

## CHIMERIC PIONEERS IN CELL THERAPY

Investor Update | July 2024

ASX: CHM



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**ASX:CHM** 



#### **INVESTMENT HIGHLIGHTS**

4 phase 1/1b clinical trials under 3 FDA INDs at 4 leading US centres

Multiple clinical updates in the next 12mths

Experienced leadership team (ø) in cell therapy clinical development

CHM-CDH17 a the ONLY CDH17 CAR-T in clinical trials

First in class CLTX-CAR for brain cancer

Robust and long life ••• patent portfolio

#### **CORPORATE PROFILE**

Exchange **ASX:CHM** 

Share Price \$0.02

52 Week Range \$0.018- 0.047

Market Cap ~\$16M

Shares on issue 841M

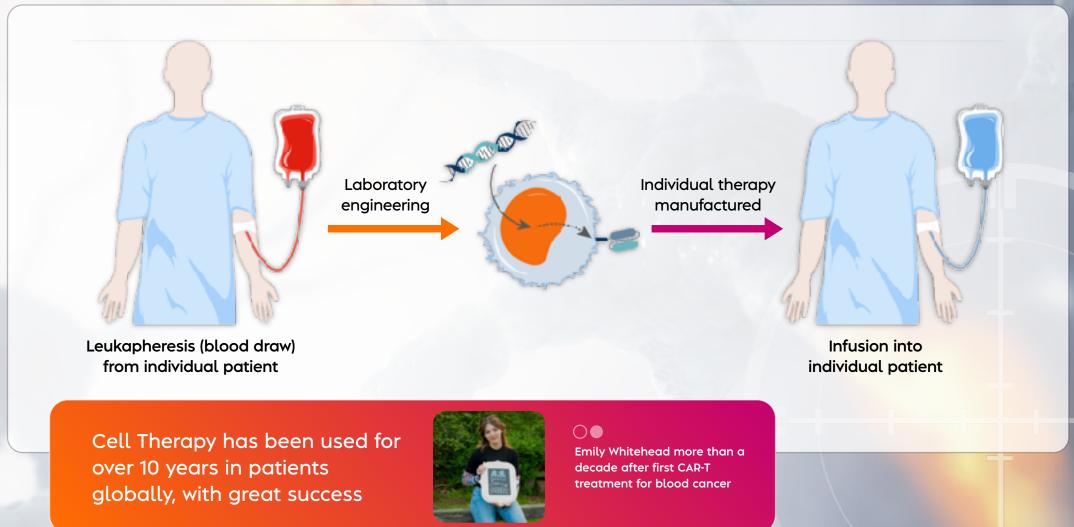
**IPO 2022** 

Capital Raised since IPO \$69M

Major Shareholder: Paul Hopper 11.1%

#### **CAR-T CELL THERAPY EXPLAINED**

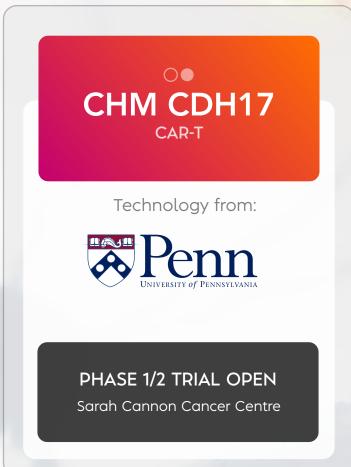
Use a patients own blood cells to make their individualised cancer therapy

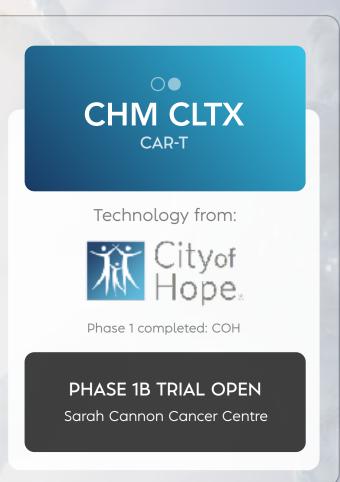




#### **CHM: BROAD PORTFOLIO**

3 Novel cell therapies; 4 Clinical Trials







# THE ONLY CDH17 CAR-T GLOBALLY IN CLINICAL TRIALS

CDH17

#### CDH17 OVERVIEW



CDH17 is protein on the surface of Gastrointestinal cancers (green on purple cells in picture)

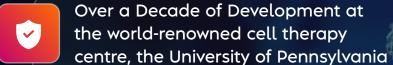


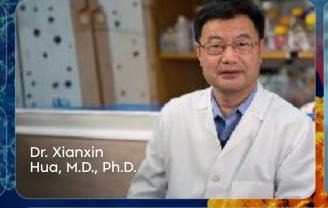
Compelling pre-clinical efficacy in Gastric, Pancreatic and Neuroendocrine cancers



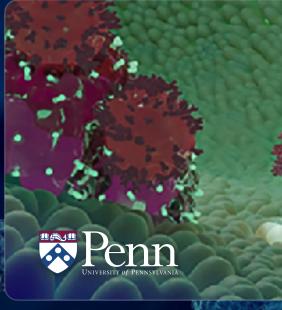
Pre-clinical models indicate no toxicity on healthy cells











#### INTENSE SCIENTIFIC INTEREST IN CDH17

200+ PUBLICATIONS IN PAST 2 YEARS



Biomater Res. 2024 Jun; 0041 (28)

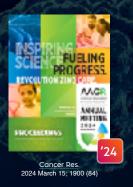
Cadherin 17 Nanobody-Mediated Near-Infrared-II Fluorescence Immunotoxin Delivery for Colorectal Cancer



Proteomics-Derived Biomarker Panel Facilitates Distinguishing Primary Lung Adenocarcinomas With Intestinal or Mucinous Differentiation From Lung Metastatic Colorectal Cancer



Novel CDH17-targeting antibodydrug conjugate exhibits anti-tumor efficacy in preclinical models of gastrointestinal cancers



TORL-3-600, a novel antibody drug conjugate directed against cadherin 17 (CDH17), has preclinical efficacy in colorectal, gastric, and pancreatic cancer



Cancer Cell Int. 2024 Feb; 67 (24)

Targeted drug delivery using nanobodies to deliver efective molecules to breast cancer cells: the most attractive application of nanobodies



J Exp Clin Cancer Res 2024 Jan 24; 31(43)

A complex of cadherin 17 with desmocollin 1 and p120-catenin regulates colorectal cancer migration and invasion according to the cell phenotype



Lung. 2023 Oct; 489-97(201)

Targeting CDH17 with Chimeric Antigen Receptor-Redirected T Cells in Small Cell Lung Cancer



Front. Pharmacol 2023 Sep; 1189799 (14)

Novel biomarkers used for early diagnosis and tyrosine kinase inhibitors as targeted therapies in colorectal cancer



JCO Glob Oncol 2023 Aug; 25 (9)

Phase 1A, first-in-human study of ARB202, bispecific antibody to CDH17 and CD3, in advanced gastrointestinal malignancies expressing CDH17



Development of allogenic nonviral RNA-based CAR-NK therapy targeting CDH17 in relapsed/ refractory gastrointestinal cancer



Sci Rep. 2023 Apr; 6493 (13)

Molecular mechanism underlying the increased risk of colorectal cancer metastasis caused by single nucleotide polymorphisms in LI-cadherin



A phase la/lb, open-label, dose escalation study of the TRAILR2 agonist BI 905711 in combination with chemotherapy (CT) in patients (pts) with advanced GI cancers



2023 Feb; 115 (41)

A phase la/b first-in-human, openlabel, multicenter study of BI 905711, a bispecific TRAILR2 agonist, in patients with advanced gastrointestinal cancers



Cancers. 2023 Feb; 1171 (15)

CAR-Based Immunotherapy of Solid Tumours-A Survey of the Emerging Targets



Cancers. 2023 Jan; 158 (15)

Integrative Clinical and DNA Population-Based Cohort Identifies CDH17 and LRP2 as Risk Recurrence Factors in Stage II Colon Cancer



Nat Cancer. 2022 May; (3)

CDH17-directed CAR T cells for solid tumors



#### CHM CDH17 IS THE FIRST CDH17 TARGETING CAR-T IN CLINICAL TRIALS

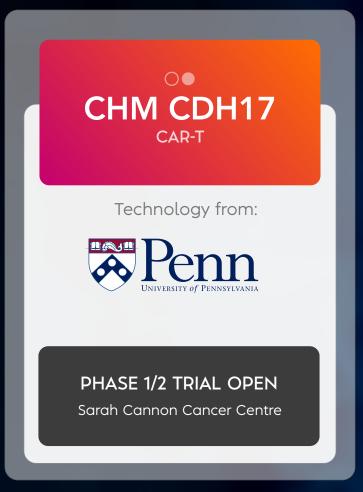
COMPANY	CHIMERIC THERAPEUTICS	ARBELE	T NA R L	Boehringer Ingelheim
ASSET	CHM-CDH171	Cabomatig2,8	TORL-3-6003,6	BI 9057114,5,7
PHASE	Phase 1/2	Phase 1	Phase 1	Phase 1
MODE	CAR-T	Antibody	Antibody	Antibody
INDICATIONS	Solid tumors (NET; CRC; GC) <sup>1</sup>	Solid tumors (Cholangio.; Liver cancer; CRC.; Panc.; G/GEJC; Eso.) <sup>2</sup>	Solid tumors (CRC) <sup>3</sup>	Solid tumors (CRC; GC; Eso.; Pan.; Cholangio.; GBC; SIA )4,5

References: 1. CHM-2101 trial; 2. Cabomatig trial; 3. TORL-3-600 trial; 4. BI 905711 trial1; 5. BI 905711 trial2; 6. TORL PR; 7. BI 905711 ASCO GI'23 Results; 8. Arbele Pipeline



#### CHM CDH17 CAR-T PHASE 1 RECRUITING

The first CDH17 CAR T cell therapy in clinical trials in the world.



### PERSONALISED CAR-T: AUTOLOGOUS

First in class CDH17 CAR T for gastrointestinal cancers

FDA IND clearance: Nov 23

Manufacturing: **GMP Ready** 

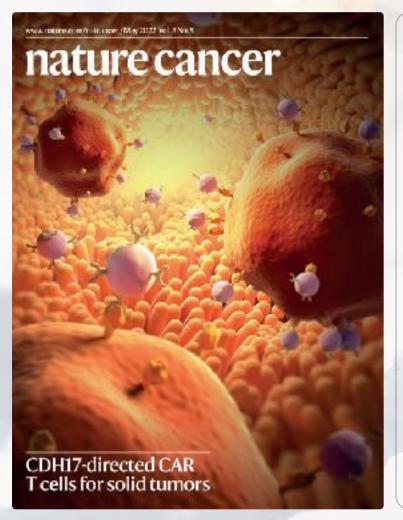
Phase 1/2 Trial Open in Colorectal, Gastric and Neuroendocrine Cancers

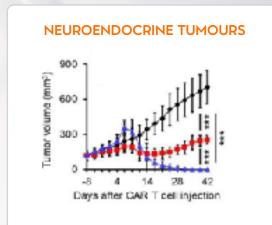
N= 15 patients

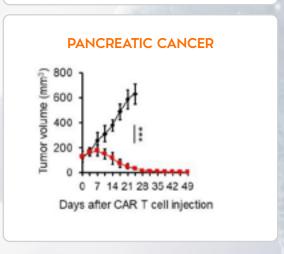


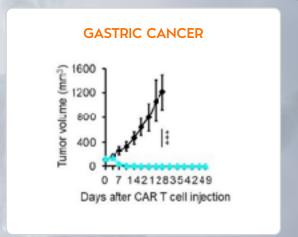
#### **ENCOURAGING PRE-CLINICAL RESULTS**

CDH17 CAR T induced complete eradication of tumours with no relapse in seven mouse models















#### CHM CDH17 CLINICAL DEVELOPMENT STRATEGY

FDA IND approved phase 1/2 | Clinicaltrials.gov Identifier NCT 06055439

**JUNE '25** 

PHASE 1 **SAFETY** 

PHASE 2 **EFFICACY** 

N=70

**REGISTRATION** 

N=15 MARKET UPDATE 3/3 + 5/5



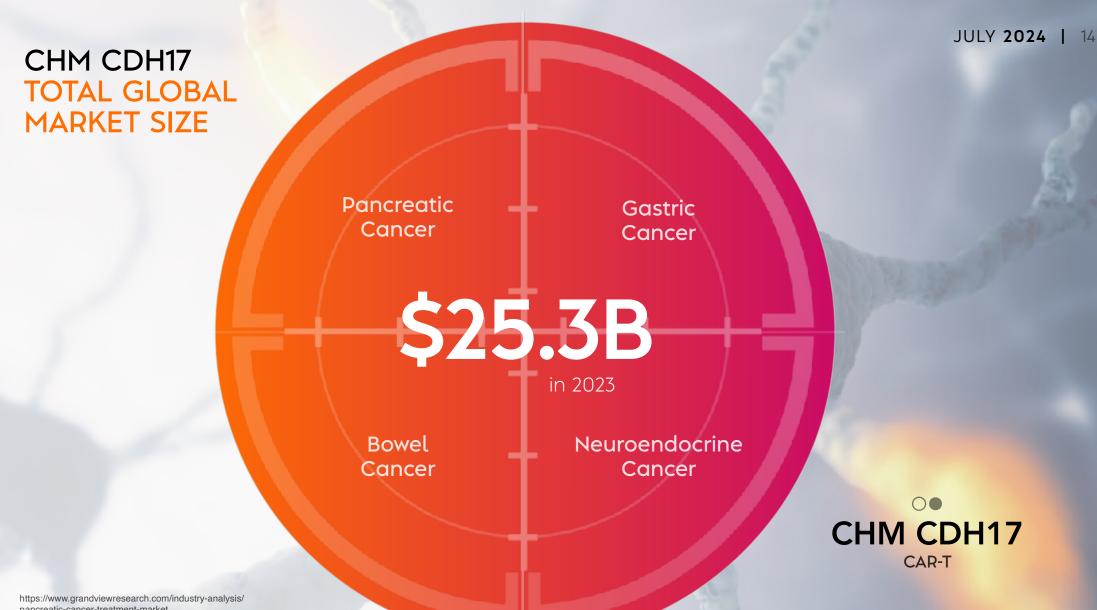






Partner or License to Big Pharma





stomach-cancer-gastric-cancer-market https://www.grandviewresearch.com/industry-analysis/ colorectal-cancer-crc-drugs-therapeutic-market

### CHLOROTOXIN (CLTX) CAR T OVERVIEW



Designed by the team at City of Hope to target **glioblastoma**, one of the most lethal types of brain cancer.



Uniquely uses **Chlorotoxin**, a peptide derived from deathstalker scorpion venom to target brain cancer.

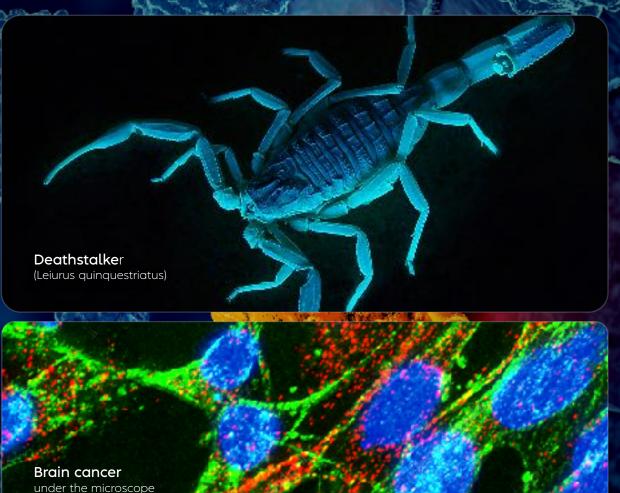


Phase 1a clinical trial completed at City of Hope showed **early and encouraging signs**.



CHM holds a global exclusive license to CLTX CAR T.







#### CHM CDH17 CAR-T PHASE 1 RECRUITING

The first CLTX CAR T cell therapy in development in the world



Technology from:



Phase 1 completed: COH

PHASE 1B TRIAL OPEN

Sarah Cannon Cancer Centre

#### PERSONALISED CAR-T: AUTOLOGOUS

First in class CLTX CAR T for brain cancer and solid tumours

Preliminary Positive Phase 1A Clinical Trial in Relapse/Recurrent Glioblastoma

Ongoing Phase 1B Clinical Trial in Recurrent Glioblastoma

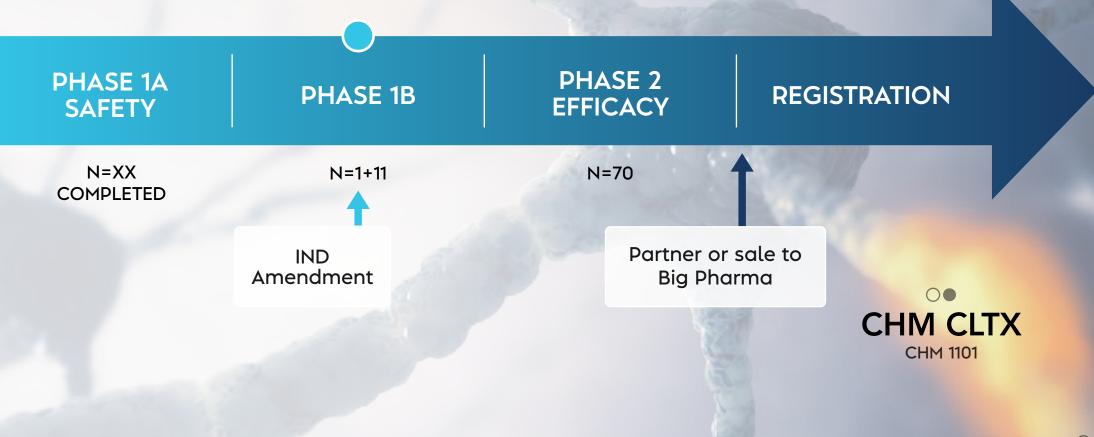
Revising Phase 1b Clinical design

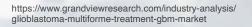
Manufacturing: GMP ready

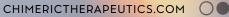


#### CHM CLTX CLINICAL DEVELOPMENT STRATEGY

FDA IND approved phase 1B









#### NK CELL THERAPY OVERVIEW



Natural killer cells (NK) are white blood cells that can destroy cancer cells and other infections in the body & are a critical part of the immune system

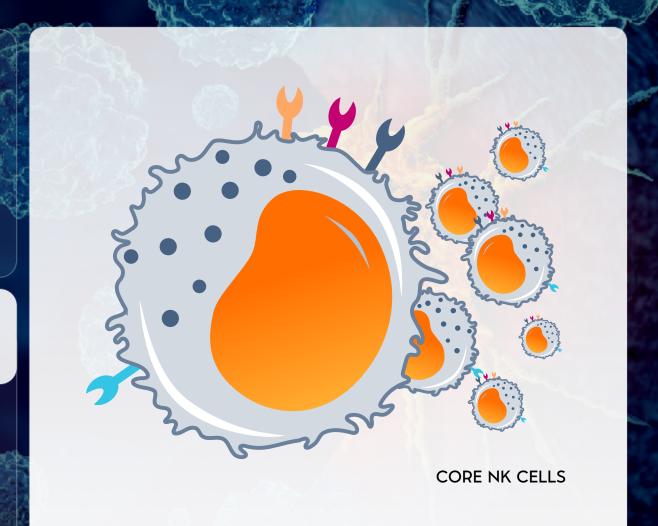
- · Can identify and kill cancer cells
- · Low risk of safety concerns
- · They constantly patrol the body to eradicate infections
- They grow in bone marrow

#### OFF THE SHELF **ALLOGENEIC**

nature

Membrane bound IL-21 based NK cell feeder cells drive robust expansion and metabolic activation of NK cells

Evelyn O. Ojo, Ashish Arunkumar Sharma, Ruifu Liu, Stephen Moreton, Mary-Ann Checkley-Luttge, Kalpana Gupta, Grace Lee, Dean A. Lee, Folashade Otegbeye, Rafick-Pierre Sekalv, Marcos de Lima & David N. Wald



## CHM CORE-NK PHASE 1 RECRUITING

Two Phase 1 trials recruiting



#### **CORE-NK: ALLOGENEIC**

Source of cells: Universal Healthy Donor

Positive Phase 1A Clinical Trial completed at Case Western

Two ongoing Phase 1B Clinical Trials in AML and CRC

AML: Cohort 1 deemed safe and moved to Cohort 2

Opportunity to combine with other technologies



#### CHM CORE NK PHASE 1 STUDY RESULTS

Ongoing Complete response

#### PATIENT #8

33-year-old female

**DIAGNOSIS:** Ovarian cancer

**HISTORY:** Progressive disease with prior allogeneic transplant

**SAFETY:** No dose limiting toxicities, no cytokine release syndrome, no GvHD CORE NK **INFUSION DAY 100** DAY 0, 14 STABLE DISEASE **DAY 28** 

COMPLETE RESPONSE

**ONGOING** COMPLETE RESPONSE

15+ MONTHS



#### AML PHASE 1B CLINICAL TRIAL OPEN

CHM CORE-NK + AZA + VEN in front-line AML Clinical Trials.gov Identifier: NCT05834244

**CELLS** 







FDA REGISTERED **BLOOD CANCER DRUG** 



**CHEMOTHERAPY** 

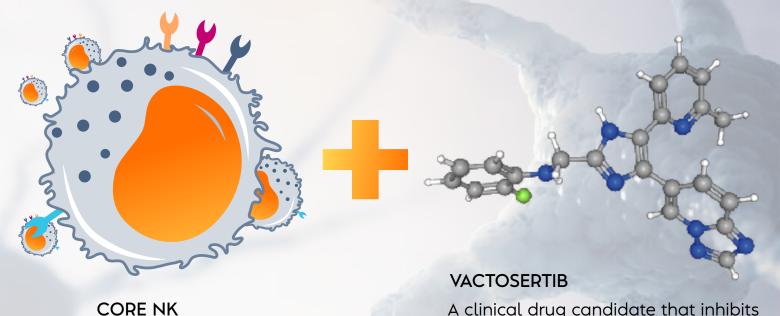


#### CRC PHASE 1B CLINICAL TRIAL OPEN

**CELLS** 

WORLD FIRST TRIAL OF NK CELLS WITH VACTOSERTIB IN BOWEL CANCER CLINICAL TRIALS.GOV IDENTIFIER: NCT05400122





A clinical drug candidate that inhibits TGF-  $\beta$  signalling, a pathway known to inhibit the effect of immunotherapy

Building upon the efficacy signal in the phase 1A CORE NK clinical trial, this trial aims to improve disease responses in patients through the coadministration of Vactosertib with CORE NK cells



#### CHM CORE-NK CLINICAL DEVELOPMENT STRATEGY

X 2 FDA IND approved phase 1B



## MULTIPLE VALUE REALISATION PATHWAYS

Sale of the Company

Develop Independently

Strategic Partnership with Big Pharma



#### MULTIPLE CLINICAL CATALYSTS IN THE NEXT 12MTHS

2023 Achievements and Deliverables in 2024

#### 2023 Achievements

2024 Deliverables



✓ FDA IND Clearance for Ph. 1/2 Trial

- ✓ Ph. 1/2 Site Open
- 1st patient dosed
- Ph. 1 Preliminary Data



- ✓ Ph. 1A trail complete in GBM
- ✓ Ph. 1A Positive Preliminary Data in GBM
- ✓ Ph. 1B 1st Patient Treated in GBM

• Ph. 1B new trial design

CHM CORE-NK
CHM 0201

- ✓ Ph. 1B ADVENT AML Site Initiation
- ✓ Ph. 1B CORE-NK 0201 + Vactosertib
  1st Patient Treated

- ✓ Ph. 1B ADVENT AML 1st Patient Treated
- Ph. 1B ADVENT AML Dose Escalation
- Ph. 1B ADVENT AML Preliminary Data

•••

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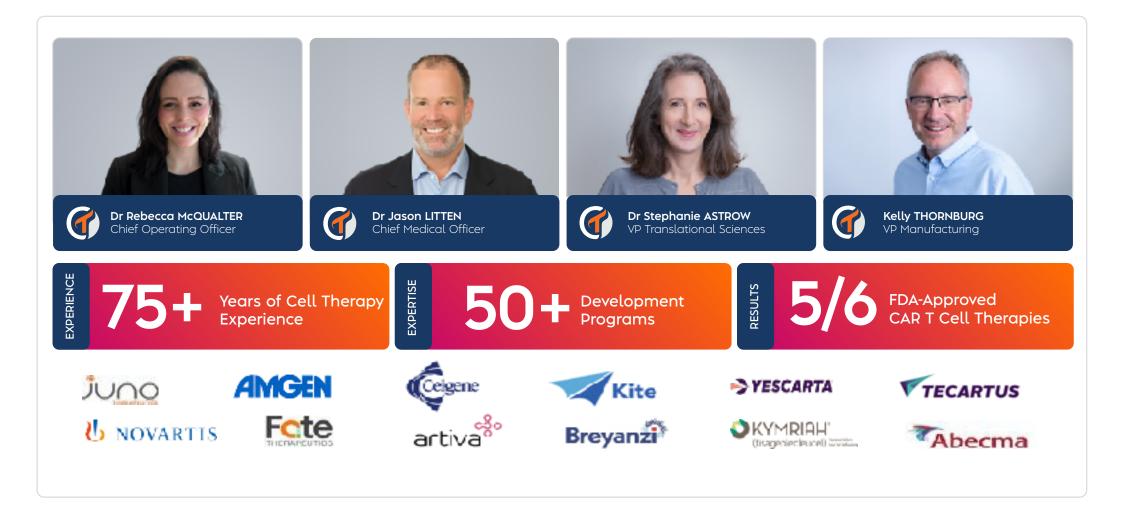
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#### CHM LEADERSHIP TEAM

#### **EXPERTS IN CELL THERAPY DEVELOPMENT & COMMERCIALISATION**

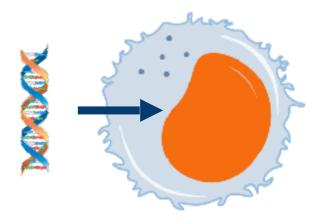




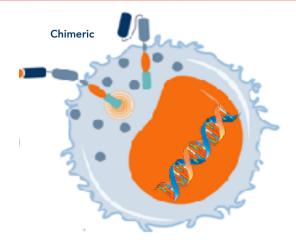
#### WHAT IS CELL THERAPY?

Cell therapy is the transfer of live cells into a patient to help lessen or cure a disease. In its most basic form is a blood transfusion.

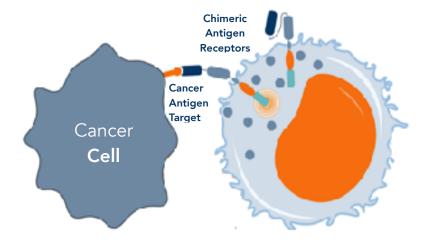
Today's cell therapies can involve the engineering of live cells to attack specific diseases



Genes programmed with the information needed to make special receptors called "Chimeric Antigen Receptors" (CARs) are inserted into live cells.



The Chimeric Antigen Receptors (CARs) become expressed on the cell surface and are activated to search for specific cancer cells.



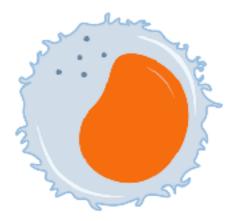
Once the Chimeric Antigen Receptor (CAR) finds the specific cancer cell it was programmed to find, it attaches itself to the cancer cell and sends a signal to kill it.



#### WHAT IS CELL THERAPY?

ALTERNATIVE CELL TYPES: T CELLS VS. NK CELLS

#### T CELLS



T cells are part of the adaptive immune system- primed to recognise a specific threat on a foreign cell surface

- $\cdot$  Proven curative efficacy in blood cancers
- Primed to target and attack specific antigens
- · Direct killing of cancer cells

#### **NK CELLS**



Natural Killer (NK) cells are part of the innate immune response - responding to anything that appears to be non-self

- · Intrinsic ability to identify and kill cancer cells
- Direct and indirect killing of cancer cells
- Low risk of safety concerns



#### CHM CDH17 CAR T

#### PHASE 1/2 CLINICAL TRIAL IN GI CANCERS

#### **OBJECTIVES:**

Characterise the safety and tolerability of CDH17 CAR and determine the recommended Phase 2 dose (RP2D) for Phase 2

#### **PRIMARY ENDPOINTS:**

- · DLT's, Safety Profile
- · AE's, CRS, ICANS

#### **SECONDARY ENDPOINTS:**

- · ORR, DCR, TTR, DOR,
- · PFS, OS
- · Cellular Kinetics

COLORECTAL **CANCER NETs** G1, G2, and welldifferentiated G3 NETs of the midgut and hindgut with ≤ 55% Ki67 expression

#### **GASTRIC CANCER**

Central laboratory confirmation of CDH17+ tumor expression by IHC (H score ≥ 5) is required.

450 **X** 106

150 **X** 106

50 X 106

**DOSE ESCALATION** 

Tumor Specific Dose Confirmation

Upon signal confirmation, dose confirmation and expansion in tumour specific cohorts

Tumor

Specific

Dose

Expansion

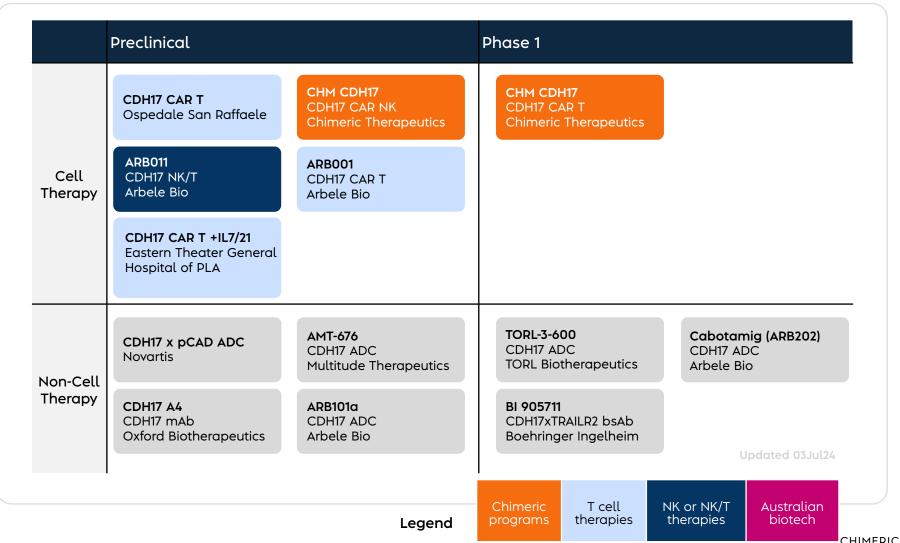
 $\bigcirc$ CHM CDH17 **CHM 2101** 





#### CHM CDH17 CAR T

#### TARGET COMPETITORS IN DETAIL









#### CHM CLTX CAR T

#### ADVANCING DEVELOPMENT TO PHASE 1B

CLINICAL TRIALS.GOV IDENTIFIER: NCT05627323



#### **OBJECTIVES:**

- · PFS, OS, ORR
- · Safety & Feasibility
- · RP2D
- · Cellular Kinetics

#### **PATIENT POPULATION:**

 Recurrent / progressive glioblastoma

## PART A DOSE CONFIRMATION



**3-6 PATIENTS** 

## PART B DOSE EXPANSION



SAFETY & EFFICACY ASSESSMENT

**12-26 PATIENTS** 







#### POSITIVE PRELIMINARY PHASE 1A CLINICAL DATA IN BRAIN CANCER (GLIOBLASTOMA)

DISEASE **CONTROL RATE** 

55%

Disease Control Rate (DCR) in heavily pretreated patients

Exceeding historical disease control rates of 20-37%1

**SURVIVAL** 

~10 months

Median survival in patients that achieved disease control

14+ months

Survival in two patients that achieved disease control

~7 month survival expectation after first recurrence2



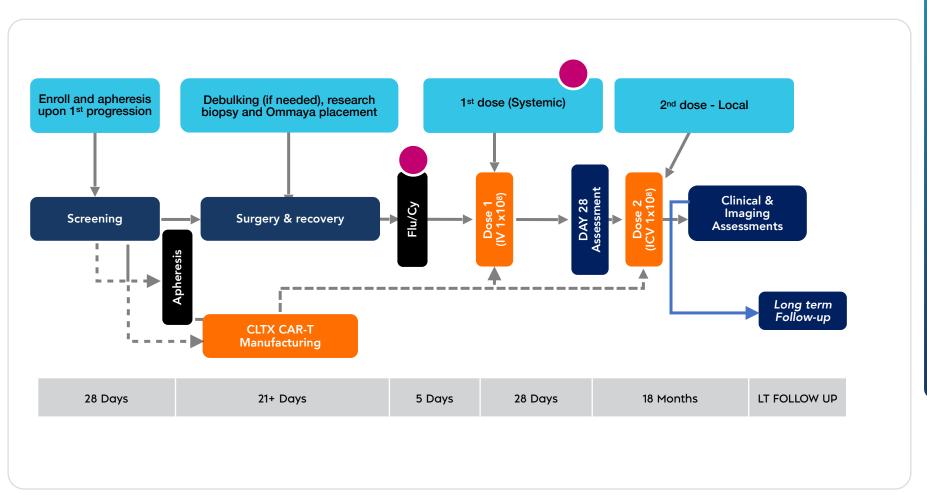


## S THERAPEUTIC

#### CHM CLTX PHASE 1B IMPROVED DESIGN

PROPOSED CLINICAL DESIGN: ADDITION OF SYSTEMIC DELIVERY AND CHEMOTHERAPY

CLINICAL TRIALS.GOV IDENTIFIER: NCT05627323







# S

#### 20 24

#### ADVENT-AML PHASE 1B CLINICAL TRIAL

CHM CORE-NK 0201 + AZA + VEN IN FRONT-LINE AML

**HIGH UNMET NEED IN AML**  Despite treatment advances, outcomes for AML patients not eligible for intensive chemotherapy or allogeneic stem cell transplant are poor

CHM CORE-NK CHM 0201

CHM CORE-NK 0201 +**AZACITIDINE +** VENETOCLAX

A Phase Ib Trial of Azacitidine, Venetoclax and CHM CORE-NK 0201 Allogeneic NK Cells for Acute Myeloid Leukemia

Study Initiation: Q1, 2024

Enrolment: 23 participants

Dose Escalation

Eligibility:

Relapse or refractory AML, or MDS/AML with 10% to

19% blasts

Dose Expansion

Newly diagnosed, older/unfit patients with adverse

Eligibility: risk AML or MDS/AML

Clinical Trials.gov

NCT05834244

Identifier:





#### CHM CORE-NK 0201 + VACTOSERTIB

FDA APPROVED FIRST EVER TRIAL OF NK CELLS WITH VACTOSERTIB

A Phase Ib Study to Evaluate Safety and Persistence of ex Vivo Expanded Universal Donor NK Cells in Combination With IL-2 and TGF-beta Receptor I Inhibitor Vactosertib

Study Initiation: Jan 2023 (paused due to staff issue)

Enrolment: 12 Patients
Est. Completion: Late 2024

Eligible Patients: Relapse or refractory solid tumours and haematological malignancies

Clinical Trials.gov Identifier: NCT05400122







#### CHM CORE-NK DEVELOPMENT PLAN

#### THE FUTURE

