TC BIOPHARM

The Global Leader in Gamma-Delta T-Cell Therapy

# Investor Presentation

Q3 2024

# Forward Looking Statements

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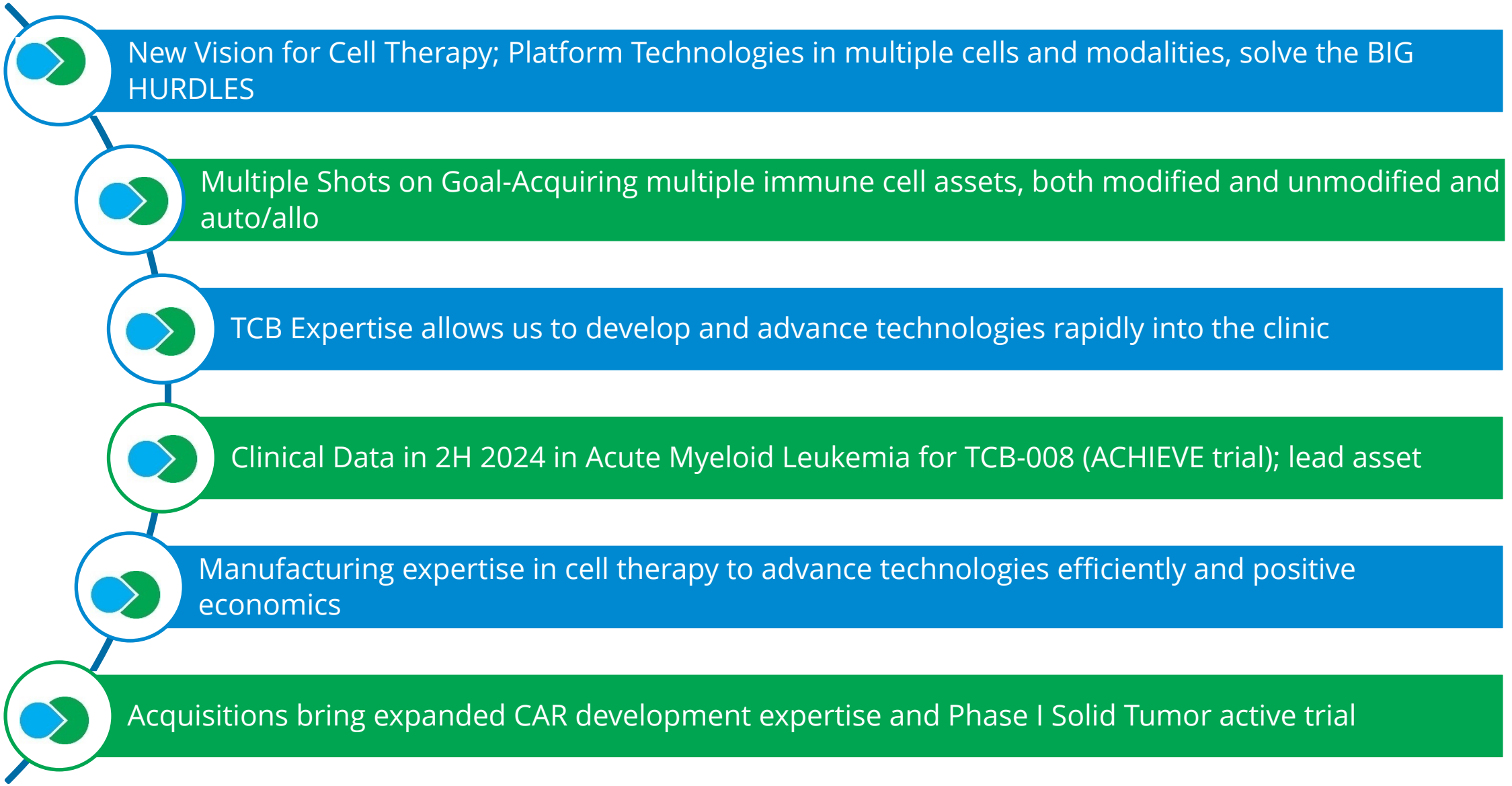
# TCBP Investment Highlights



# Combined Clinical Development Pipeline

## Next generation GDT cell therapies for both solid tumors and blood cancers

| Program | Indication | Pre-clinical | Phase 1 | Phase 2 | Phase 3 | Status / Upcoming Milestone |
|---|---|---|---|---|---|---|
| **OmnImmune** (Vδ2 subtype) Allogeneic (Unmodified) | **AML** | | | 2b | | Phase 1b/2a complete H1 2020 – PR & CR achieved **Phase 2b launched, 5 patients dosed to date** |
| **TCB-008** (Vδ2 subtype) Allogeneic (Unmodified) | **AML** | | 1b | | | **Announced FDA Clearance of Phase 1B IND for TCB-008** |
| **CAR-T** Acquisition Assets | **Solid Tumors** | | Phase 1/2 | | | **Granted MHRA** Clinical Trial Authorization for Lateral NKG2D CAR-T Cell Therapy |
| **Anti-Fungal** | | | | | | **Proof of Concept & Pre-clinical Work** |
| **CAR-NK** Acquisition Assets | **Renal Carcinoma / NSCLC** | | | | | **Demonstrated tumor regression** and functional persistence in multiple CD70 expressing tumor models<br><br>Efficacy established in multiple xenograft models |

## Program that does not involve any current development or clinical activity by the Company

| Program | Indication | Pre-clinical | Phase 1 | Phase 2 | Phase 3 | Status / Upcoming Milestone |
|---|---|---|---|---|---|---|
| **TCB001** Autologous (Unmodified) | Melanoma | | | | | Phase 1b/2a POC complete – evidence of tumor shrinkage (not pursuing further development) |

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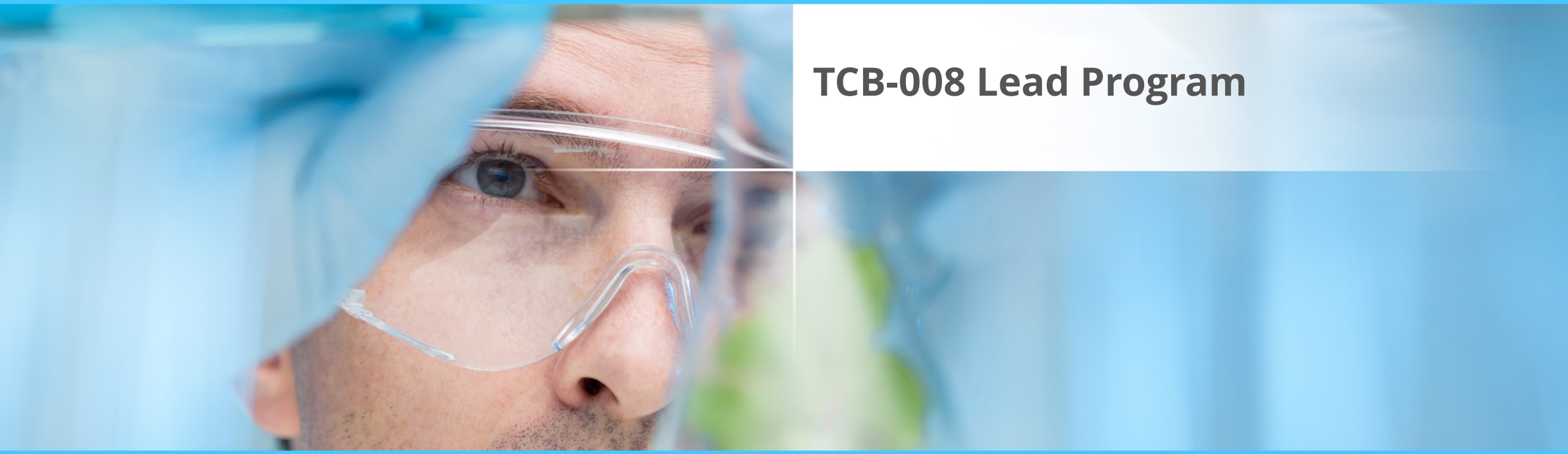

# TCB-008 Lead Program

# ACHIEVE (TCB-008-001) Ph II UK Study Update

- Completed Safety Cohort and received positive review from the Data Safety Monitoring Board (DSMB)
- Amended Protocol to increase dosing to $12.0 \times 10^7$ to $23.0 \times 10^7$ cells
- Trial to date
  - 7 patients screened, 1 screen failure, 1 patient discontinued prior to treatment with TCB0008, 4 patients dosed with one dose of TCB-008 (7 X $10^7$ cells administered IV), 1 patient dosed with two doses of TCB008 (7 X $10^7$ cells administered IV)
  - None of the adverse events were considered related to TCB008 and no dose limiting toxicities were reported in these 5 patients
    - All 5 patients reported no treatment emergent serious adverse events (TESAEs) related to TCB-008.
    - 2 patients died during the study (*post transplant lymphoproliferative disorder* and *disease progression*), 2 patients withdrew consent, and 1 subject was withdrawn due to disease progression.
- The overall response per ELN 2020 Criteria was stable disease (2 patients, 40%)

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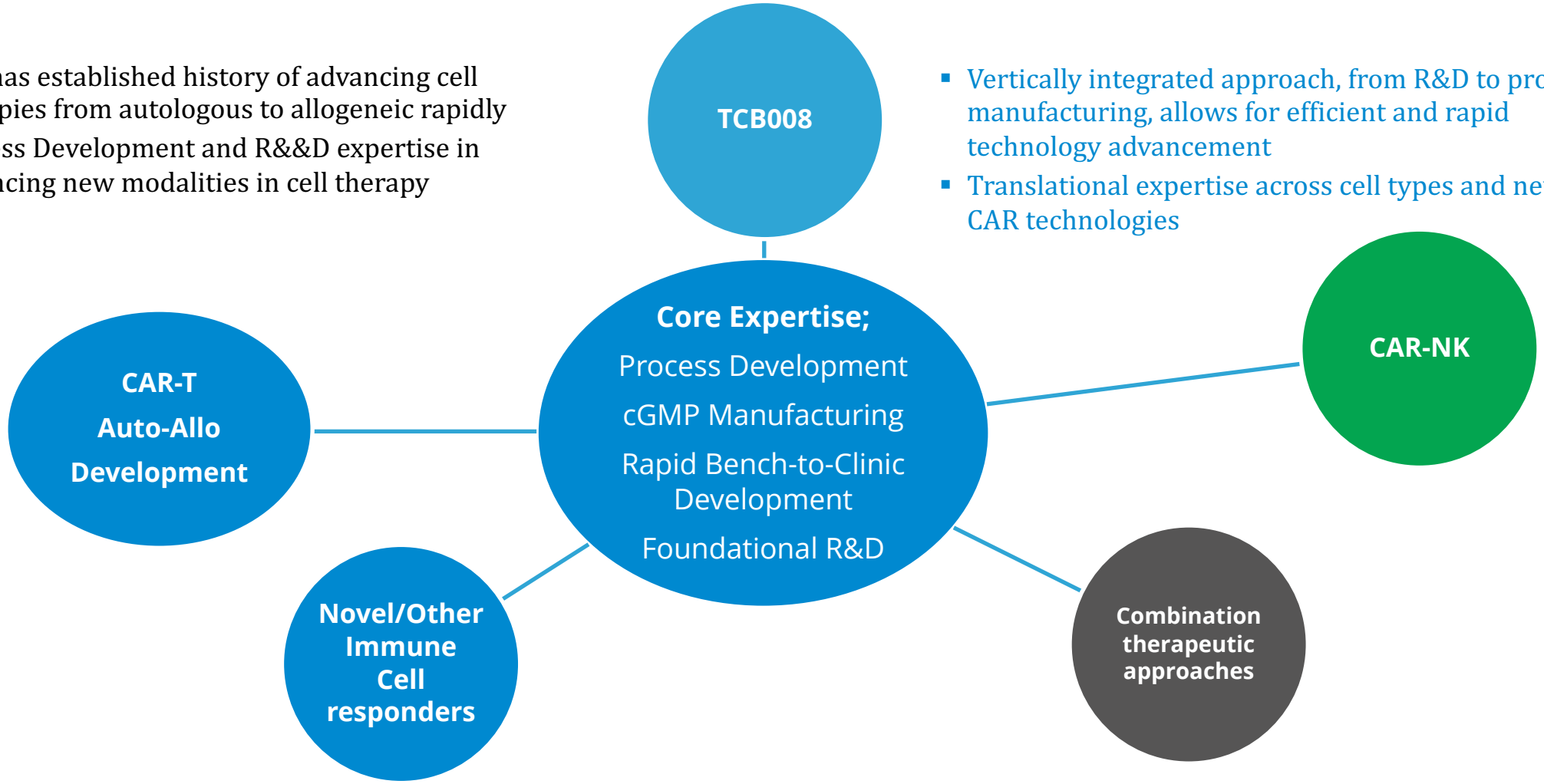
# Acquisition Strategy

# TCBP's Enhanced Platform

## TC BioPharm's GDT, CAR-T and NK Cell assets provide a unique product development platform targeting blood cancer and solid tumors

- TCB has established history of advancing cell therapies from autologous to allogeneic rapidly
- Process Development and R&&D expertise in advancing new modalities in cell therapy

- Vertically integrated approach, from R&D to product manufacturing, allows for efficient and rapid technology advancement
- Translational expertise across cell types and new CAR technologies



# M&A Focus

- TCBP seeks to opportunistically pursue complimentary cell therapy companies
- Market conditions provide attractive valuations for desirable assets
- Currently negotiating with specific acquisition targets
  - Candidates would provide both stand alone treatments and complimentary therapeutics
- Capable of developing proprietary γδ T cell therapy platforms, which can support a pipeline of innovative cell therapies
- TCB-008 has an ideal profile for combination therapies
  - No drug related toxicity
  - Allogeneic, should not cause drug on drug interaction
  - Chemo resistant when activated
- Company focus for TCB-008 will be on multiple exclusive partnerships/agreements for TCB-008 in Combination trials
  - Upfront payments, non-dilutive with royalty agreements

# TCBP: Synergies for M&A

***Acquisition Mason/TCB Synergies***

- CAR-T development expertise; helps TCBP move Co-stimulatory forward as well as entrée into modified cells in clinic
- Strong clinical team
- Senior level management
- TCB expertise in process development
  - Can advance Mason assets from autologous to allogeneic rapidly
- TCB gamma delta expertise
  - Advances Mason CAR rapidly from alpha betas
- TCB manufacturing expertise
  - Allows for in-house manufacturing advancements for Mason assets

***Acquisition LION/TCB Synergies***

- LION brings CAR-NK expertise
- New immune cell asset expertise
- Expanded asset base with IP/Patent families
- TCB Process Development expertise to update LION manufacturing to remove feeder cell component
- TCB-008 has strong rationale for combination therapy with NK and CAR-NK cells

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# M&A Transactions

# Acquisition MASON; CAR-GDT/AB Technology Platform – Signed LOI

*Pursuing the development of more durable CAR-T therapies for the treatment of cancer and autoimmune diseases*

## Strength of Lateral CARs

- Optimized architecture for CAR constructs versus traditional linear CAR design with key advantages:
  - Decreased cell exhaustion
  - Increased cell persistence
  - Increased anti-tumour activity
- Lateral design is highly flexible and can be applied to improve any CAR in development
- Two variations of Lateral CARs:
  - Adaptor and Parallel (pCAR)
- Lead candidate – best-in-class, autologous NKG2D CAR-T for solid tumours
  - Phase 1 study on-target to begin in first half 2024

## Novel Allogeneic T2γδ Platform

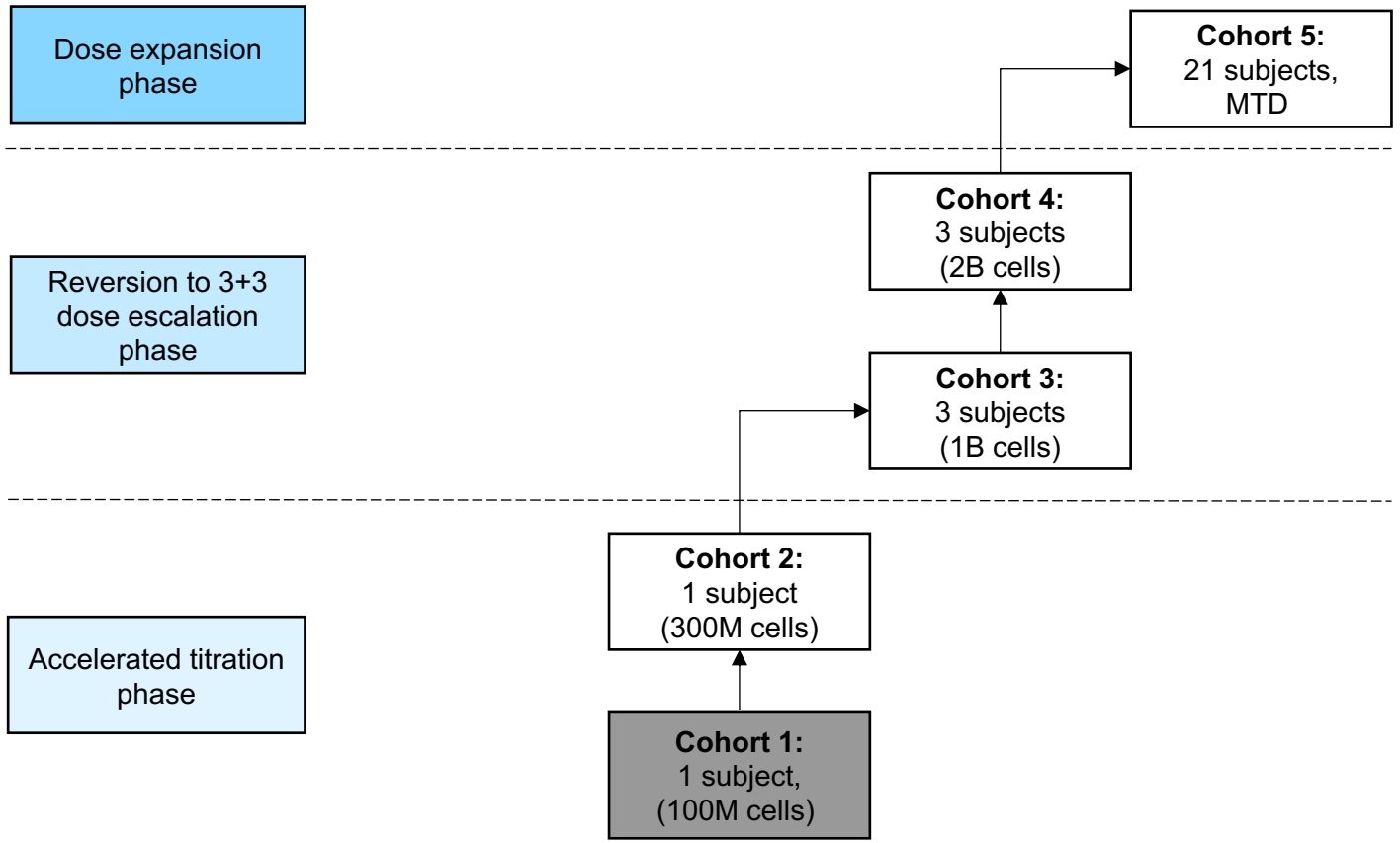
- Underpinned through the utilization of TGF-β-educated γδ T-cells
- Strategic approach focused on:
  - Enhancing intrinsic γδ T-cell function
  - Engineering therapy with optimized Lateral CARs
  - Co-expression of optimized armoring technology
- Currently evaluating multiple Lateral CARs in T2γδ cells for the treatment of both autoimmunity and cancer
- Secondary Asset – anti-CD19 T2γδ CAR-T for autoimmune diseases
  - Submission of CTA expected in 2025

## Innovative Add-On Technologies

- Cell trafficking and infiltration
  - CXCR2, others
- Armoring
  - Functionally conditional IL-18, others
- Optimized signaling
- Non-genome-edited engineering technologies
- Streamlined and robust manufacturing process

# First-in-Human Phase 1b Trial in Solid Tumors

*Set to evaluate Lead Asset following CyFlu preconditioning in patients with r/r solid tumours with NKG2D ligands*




## Key Milestones

| | |
|---|---|
| Q3:22 | Granted ILAP Designation |
| Q1:23 | Collaboration with GOSH |
| Q3:23 | Received MHRA Authorisation |
| H1:24 | Initiate Dose Escalation |
| Q1:25 | Initiate Dose Expansion |

CyFlu: Cyclophosphamide / fludarabine; r/r Relapsed or refractory.



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# Best-in-Class NKG2D CAR-T Therapy

*Potential to be first NKG2D CAR-T therapy to drive deep clinical responses in solid tumors*

## Addresses Several Hurdles Posed by Solid Tumors

- Trafficking to tumour site
- Immunosuppressive TME
- Antigen loss
- Antigen heterogeneity
- T-cell ‘functional persistence’
- Paucity of suitable antigens

## Optimized Construct, Optimized Trial Design

- Greater anti-tumour activity with similar safety compared to second-generation linear NKG2D CARs
- Infusion of treatment following standard CyFlu preconditioning for achievement of optimal cell kinetics
- Enrolment in Phase 1b trial to include patients positive for NKG2D ligands assessed by investigational IVD

# Significant Opportunity in NKG2DL-Expressing Solid Tumors

*Enormous total addressable market for CAR-T targeting NKG2D stress ligands*

**Colorectal Carcinoma**
- 36.6 per 100,000 incidence rate in the US[1]
- Estimated 153,020 new cases in the US in 2023[2,] with 22% of mCRC patients diagnosed at a late stage[3]

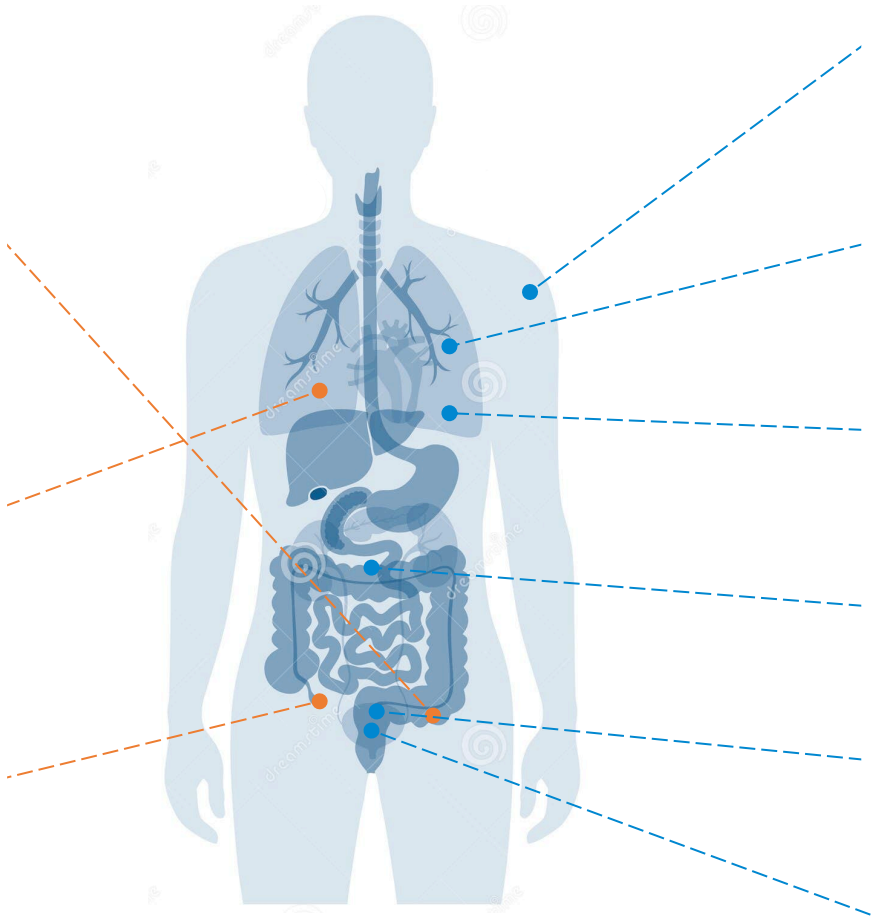
100%

**Triple negative breast cancer**
- 13.2 per 100,000 incidence rate in the US[1]
- Estimated 25,000 new cases in the US in 2023

93%

**Ovarian Cancer**
- 10.3 per 100,000 incidence rate in the US[1]
- Estimated 19,710 new cases in the US in 2023[2]

88%



74%

**Melanoma**
- Estimated 97,610 new cases in the US in 2023

72%

**Mesothelioma**
- 0.8 per 100,000 incidence rate in the US[1]

98%

**NSCLC**
- Estimated 193,055 new cases in the US in 2023[3]

100%

**Pancreatic adenocarcinoma**
- Estimated 64,050 new cases in the US in 2023[2]

91%

**Bladder cancer**
- Estimated 82,290 new cases in the US in 2023[2]

80%

**Prostate**
- Estimated 288,300 new cases in the US in 2023[2]

**Percent of Patients with NKG2D Ligand Expression**

[1] SEER*Explorer, accessed 11/12/2023.
[2] Siegel *et al* Cancer statistics 2023, CA Cancer J Clin (2023) 17-48.
[3] Cancer Net 2023 weblink.

# Mason Lead Asset – Summary of Preclinical Safety

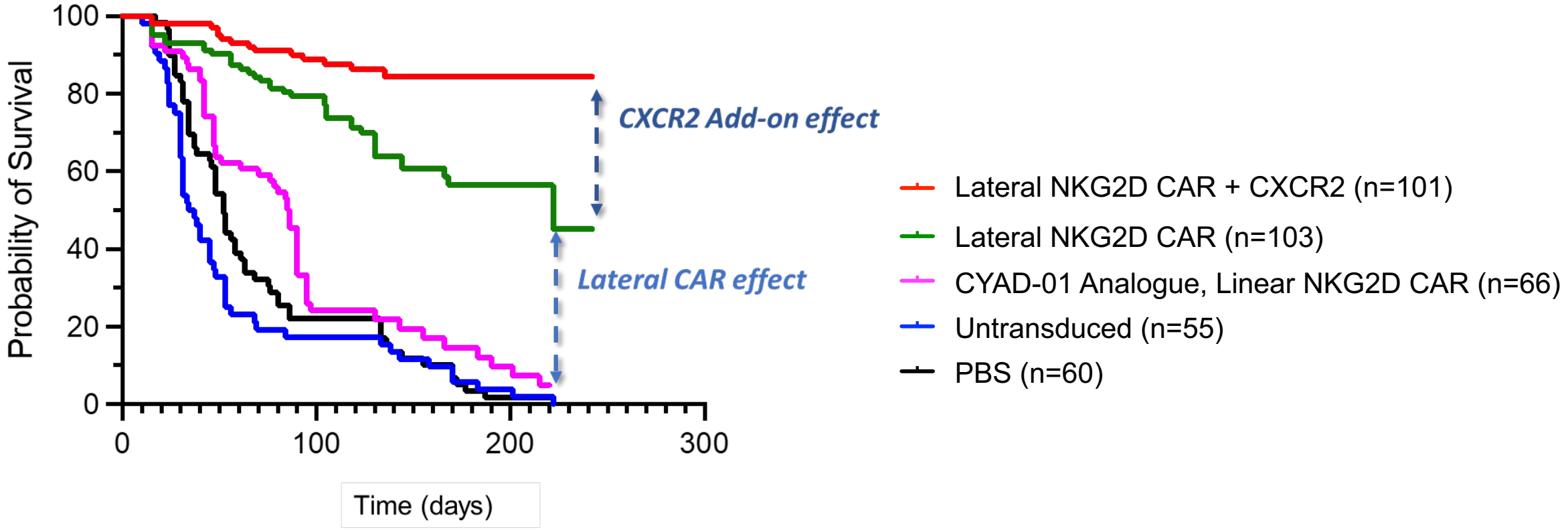
*Despite Asset's enhanced anti-tumor activity, preclinical data shows comparable safety to second-generation NKG2D CAR*

- Mouse NKG2D extracellular domain was substituted for human orthologue, enabling human CAR T-cell-mediated recognition of mouse ligands *in vivo*
- Escalating doses were infused i.v. in immunodeficient mice, benchmarking toxicity against a mouse analogue of the clinical stage CAR-T candidate, CYAD-01
- Using doses of up to 20 million CAR T-cells, toxicity was observed in a dose-dependent manner
  - Toxicity was transient and all mice recovered rapidly
  - Extrapolating from mouse to man, doses evaluated were between 7.5-fold and 37.5-fold higher than the top dose planned for the Phase 1/2 trial
- Independent histopathological analysis concluded there was no evidence of toxicity within the organs
- Toxicity profile was identical between Mason lead asset and CYAD-01 analogue

***Data confirm that the significantly enhanced efficacy of Mason lead asset is achieved without an increase in toxicity***

# Lead Asset – Striking Improvement in Survival in Preclinical Models

*Asset demonstrates over* **17-fold improvement in survival** *versus linear NKG2D CAR*




***Aggregate of Kaplan-Meier survival curves for thirteen in vivo models highlights the differentiation of a Lateral CAR design and Lead Asset***

*In vivo* models include pancreatic, mesothelioma, ovarian (epithelial, endometrioid and high grade serous), TNBC and mCRC

# Streamlined and Robust Manufacturing Process for Phase 1b Trial

- The Company's proprietary cell therapy manufacturing process allows for the creation of clinical product from the patient's whole blood, allowing for a streamlined process which can be efficiently scaled
- Leverages similar robust CAR-T manufacturing process established in prior program development

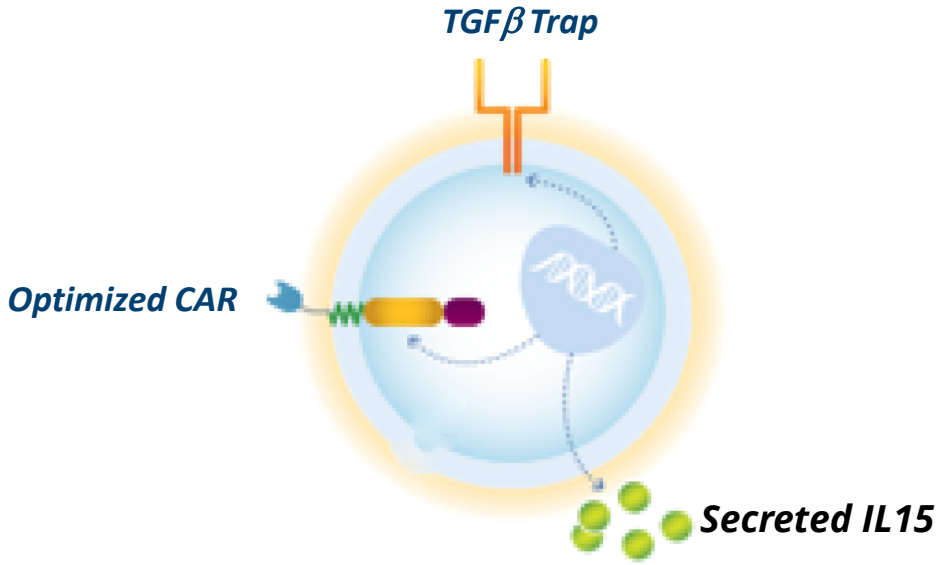
***In March 2023, gained access to start-of-the-art GMP production facilities at Great Ormond Street Hospital (GOSH)***

# NK Acquisition (LION)– Signed LOI

## ”LION” was established to enable allogeneic cell therapy for solid tumors


- **‘Platform’: A versatile, allogeneic CAR-NK platform for solid tumors**
  - Donor-derived NK cells are engineered and expanded to produce doses at scale
  - Non-viral engineering method enables large payloads and efficient manufacturing
  - Synthetic biology modules to address solid tumor microenvironment
- **In vivo efficacy demonstrated with multiple products in preclinical models**
  - Lead CAR-NK programs targeting CD70 (RCC, NSCLC) and HER2 (Breast, Gastric CA)
  - In vivo efficacy established in multiple xenograft models, demonstrating durable efficacy and NK cell persistence
- **Company and Financing history**
  - $75M capital raised to date since company founding in March 2020
  - Investor syndicate includes SV Health Investors, Sofinnova Partners, Lightstone, Takeda Ventures, and Astellas Venture

# “LION” platform addresses key hurdles to durable solid tumor efficacy




| Hurdles to Efficacy | “Company A” |
|---|---|
| Potency in Tumor Microenvironment | 1 **TME Toolkit**<br>• TGFb-DNR<br>• Second Gen Switch receptors |
| Persistence of allogeneic cells | 2 **Built-in Cytokine Support**<br>• Soluble IL-15<br>• In vivo persistence >6 mo |
| Manufacturability | 3 **Flexible Manufacturing System**<br>• Nonviral engineering method<br>• Expansion and cryo solutions |

The platform has now produced two programs which demonstrate in vivo efficacy across multiple xenograft models, with potential IND in 2025 timeframe

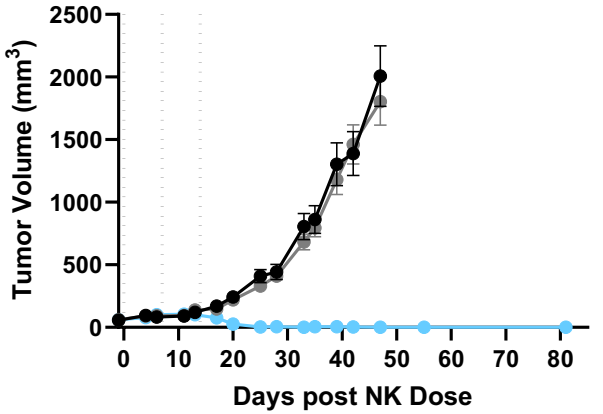
Core technology has potential to be more broadly applied beyond PBMC-derived NK cells

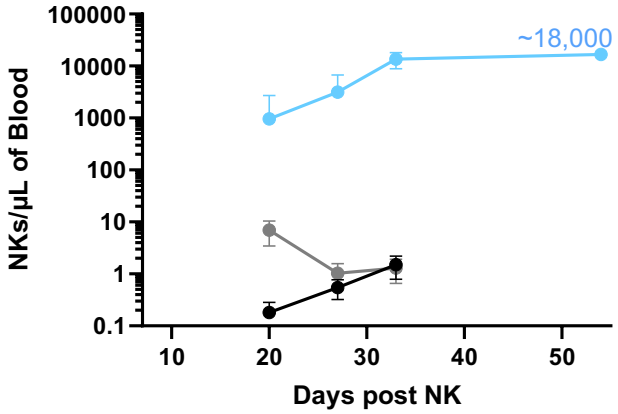
# LION-O CAR-NK Expands, Persists and Durably Regresses CD70 Expressing Tumors

Anti-tumor efficacy

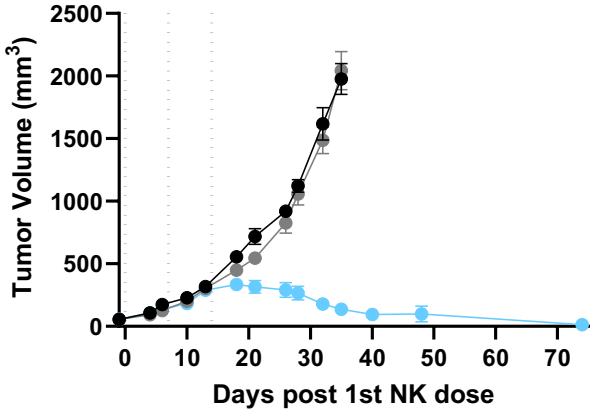
NK cell persistence

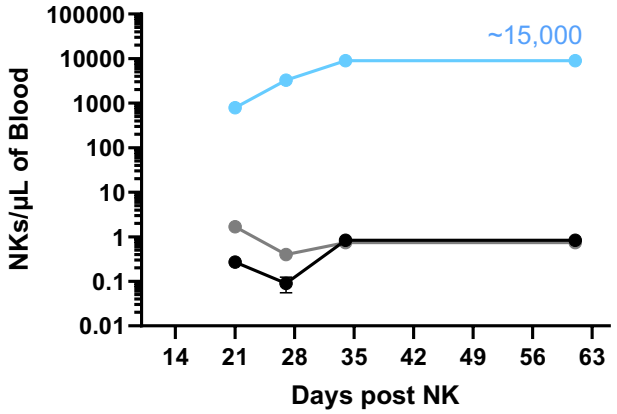
## A. A498 (RCC, CD70 high)



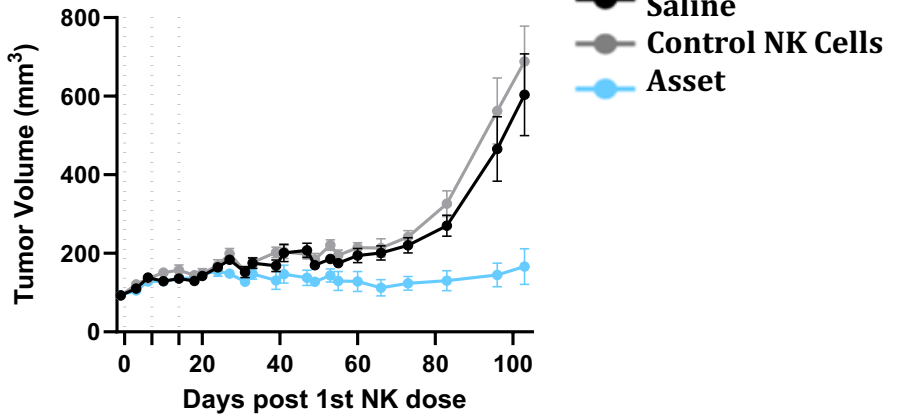



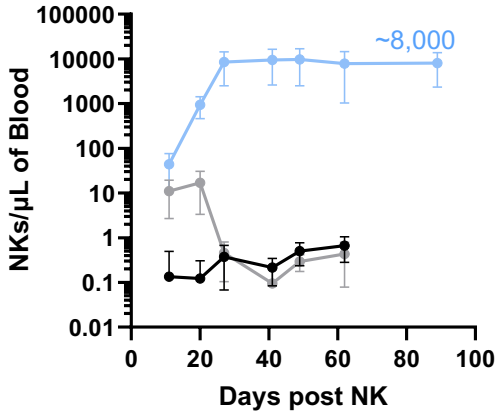

## B. NCI-H1975 (NSCLC, CD70 low)



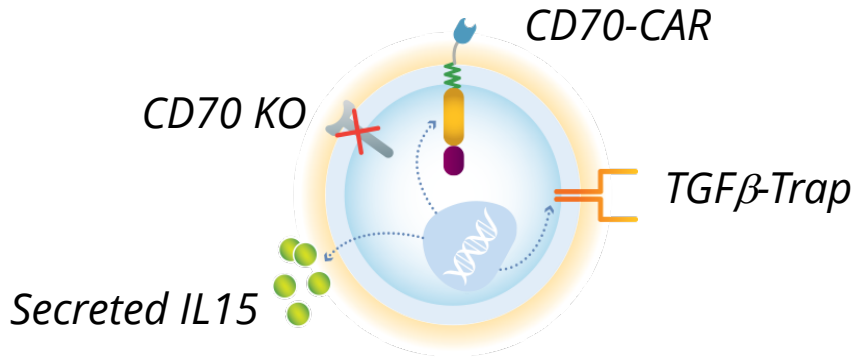
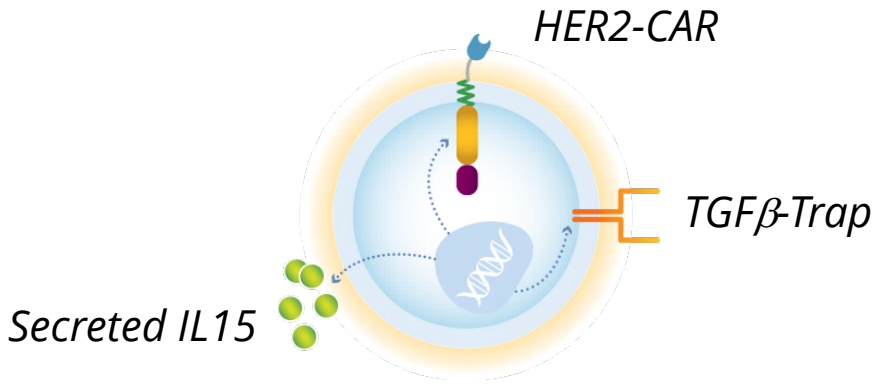




## C. Caki-2 (RCC, CD70 medium)



# Pipeline: Two CAR-NK programs with *in vivo* efficacy data

| PROGRAM (TARGET) | INDICATIONS | DEVELOPMENT STATUS | CAR-NK CELL DESIGN |
|---|---|---|---|
| **LION-O CD70** | RCC<br>NSCLC<br>Other solid & heme malignancies | Preclinical efficacy<br><br>IND planned 2025 |  |
| **CAR-NK (HER2)** | Breast & Gastric Cancer | Preclinical efficacy<br><br>Candidate Selected<br><br>Partnership discussions ongoing |  |

# Thank you

**Chris Camarra**
*EVP, Communications*
TC Biopharm
c.camarra@tcbiopharm.com

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# Appendix

Q2 2024

# ACHIEVE2 (TCB008-003) Ph I US Study (IND Accepted)

## *FDA clearance of investigational New Drug (IND) application for a Phase 1B study in relapse/refractory AML*

Open-label, multi-center study conducted in 2 parts (dose escalation followed by dose expansion) to evaluate safety, persistence/expansion, and preliminary efficacy of single and multiple IV doses of TCB008 in patients with AML or MDS/AML, MRD-persistent AML, or MDS/AML who have failed or are intolerant to the current standard of care.

**Proposed Primary Objectives:**

- To establish the recommended dose for further investigation in the dose-expansion part of the study, in patients with previously treated relapsed or relapsed refractory AML or MDS/AML, or MRD persistent-AML or MDS/AML (dose escalation part only)
- To determine the safety and tolerability of TCB008 in patients with previously treated relapsed or relapsed refractory AML or MDS/AML, or MRD-persistent AML or MDS/AML

**Proposed Number of Patients:**

- Dose escalation: approximately 9 to 24 DLT evaluable patients are planned to follow a 3 + 3 enrollment design. Non-DLT-evaluable patients will be replaced.
- Dose expansion: Up to 60 patients are planned (up to 20 patients in each of the 3 cohorts)

**Proposed Dosing Regime:**

- Dose escalation:
  - Cohort 1: 1.5 mL TCB008 ($3.6\times10^7$ to $6.9\times10^7$ cells)
  - Cohort 2: up to 5 mL TCB008 ($12.0\times10^7$ to $23.0\times10^7$ cells)
  - Cohort 3: up to 18 mL TCB008 ($43.2\times10^7$ to $82.8\times10^7$ cells)
- The dose level for the dose expansion will be based on the recommended dose for further investigation (RDE) determined in the dose escalation part of the study

Patients may be reinfused with TCB008 up to 3 times following initial infusion (at the same dose as the initial infusion) as deemed appropriate by the investigator or designee should protocol specified criteria be met.

**First Patient will be dosed 2H 2024**

# Relapse/Refractory Acute Myeloid Leukemia Phase 1b Trial Summary

**Based on compelling clinical data in non-responding patients TCB has progressed to phase 2/3 studies**

**AML patients, late-stage, non-responders**

- Poor life expectancy (often days/weeks)
- Prior clinical options have failed in all patients

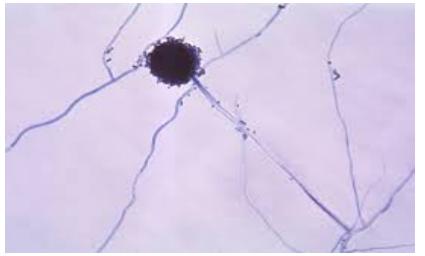
## Results

- Average cancer levels in bone **decreased from 38% to 6%**
- One patient had a complete response; another classified MLFS* following treatment; and one stable disease
- No serious adverse treatment-related safety events
- No grade 3≥ OmnImmune® (TCB002) treatment related toxicities were noted
- One patient died because of bilateral pneumonia determined unrelated to study medication

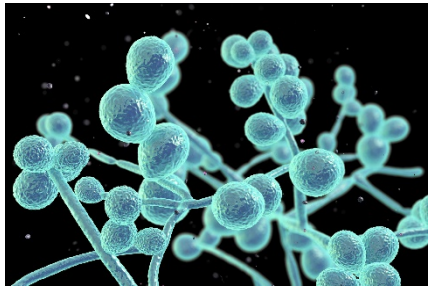
*MLFS: morphologic leukemia-free state

# QMUL Collaboration

- Formed a collaboration agreement with Queen Mary University of London (QMUL) to research the therapeutic benefits of gamma-delta T cells for the treatment of mucosal infections
- The study is aimed to understand how gamma delta T-cell function becomes dysregulated in infectious and inflammatory diseases and could potentially be restored by novel agonist / antagonist immunotherapies
- The project includes grant funding from The Queen Mary Impact Fund (QMIF) to finance the study
- Research will be conducted at a leading institution in the gamma delta field focusing on gut health and microbial infections
- TC BioPharm aims to target ***Candida*** and ***Aspergillus***
  - *Candida* is a fungal infection that affects bloodstream and/or internal organs such as the kidney, heart, or brain
  - *Aspergillus* can invade areas of your body other than your lungs, such as your sinuses



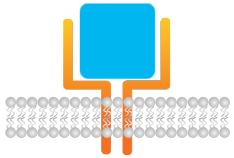
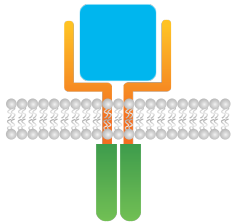
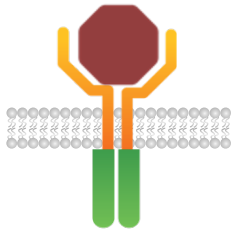
***Aspergillus***



***Candida Albicans***

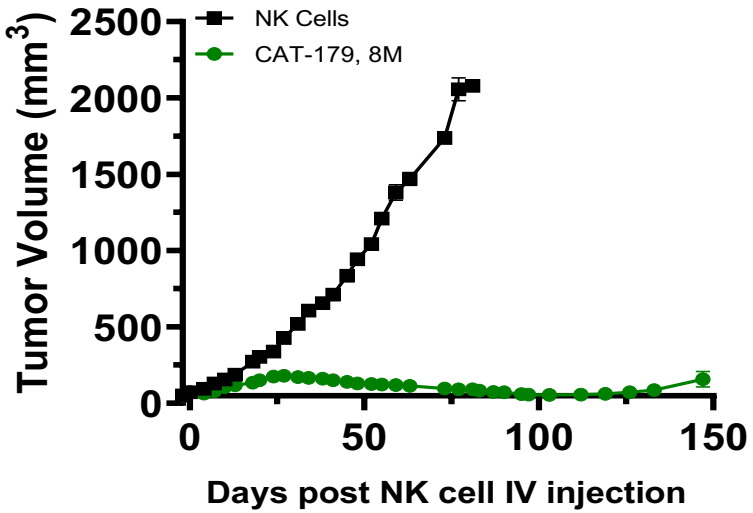
# Switch Receptor (SR) Platform

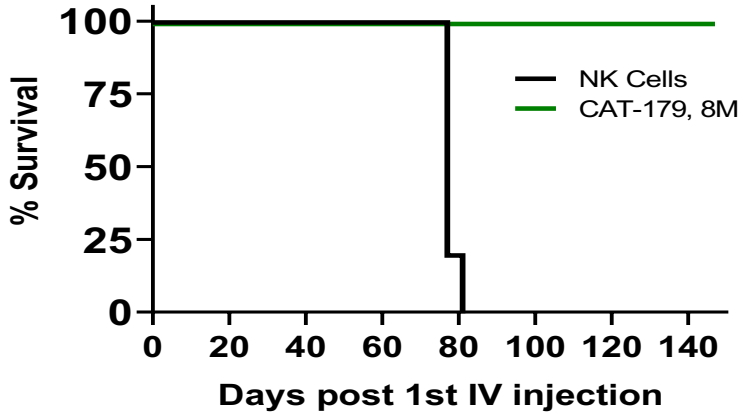
## Tailored Modules for Durable Solid Tumor Efficacy

| | | TGFβ-Trap  | TGFβ-Switch Receptor  | TME-Switch Receptor  |
|---|---|---|---|---|
| BENEFITS | | **PRESERVE** CAR-NK activity and function in high TGFβ tumors. | **ENHANCE** CAR-NK proliferation and function in high TGFβ tumors | **EXTEND** to other TME factors to broadly enable solid tumor efficacy |
| STRUCTURE | Extracellular domain | TGFβRII | TGFβRII | Various TME factors |
| | Intracellular domain | None | Signaling optimized for function | Signaling optimized for function |
| FUNCTION | Protect engineered and surrounding cells | +++ | +++ | +++ |
| | Enhance function | - | +++ | +++ |
| | Modularity | CAR + TGFβ Trap<br>LION-0, LION-2 | CAR + TGFβSR | Multifunctional NK cells |

# Extends Survival of Mice with HER2 Xenografts

## LION-2 durably regresses N87 (gastric CA) xenografts and enhances survival




## LION-2 is effective in SKOV3 (ovarian CA) intraperitoneal xenograft model