922m (A$3,210m) a year for the therapy. It is important to note that we are not currently modelling the receipt of a priority review voucher (PRV) following anticipated approval of the programme. If approved, we believe CLTX-CAR T would likely be eligible to receive a PRV through the rare paediatric disease designation pathway. As a reminder, a PRV can be used to gain priority review for a subsequent compound and can be sold. Based on recent transactions the value of a PRV is around US$100m. In March 2019, GW Pharmaceuticals sold a PRV to Biohaven for US$105m and in August 2019, Sobi announced a sale of a PRV to AstraZeneca for US$95m.

We apply a 10% probability of success, our standard level for therapies at this stage of development. We also model revenues out to 2039 as CLTX-CAR T would be eligible for 12-year exclusivity (given that it is a biologics drug) upon approval, which we project in 2027. There are patents pending in all major markets with an October 2016 filing date, indicating patent protection until at least 2036, which can be extended by up to five years in both the US and EU. Additionally, further patent applications may extend the life of patent protection for the product even further, if additional patents are granted.

Outside of GBM

The company is clearly focusing on the opportunity with GBM initially but as mentioned previously, the potential exists to expand into other tumours such as melanoma. Melanoma is a relatively common cancer and the National Cancer Institute estimates there will be approximately 100,350 new cases in the US in 2020 with another 144,209 cases in Europe according to the the International Agency for Research on Cancer. However, unlike with GBM, the five-year survival rate is relatively high at 92.7%, as 83% of cases are localised and can be removed, according to the

National Cancer Institute. However, in the 4% of people who have metastatic disease, five-year survival is reduced to 27.3%. Generally, these patients are either given chemotherapies such as dacarbazine or temozolomide or checkpoint inhibitors. If CLTX-CAR T is developed for melanoma, it would be one of the few treatments using the CAR T mode of action. Of the five ongoing CAR-T trials that include melanoma patients, four include multiple tumour types and do not necessarily focus on the indication.

Exhibit 7: CAR T pipeline for melanoma

Trial name	Phase	Patients	Target	Sponsor
Administering Peripheral Blood Lymphocytes Transduced With a CD70-Binding Chimeric Antigen Receptor to People With CD70 Expressing Cancers	I/II	124	CD70	National Cancer Institute
Autologous CAR-T/TCR-T Cell Immunotherapy for Malignancies	I/II	73	NY-ESO-1	Shenzhen BinDeBio
MB-CART20.1 Melanoma	I	15	CD20	Miltenyi Biomedicine GmbH
C7R-GD2.CART Cells for Patients With Relapsed or Refractory Neuroblastoma and Other GD2 Positive Cancers (GAIL-N)	I	94	C7R-GD2	Baylor
B7H3 CAR T Cell Immunotherapy for Recurrent/Refractory Solid Tumors in Children and Young Adults	I	68	B7H3	Seattle Children's Hospital

Source: Clinicaltrials.gov

Sensitivities

There is significant development risk for the CLTX-CAR T programme as it is targeting a historically intractable cancer and we have not yet seen human efficacy data for it. However, chlorotoxin has been shown to bind to a wide variety of GBM cells in preclinical testing, which may make it a better GBM-targeting mechanism than others that have been tried (though this needs to be demonstrated in human clinical trials). Further, CAR T therapies to date have been approved for hematologic tumours only and there may be additional delivery challenges associated with generating efficacy in solid tumours such as GBM.

With regards to commercial risk, it is hard to predict what the GBM treatment paradigm will look like in 2027 and whether other therapies may be approved by then, though the lack of treatment options may mean it may look a lot like today as it is a very difficult disease to find an effective treatment for. Also, while there are a lot of CAR T programmes ongoing for GBM, most are sponsored by academia and not by well-funded corporates that can develop the medicines to approval. Additionally, if the data is strong enough, the approval timeline may be accelerated due to the high unmet medical need in GBM. There is also operating risk as the company was only recently founded in 2020, with the management team joining in Q4. However, management comes from established biopharmaceutical companies, providing Chimeric with a greater level of experience than many other firms at the same stage. Chimeric's chief operating officer (COO) is Jennifer Chow, who was head of global marketing, analytics and commercial operations at Kite Pharmaceuticals/Gilead Sciences. She was responsible for assessing and prioritising research and external assets for commercial development at the CAR T focused company. Prior to that, she was global cell therapy commercial lead at Celgene where she was responsible for designing and developing a global commercial strategy for CAR T. The chief medical officer, Syed Rizvi, was vice president of clinical development & medical affairs at Legend, a US$3.7bn Nasdaq-listed firm. Prior to Legend, he was head of the CAR-T programme in Global Medical Affairs at Celgene, responsible for the strategic direction of the CAR-T and immuno-oncology portfolios.

The company also faces risks associated with the need to raise financing to execute its business plan, which can lead to potentially significant dilution if funding needs are met through equity issuances. Share issuance over the next few years may be higher than current shares outstanding, depending on the stock price at the time of any such raise(s).

Valuation

We are initiating coverage of Chimeric Therapeutics at A$307m or A$0.93 per basic share (A$0.87 per diluted share) using a risk-adjusted NPV model focusing strictly on the CLTX-CAR T programme. We attribute a 10% chance of success to CLTX-CAR T, our standard probability of success for a programme in Phase I. We are also modelling peak sales of A$3,210m and a launch in 2027. We will adjust our assumptions as CLTX-CAR T advances through clinical studies.

Exhibit 8: Chimeric valuation table

Product	Main indication	Status	Probability of successful commercialisation	Approval year	Peak sales (A$m)	Economics	rNPV (A$m)
CLTX-CAR T	GBM	Phase I	10%	2027	3,210	100% less single digit royalty to COH	269.8
Total							269.8
Net cash (as of 30 June 2020 + IPO)							36.9
Total firm value (A$)							306.72
Total basic shares (m)							330.5
Value per basic share (A$)							0.93
Options (m)							23.0
Total number of shares (m)							353.5
Diluted value per share (A$)							0.87

Source: Edison Investment Research

Financials

Chimeric reported a minimal level of cash as of 30 June 2020 and proceeded to raise A$4.3m worth of convertible debt on 1 September. The debt is payable in company shares that are expected to convert at the IPO (assuming conversion, noteholders would own approximately 9% of the company). The pro-forma cash and cash equivalents is expected to be A$36.9m following Chimeric's IPO on the ASX. Use of funds over the next 24 months has been estimated by the company to include A$11.2m in SG&A and employment expenses, A$7.0m in licence fees to City of Hope and A$5.6m in Phase I clinical trial costs and manufacturing.

The company has also stated that it may spend (also over the next 24 months) an additional A$1.9m on R&D on additional cancer targets, A$5m on additional sites for the Phase I and A$5m on other commercial and academic collaborations, but we believe that these spending initiatives will depend on the clinical data as well as market conditions.

Based on our estimates for burn rates (operating cash burn of A$16.2m and A$11.2m for FY21 and FY22, respectively), the company's current cash on hand should last the company into FY23. We project a need to raise an additional A$52.5m through 2026, modelled as illustrative debt, to fund operations based on the current business plan. As the company is new with little operating history, we may need to adjust our operating expense estimates as the company proceeds with its business plan.

Exhibit 9: Financial summary

A$'000s	2020	2021e	2022e
Year end 30 June	AIFRS	AIFRS	AIFRS
PROFIT & LOSS			
Revenue	0	0	0
Cost of Sales	0	0	0
Gross Profit	0	0	0
Sales, General and Administrative Expenses	(64)	(7,203)	(4,007)
Research and Development Expense	0	(9,068)	(7,254)
EBITDA	(64)	(16,271)	(11,261)
Operating Profit (before amort. and except.)	(64)	(16,271)	(11,261)
Intangible Amortisation	0	0	0
Other	0	0	0
Exceptionals	0	0	0
Operating Profit	(64)	(16,271)	(11,261)
Net Interest	0	0	0
Other	0	0	0
Profit Before Tax (norm)	(64)	(16,271)	(11,261)
Profit Before Tax (FRS 3)	(64)	(16,271)	(11,261)
Tax	0	0	0
Deferred tax	(0)	(0)	(0)
Profit After Tax (norm)	(64)	(16,271)	(11,261)
Profit After Tax (FRS 3)	(64)	(16,271)	(11,261)
Average Number of Shares Outstanding (m)	0.0	335.5	338.9
EPS - normalised (c)	(6,200.80)	(4.85)	(3.32)
EPS - Reported (A$)	(63.02)	(0.05)	(0.03)
Dividend per share (c)	0.0	0.0	0.0
BALANCE SHEET			
Fixed Assets	0	15,983	16,793
Intangible Assets	0	15,185	15,165
Tangible Assets	0	798	1,628
Other	0	0	0
Current Assets	(0)	24,742	13,117
Stocks	0	0	0
Debtors	0	0	0
Cash	(0)	19,941	7,948
Other	0	4,801	5,169
Current Liabilities	(64)	(16,219)	(16,219)
Creditors	(30)	(16,219)	(16,219)
Short term borrowings	(34)	0	0
Long Term Liabilities	0	0	0
Long term borrowings	0	0	0
Other long term liabilities	0	0	0
Net Assets	(64)	24,506	13,691
CASH FLOW			
Operating Cash Flow	(34)	(16,171)	(11,161)
Net Interest	0	0	0
Tax	0	0	0
Capex	0	(800)	(832)
Acquisitions/disposals	0	0	0
Financing	0	32,646	0
Dividends	0	0	0
Other	0	0	0
Net Cash Flow	(34)	15,675	(11,993)
Opening net debt/(cash)	0	34	(19,941)
HP finance leases initiated	0	0	0
Exchange rate movements	0	0	0
Other	0	4300	0
Closing net debt/(cash)	34	(19,941)	(7,948)

Source: company accounts, Edison Investment Research

Contact details	Revenue by geography	Re
The CFO Soluton Level 3, 62 Lygon Street, Carlton Victoria 3053 +61 83 98245254 www.chimerictherapeutics.com/	N/A	

Management and board

Executive chairman: Paul Hopper	Chief operating officer (COO): Jennifer Chow
Paul Hopper is the founder of Chimeric Therapeutics. He has over 25 years' experience in the biotech, healthcare and life sciences sectors. Focused on start-up and rapid growth companies, he has served as either founder, chairman, non-executive director or CEO of more than 14 companies in the US, Australia and Asia. Previous and current boards include Viralytics, Imugene, Prescient Therapeutics, Polynoma and Suda Medical. His experience covers extensive fund-raising in the US, Australia, Asia and Europe, and he has deep experience in corporate governance, risk and strategy. He also has many years' experience in providing corporate advice and guidance, financial analysis and management of companies of differing sizes and financial circumstances.	Until recently Ms Chow was Head of Global Marketing, Analytics and Commercial Operations at leading global CAR T company Kite Pharmaceuticals (acquired by Gilead Sciences in 2017 for US$11.9bn). Ms Chow was responsible for assessing and prioritizing research and external assets for development, ensuring optimal clinical development of the Kite pipeline for global commercialisation. Ms Chow has more than 20 years of commercial strategy and marketing experience focused in cellular therapy, haematology and oncology. Formerly Ms Chow was the Global Cell Therapy Commercial Lead at Celgene Corporation and was responsible for designing and developing the global CAR T commercial strategy and operating model. Ms Chow was also formerly at Roche, Nycomed/Takeda and Schering Canada.
Chief medical officer: Syed Rizvi	**Director (non-executive): Leslie Chong**
Dr Syed Rizvi joined the company in 2020. Prior to that, he served as vice president of clinical development and medical affairs at Legend Biotech. Dr Rizvi brings more than 20 years of successful oncology drug development experience and has been responsible for setting the medical/clinical strategy for clinical development resulting in new indications and potential label expansion. Before Legend, he was Celgene's head of the CAR-T programme in Global Medical Affairs and also served as head of hematology for US Medical Affairs. At Celgene, he was responsible for the strategic direction and management of the CAR-T and immuno-oncology therapy portfolios, built a comprehensive clinical research alliance, and developed an immuno-oncology network with researchers to harness scientific discovery for targeted patient outcomes. Prior to Celgene, Dr Rizvi held global clinical leadership roles in oncology programs at Novartis Oncology and Merck.	Leslie Chong has more than 21 years of oncology experience with comprehensive clinical development experience in global Phase I–III studies from start-up to registration. She was senior clinical program lead at Genentech, one of the world's most successful biotech businesses, developing therapies across all cancer indications. She was previously at global majors GlaxoSmithKline and Exelixis in cancer therapy development. She has development experience in oncology with small molecules, immunotherapies, cancer vaccines, oncolytic viral therapies, epigenetics, monoclonal antibodies et al. Ms Chong has extensive experience in leading clinical development of brain cancer therapies. Ms Chong is currently chief executive officer and managing director of Imugene Limited; and non-executive director of Cure Brain Cancer Foundation.

Principal shareholders	(%)
Paul Hopper	25.0

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